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Editorial

Vietnamese Dermatology

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Abstract

BACKGROUND: The World Health Academy of Dermatology, the Vitiligo Research Foundation, the Military Medical Academy of Belgrade Serbia, the University of Parma-Italy and the University of Rome Guglielmo Marconi, Rome-Italy have successfully joined Vietnamese Dermatology Community in the ambitious project of positionìng Vietnam in the Dermatologic Olympus.

AIM: The aim of our special issue is to present some pearls of the Vietnamese Dermatology devoted to the description of the national and hopefully international declining of traditional therapies.

METHODS: We present 36 contributions from all academic hospitals of Vietnam reflecting the therapeutic strategies and every day's dermato-venereology practice in Vietnam.

RESULTS: This special issue show the efficacy and safety of our Vietnamese approach continuously embracing the concept that "old and traditional is beautiful when safe, effective and cheap".

CONCLUSION: Vietnamese Dermatology is deeply concerned with any possible marketing orientated lucrative therapies, thus emphasising the risk/benefits ratio of "old-traditional" versus "new" therapeutic strategies.

Vietnamese Dermatology is presently proudly living an exciting era of great changes thanks to the fertile continuous cooperation with international leaders and associations [1], [2], [3].

The World Health Academy of Dermatology, the Vitiligo Research Foundation, the Military Medical Academy of Belgrade Serbia, the University of Parma-Italy and the University of Rome Guglielmo Marconi, Rome-Italy have successfully joined our Vietnamese Dermatology Community in the ambitious project of positionìng Vietnam in the Dermatologic Olympus.

Other private and public institutions are joining and will join us.

In this very peculiar issue, you'll find 35 contributions from all academic hospitals of Vietnam reflecting the therapeutic strategies and every day's dermato-venereology practice in Vietnam.

Our publications are mainly directed to the large General Medicine Community and only secondarily to the smaller Dermatology Community.

Some pearls of this Vietnamese Dermatology Special Issue are devoted to the description of the national and hopefully international declining of traditional therapies.

PUVA Therapy is becoming increasingly unpopular in Vietnam while the Narrow Band and Broad Band Phototherapies are prevailing. This is just one example among others.

Other sections of this special issue show the efficacy and safety of our Vietnamese approach continuously embracing the concept that "old and

traditional is beautiful when safe, effective and cheap".

Last, our Vietnamese Dermatology is deeply concerned with any possible marketing orientated lucrative therapies, thus emphasising the risk/benefits ratio of "old-traditional" versus "new" therapeutic strategies.

This is the "file rouge" of this Vietnamese Special Issue.

A strict therapeutic Ethical approach is the basis for our victorious international leadership.

This is our vision and mission.

The new Era of Vietnamese Dermatology culminated with the World Dermatology Summit of Hanoi of December the 2nd, 2017 [4].

After this spectacular international event, many other international meetings and round tables and workshops have enriched the Vietnamese Dermatology.

We are now ready to proudly show our Leaders attitudes with the organisation of the World Vitiligo Day in Ha Noi on June 25th, 2019 [5].

We're waiting for you all to be warmly welcomed.

This Special Vietnamese issue is something more than a series of medical and surgical reports.

It is, in fact, the description of what Vietnamese Dermatology is in the moment in which everyone perceives that everything is changing.

We proudly work as an International Team being aware that medical and surgical developments are nowadays a challenging global issue - we accept the challenge for a better Dermatology in a better World.

Hopefully, the readers will give us their precious comments, criticism and advice.

Here we are today in Vietnam, ready for sharing and absorbing from every corner of the Planet what's good for all our patients.

Enjoy the reading!

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Basic Science

In Vitro Antibiotic Resistance in Bacterial Infected Eczema at Ho Chi Minh City Hospital of Dermatology

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Keywords: Infected eczema; Antibiotics resistance

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Abstract

BACKGROUND: Infected eczema is one of the most common complications of eczema. The progression and treatment of infected eczema have become more complex and difficulty due to the antibiotic resistance of bacteria and the abuse of antibiotics in treatment.

AIM: Our research was conducted with the aim of investigating the severity of in vitro antibiotic resistance in patients with bacterially infected eczema at Ho Chi Minh City Hospital of Dermatology.

METHODS: We studied 40 cases of patients, suffering from atopic dermatitis, contact dermatitis, vesicular palmoplantar eczema, with positive results of infected eczema.

RESULTS: *S. aureus* accounted for 82.5%, followed by *S. epidermidis* (15%), *P. aeruginosa* (12.5%), *S. pyogenes* (5%) accounted for a small percentage. *E. coli* (2.5%) and *M. morganii* (2.5%) accounted for the lowest percentage. Both MSSA and MRSA were completely resistant to penicillin. MRSA is completely resistant to penicillin, erythromycin, and cefuroxime, highly resistant to clindamycin (82.35%). Our research showed that *Pseudomonas aeruginosa* was not resistant to a variety of antibiotics. It was completely resistant to tetracycline, trimethoprim/sulfamethoxazole (100%). Most bacteria are highly sensitive to linezolid, vancomycin as other studies in the world shown. There are also rifampicins, pristinamycin. Hence, it`s prioritised to be used for only patients with eczema infected with multidrug-resistant bacteria.

CONCLUSION: Penicillin is not recommended for the treatment for infected eczema. Linezolid, vancomycin has a high sensitivity to bacteria including multidrug-resistant bacteria like MRSA.

Introduction

Eczema is a common and recurrent disease making up a large percentage among patients who come for dermatological examination and treatment. The disease greatly affects patients' life quality. In the current context of industrialisation, the percentage of patients tends to increase, creating a burden for the patients, families and whole society.

One of the common reasons why eczema is becoming more prevalent is bacterial superinfection. Particularly with the emergence of multidrug-resistant bacteria at present, it's becoming increasingly difficult to treat eczema.

Therefore, our research was conducted with the aim of investigating the severity of *in vitro* antibiotic resistance in patients with bacterially infected eczema at Ho Chi Minh City Hospital of Dermatology. With this research, we hope to support the treatment for patients with eczema.

Population and Method

Research design

Our research was designed as a case series

report to investigate the prevalence of in vitro antibiotic resistance in bacterially infected eczema in atopic dermatitis, contact dermatitis, vesicular palmoplantar eczema at Ho Chi Minh City Hospital of Dermatology, from October 2014 to May 2015. Patients presented at least 1 out of 3 clinical features of bacterial superinfection: Fluid leakage and signs of acute inflammation, like swollen, hot, red, painful; Yellow flakes; Pustules combines with positive bacteria culture results. Exclusion criteria included: patients who are not diagnosed to get one of the three types of eczema analyzed through clinical examination; Patients drank or applied antibiotics a month ago; Patients immunodepressed.

Results

In our study there were 40 infected eczema patients with positive bacterial culture results, in which the group aged between 13 and 37 accounted for the highest percentage (35%); Male (65%) accounted for a higher percentage than female (35%); The number of patients living in cities (52.5%) was higher than in rural areas (47.5%); Patients with a history of allergy accounted for 45%. Atopic dermatitis accounted for the highest percentage (70%), in which patients in the acute stage made up a higher percentage (65%). The symptoms of itching (100%) and pain (100%) accounted for the highest percentage. The symptom of fever accounted for the lowest percentage (17.5%). Lesions on limbs accounted for the majority (77.5%), in which the lower limbs accounted for a higher percentage than the upper limbs.

Among transplantable bacteria in the patients with infected eczema, *S. aureus* accounted for 82.5%, followed by *S. epidermidis* (15%), *P. aeruginosa* (12.5), *S. pyogenes* (5%) accounted for a small percentage. *E. coli* (2.5%) and *M. morganii* (2.5%) accounted for the lowest percentage. MRSA occupied 51.52% that was higher than MSSA with the percentage of 48.48%.

MRSA is completely resistant to penicillin, erythromycin, cefuroxime, highly resistant to clindamycin (82.35%), lowly resistant to gentamycin (58.82%), ciprofloxacin (52.91%), chloramphenicol (23.53%), cotrimoxazole (5.88%), no resistance to tetracycline, vancomycin, linezolid, rifampicin, pristinamycin.

MSSA is also completely resistant to penicillin (100%), erythromycin (50%), clindamycin (43.75%), gentamycin (31.25%), ciprofloxacin (12.5%), tetracylin (6.25%), chloramphenicol (6.25%), no resistance to chloramphenicol, ciprofloxacin, vancomycin, linezolid, rifampicin, pristinamycin.

S. epidermidis was also resistant to penicillin at a high rate (83.33%). MRSA had the highest percentage of resistance to antibiotics in comparison with MSSA and S. epidermidis. MRSA, MSSA, S. epidermidis was completely non-resistant to vancomycin, linezolid, rifampicin, pristinamycin.

In our study, 5 cases *Pseudomonas aeruginosa* was completely resistant to tetracycline, trimethoprim/sulfamethoxazole (100%), in which only one case was resistant to ceftriaxone (20%). *Pseudomonas aeruginosa* was completely non-resistant to the remaining antibiotics

Discussion

In our study, among transplantable bacteria in patients with infected eczema, S. aureus accounted for the highest percentage (82.5%), followed by *S. epidermidis* 15% and *P. aeruginosa* 12.5% and *S. pyogenes* 5%, *E. coli* 2.5%, and *M. morganii* 2.5% (82.5%), accounted for the lowest percentage. This finding is consistent with conclusions of the study of Hon KL1 and et al., [1] were the most common bacterium in eczema from the moderate to severe levels was *S. Aureus*. MRSA rate in our study was higher than other researches on bacterially infected eczema in literature. In our opinions, the purchase and sale of antibiotics are not carefully regulated in Vietnam. According to the survey on the sale of antibiotics in rural and urban drug stores in the Northern provinces done by the University of Pharmacy and Agency of Health Examination and Treatment, most of the antibiotics are sold without prescriptions, 88% in the urban areas and 91% in the rural areas [2].

Moreover, drug sellers and citizens have low awareness of antibiotics and antibiotic resistance. The increased rate of MRSA infection, apart from the hospital-acquired MRSA (HA-MRSA), also includes Community-associated MRSA (CA-MRSA). This CA-MRSA is different from the previous strains of MRSA, which is closely related to health care, age, and rapidly transmits to healthy individuals in the community and frequently causes infectious diseases outside the hospital environment. This explains why MRSA increases rapidly even without the nosocomial infection. We need further research to clarify this issue.

The results showed that both MSSA and MRSA are completely resistant to penicillin (100%). S. epidermidis was also highly resistant to penicillin (83.33%). Compared to MRSA, MSSA was sensitive to a variety of antibiotics. In a study by Horvath A et al., [3], all strains of MSSA were highly sensitive to vancomycin, except penicillin, but other antibiotics were still susceptible to MSSA.

MRSA is completely resistant to penicillin, erythromycin, cefuroxime, highly resistant to clindamycin (82.35%), lowly resistant to chloramphenicol, cotrimoxazole, no resistance to vancomycin, linezolid, rifampicin, pristinamycin found. The resistance percentage of gentamycin, erythromycin are similar to other studies in the world. Although the resistance percentages of chloramphenicol, cotrimoxazole and tetracycline in other studies are higher than ours, studies in Ardabil Hospital in Iran [4] showed consistent results. Tang CS et al., [5] conducted a study evaluating the sensibility of *S. aureus* to antibiotics among the children with atopic dermatitis. Results of antibiogram showed that followed by penicillin, S. aureus has the highest resistance to erythromycin and clindamycin. Besides penicillin, gentamycin, erythromycin and clindamycin achieved higher percentages of resistance than the remaining antibiotics.

S. epidermidis was resistant to lots of other antibiotics and was rarely resistant to linezolid. According to the study by Khan MM, Faiz A, Ashshi AM [6] *S. epidermidis* was found to have a high antibiotic resistance. The overall drug resistances were ranged from 1.6% to 99.5% for all test drugs, except vancomycin and linezolid that were 100% sensitive. Thus, there is a similarity in our results when *S. epidermidis* mostly showed the resistance to antibiotics and the high resistance to penicillin. Particularly, vancomycin, linezolid was highly sensitive to *S. epidermidis.*

Our research showed that *Pseudomonas aeruginosa* was not resistant to a variety of antibiotics. It was completely resistant to tetracycline, trimethoprim/sulfamethoxazole (100%). In which only one case is resistant to ceftriaxone (20%). In comparison with other studies, our results are different because *P. aeruginosa* has been reported to be resistant to most antibiotics with different percentage of resistance in regions in the world, but have a high resistance to tetracycline, trimethoprim/ sulfamethoxazole, which is consistent with the majority of studies. In our study, the bacterially infected eczema was recurrent, but there was no surgical intervention, no use of invasive devices, most of the patients came for examination in the daytime. Therefore, they were less susceptible to infection and the transmission of the drug-resistant gene of *P. aeruginosa* in the hospital. As a result, the drug resistance of *P. aeruginosa* in our study was not as high as other studies [7], [8], [9], [10].

In conclusion, penicillin is not recommended for the treatment for infected eczema. Linezolid, vancomycin has a high sensitivity to bacteria including multidrug-resistant bacteria like MRSA. Hence, it`s prioritized to be used for only patients with eczema infected with multidrug-resistant bacteria. The patient with infected eczema and manifestations of popular infection should be appointed for the antibiogram.

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Basic Science

Distribution of Malassezia Species from Scales of Patient with Pityriasis Versicolor by Culture in Vietnam

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Keywords: Pityriasis versicolor; Yeast; Malassezia spp.

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Abstract

BACKGROUND: The detection of pathogenic fungus is an important step and key to assessing the sensitivity of the antifungal drugs, and therefore choosing an effective treatment method.

AIM: To identify Malassezia species from scales of a patient with pityriasis versicolor.

METHODS: Three hundred patients with pityriasis versicolor who were positive with direct examination, were isolated by culture.

RESULTS: Identification of Malassezia species by culture: the growth rate was 90.3%; the detection rate was 97.0%, including 11 species: *M. globosa* (42.4%), *M. dermatitis* (17.3%), *M. furfur* (14.4%). *M. globosa* was the most prevalent species in the 20-29 group 36.5%, in hyphae and yeast cells (42.2%).

CONCLUSION: *M. globosa* is the main cause of pityriasis versicolor in Vietnam.

Introduction

Malassezia spp. Is lipophilic yeast which is of the normal cutaneous commensal flora on humans and animals. Malassezia includes 14 species in which *M. globosa, M. furfur, M. sympodialis* are the most common. Symptoms of Malassezia fungal diseases include pityriasis versicolor, seborrheic dermatitis, atopic dermatitis, Malassezia folliculitis, psoriasis, even skin cancer [1], [2] in all parts of the world, especially in tropical countries (18% of the population) [3].

In the world, depending on climate, geographic conditions, there is a difference between the distribution of Malassezia species in other areas.

Therefore, we carried out a study to identify Malassezia species that caused pityriasis versicolor (PV) by the culture at National Hospital of Dermatology and Venereology (NHDV), Viet Nam.

Methods

A cross-section study of 300 patients with PV who had a positive direct examination test at NHDV from January 2016 to December 2016. Skin scales samples: Identification culture. MDixon media culture, SDA, TABLE 20, Tween 40, Tween 60, Tween 80, Malassezia Chromatase. Data were collected by SPSS 23.0 software and statistical tests study, to determine the incidence of Malassezia species.

Results

On 271 cultured samples, 11 *Malassezia* species were identified: *M. globosa, M. furfur, M. dermatis, M. sympodialis, M. restricta, M. obtusa, M. slooffiae, M. pachydermatis, M. japonica, M. equina,* and *M. cuniculi*.

Table 1: Identification of Malassezia species by culture

Species	N	%
M. globosa	115	42.4
M. furfur	39	14.4
M. dermatis	47	17.3
M. sympodialis	13	4.8
M. restricta	12	4.4
M. obtusa	16	5.9
M. slooffiae	5	1.8
M. pachydermatis	1	0.4
M. japonica	11	4.1
M. equine	3	1.1
M. cuniculi	1	0.4
Malassezia spp.	8	3.0
Total	271	100

We tested the development of M. pachydermatis on Sabouraud agar (SDA). *M. restricta* has a negative Catalase test. Then, proceeding with the reaction with Tween 20, Tween 40, Tween 60, Tween 80. Next, comparing with colony morphology and microscopic staining of three species including *M. sympodialis, M. japonica, M. slooffiae*. Some other species cultured in CHROM agar Malassezia, based on morphology, colour and colony characteristics, identified six species including *M. furfur, M. dermatis, M. globosa, M. obtusa, M. cuniculi,* and *M. yamatoensis*.

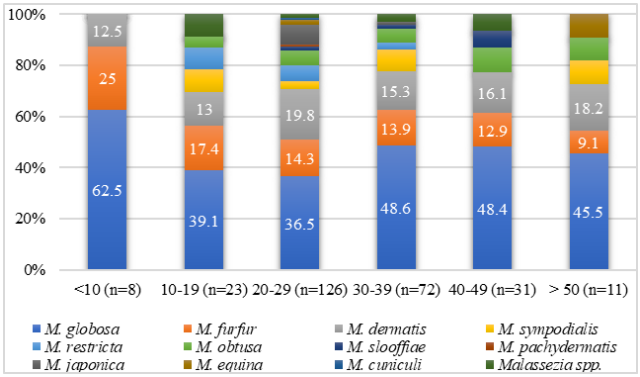

Figure 1: Distribution of Malassezia species isolated according to a group of ages

In different age groups, *M. globosa* is a common species, following *M. dermatis, M. furfur*. We did not find *M. furfur* in humans who was over 50 years old, while *M. obtusa* which was normal flora, had a higher rate. In the group of under 10 years old, only found 3 species: *M. globosa, M. furfur, M. dermatis*. The male/female ratio is approximately 2/1. Men may be the main occupational and physical activity partners, so exposure to a variety of environmental factors may be a favourable factor for the pathogenicity of the fungus, which can lead to infection rate.

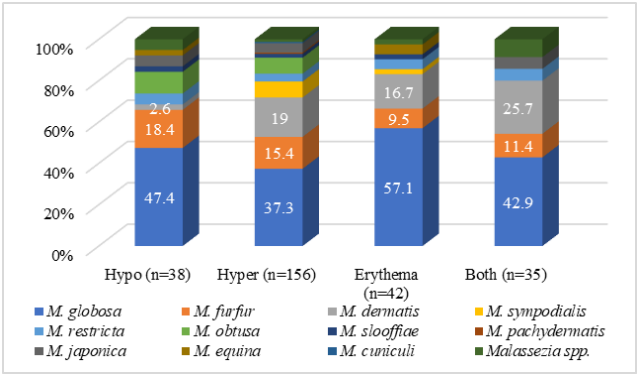

Figure 2: Distribution of Malassezia species isolated according to colour lesions

Fungus infection in the male is higher than female. In the study, we found that hyperpigmented was the most common with 58.3%, following Hypopigmented, Erythema and Both.

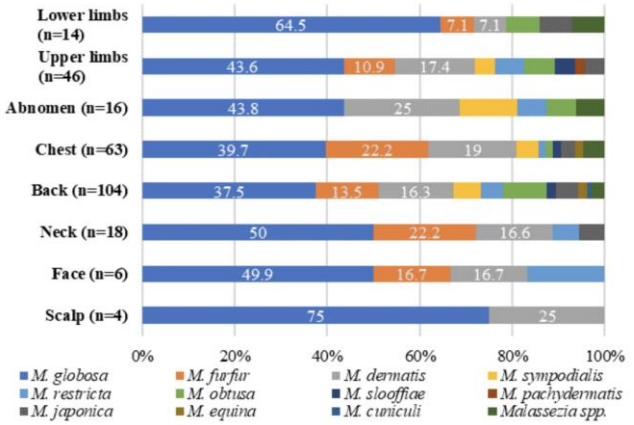

Figure 3: Distribution of Malassezia species isolated according to the site of lesions

Discussion

Results in the study showed a higher method of Abbas Rasi và cs (2009) [4], Kaneko Takamasa et al., (2011) [5], Rezvan Talaee et al., (2014) [6]. Nguyen Dinh Nga et al., (2007) [7]. However, in addition to the culture environment, climate and geography are also a major factor influencing the distribution of Malassezia species. Also, some new species have been discovered in recent years, such as *M. equina, M. caprae* (2007), *M. cuniculi* (2011), can increase the number of species discovered.

Results matched with Karakas et al., (2009) [8] with 47.7%. As such, *M. globosa* was found in the different area of the world and Vietnam. *M. furfur* was referred to as the most frequent species and most common disease, but in our study, only 14.4% was ranked third after *M. globosa* (42.4%) and M. dermatis

(17.3%). In particular, *M. furfur* grows well in mDixon agar, which is more easily indentified than other species. Our results are similar to those of other authors: Karakas et al., (2009) [8], Rezvab Talaee et al., (2014) [6].

A study by Nguyen Dinh Nga et al., (2007) conducted in Vietnam showed that the majority of species were *M. furfur* (57.33%) and *M. globosa* [7]. Our results from Table 1 show that *M. globosa* is the common species (42.4%), *M. furfur* (14.4%).

In comparable climates, our findings are similar with other authors: Talaee et al., (2014) [6] with hyperpigmented 50%; Karakas et al., (2009) [8] with 47.4%. We found that the hyperpigmented lesions were mainly related to *M. globosa* by Talaee et al., (2014), Karakas et al., (2009) *M. dermatis* is quite common in erythema lesions [6], [8]. *M. sympodialis* is mainly found in hyperpigmented [9].

In conclusion, using culture method, we identified 11 Malassezia species including *M. globosa* (42.4%); *M. dermatis* (17.3%); *M. furfur* (14.4%). M. globosa is the main cause of pityriasis versicolor in Vietnam.

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Clinical Science

The Effectiveness of Local Surgical Technique in Treatment of Axillary Bromhidrosis

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Keywords: Axillary bromhidrosis; Bromhidrosis

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Abstract

BACKGROUND: Up to now, surgical excision of apocrine glands still has been a method that yields high treatment results and low rate of odour recurrent for patients, but many people worry about some serious complications that have been observed postoperatively, such as hematoma and skin necrosis. These prolong wound healing, leading to unsightly scars in the axillary fossae.

AIM: We conducted this research to investigate the effects and complications of our surgical technique for axillary bromhidrosis.

METHODS: Forty-three patients with axillary bromhidrosis were treated. An elliptical incision was made at a central portion of the area marked, with both tips of the ellipse along the axillary crease. The elliptical skin with the subcutaneous tissue was removed en lock. The adjacent skin was undermined to the periphery of the hair-bearing area with straight scissors. The undermined subcutaneous tissue was removed with curved scissors, and the skin was defatted to become a full-thickness skin flap. Any suspected hemorrhagic spots were immediately coagulated electrosurgically. Appropriate drains were placed, and the treated area was covered with thick gauze to each axilla. Arm movement was strictly controlled in the first 3 days post-operatively.

RESULTS: Thirty-one patients have been followed up and evaluated for 6 months. 56 out of 62 axillae (90.3%) showed good to excellent results for malodor elimination. All patients reported a reduction in axillary sweating. There were two axillae of skin necrosis and three axillae of hematoma, with one patient receiving an anticoagulant from a cardiologist after the first day of surgery, to treat heart valve disease. The Dermatology Life Quality Index (DLQI) score decreased significantly, and the quality of life improved after the operation.

CONCLUSION: Our technique is a simple surgical procedure and easy to perform helping to achieve results for high malodor elimination, with almost no serious complications. Patient's life quality improved significantly after the operation.

Introduction

Axillary bromhidrosis is a disease characterised by excessive malodour due to the hyperfunction of apocrine glands. Although this disease is not life-threatening, it can have a serious effect on the patients' quality of life, especially in an Asian society. Various treatment methods have been developed, but the effect of nonsurgical methods such as topical antiperspirants and deodorants, lasers and botulinum toxin A, is temporary and limited [1], [2]. Systemic medication with anticholinergics cause major side effects, and long-term use is not possible. Thus, surgical treatment seems to be the most logical and effective method available.

Since Skoog and Thyresson introduced the first surgical treatment for axillary hyperhidrosis in 1962 [3], a variety of surgical techniques have been reported in recent years. Minimal invasive procedures, such as superficial liposuction, suction curettage, allow for short recovery time and leave only minor

scars [4]. However, the techniques are unsatisfactory to doctors and patients due to recurrent odour. Up to now, local surgical excision of apocrine glands has been a method that still yields high treatment results and low rate of odour recurrent for patients, although it is often accompanied by wound complications and relatively long recovery period [5], [6], [7], [8].

The purpose of this study is to evaluate the effectiveness and safety of local surgical technique that partially removes skin and subcutaneous cellular tissue in the treatment of axillary osmidrosis.

Methods

Patients

From July 2017 to July 2018, 43 patients were operated on for bilateral axillary bromhidrosis. All operations were carried out in our hospital. The results were assessed by the patients themselves and their family members and/or close friends. The results of malodor elimination were graded by the patients as excellent, good, fair, and poor. Elimination of sweating was evaluated using the Hyperhidrosis Disease Severity Scale (HDSS) [9]. Changes in hair growth and patient satisfaction degree were also evaluated. The quality of life was assessed using the modified Dermatology Life Quality Index [10], which includes a 10 item questionnaire aiming to measure the effects of skin problem on usual life. There were four possible answers for every question: ‘‘not at all’’, ‘‘mild,’’ ‘‘moderate’’, or ‘‘severe’’’, with corresponding scores of 0, 1, 2, and 3 respectively. Total scores ranged from 0 to 30, with higher scores indicating a lower quality of life. Post-operative complications were investigated.

Statistic analysis

Statistical analysis was performed using non-parametric testing, with statistical significance at the 95% level. The calculations were performed using the STATA13.0.

Surgical Technique

Patients were placed in the supine position and arms were abducted to about 90. The axillary hair-bearing area was marked before the operation. After regular sterilisation of the area, local anaesthesia was given using 0.5% lidocaine with 1:200,000 epinephrine. An elliptical incision was made at a central portion of the area marked, with both tips of the ellipse along the axillary crease. The widest diameter of the elliptical incision was 1.5 cm. The elliptical skin with the subcutaneous tissue was removed en lock. The adjacent skin was undermined to the periphery of the hair-bearing area with straight scissors. The undermined subcutaneous tissue was removed with curved scissors, and the skin was defatted to become a full-thickness skin flap. Any suspected hemorrhagic spots were meticulously coagulated electro surgically. The incisions were closed in two layers with 5-0 vicryl subcuticularly and 5-0 nylon for the skin. A drain was made of a butterfly needle, and a 20ml syringe placed, which was removed 24 -28 hours postoperatively. The axillary wounds were covered with bulky gauze. Arm movement was strictly controlled in the first 3 days post-operatively. Sutures were removed 10 days after the operation.

Results

The operations were performed in 32 female and 11 male patients, the average age was 29.9 years (ranged 18-63 years), and the female-to-male ratio was 3 : 1. The mean onset of disease was 16.7 years. The mean body-mass-index (BMI) was 20.9 kg/cm^2. Of 43 cases, 32 cases (74.4%) had family histories of this condition.

Table 1: Postoperative evaluation of 31 patients (62 Axillae) after local excision for Axillary Osidrosis

Variable		*N (%)*
Malodor elimination		
– Excellent (neither the patient nor close persons were aware of malodor)		15/62 (24.2)
– Good (very marked improvement and minimal malodor sometimes occurs during heavy perspiration)		41/62 (66.1)
– Fair (marked improvement but can be aware of light malodor by her/himself sometimes during daily activity)		6/62 (9.7)
– Poor (limited improvement and both the patient and persons nearby were easily aware of malodor)		0 (0)
Reduced hair growth		
– Significant (>75%)		12/62 (19.4)
– Moderate (50–75%)		28/62 (45.2)
– Mild (25–50%)		18/62 (29)
– No significant (<25%)		4/62 (6.5)
Mean HDSS score		
Before surgery	Before surgery	
2.6 ± 0.9	1.3 ± 0.5*	
Patients' satisfaction		
– Satisfactory		27/31 (87.1)
– Neutral		4/31 (12.9)
– Regretful		0 (0)
Scar form		
– Flat scar		45/62 (72.6)
– Atropic scar		0 (0)
– Hypertrophic scar		16/62 (25.8)
– Keloid		0 (0)
– Contrative scar		1 (1.6)
Complications		
– Hematoma		3/62 (3.4)
– Seroma		0(0)
– Skin edge necrosis		2/62 (2.3)
– Local infection		0 (0)
– Upper limb oedema		3/62 (3.4)
– Shoulder movement limitation		0 (0)

HDSS: Hyperhidrosis Disease Severity Scale
*p < 0.05

There were 31 patients followed up for a minimum of 6 months, with an average of 8 months (6-12 months). A summary of the results, including malodor elimination, changes in axillary sweating and hair growth, post-operative scar, patient satisfaction degree, and post-operative complications as presented in Table 1.

Of the total of 62 axillae (31 cases), 56 (90.3%) showed good to excellent results; hair growth decreased in 58 (93.6%). The mean HDSS score decreased significantly, 2.6 before the treatment and 1.3 after the surgery ($p < 0.05$). Quality of life was assessed before and 6 months after the operation. The mean DLQI score was 16.1 (ranged from 5 to 28) before the treatment and decreased to 3.3 after the surgery.

All subscores of questions and mean DLQI score significantly decreased after the procedure ($p < 0.05$) as shown in Figure 1. Overall, 27 (87.1%) patients were satisfied, and 4 (12.9%) patients were neutral with the procedure.

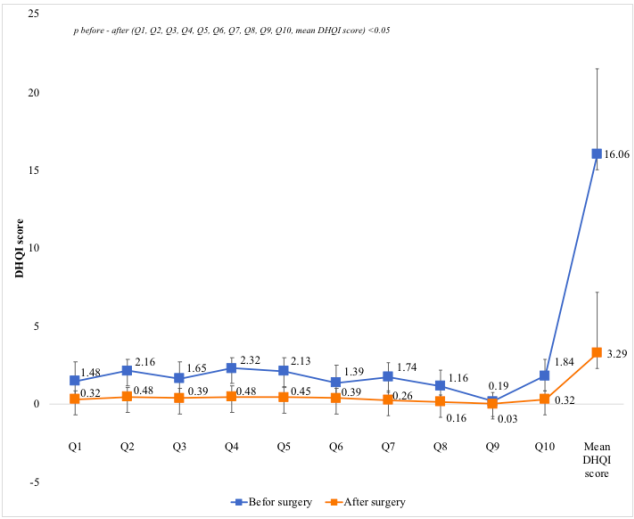

Figure 1: Mean of DQLI score before and six months after surgery

There were three cases of haematoma, two cases of skin edge necroses and three instances of upper limb oedema. For patients with upper limb oedema, oedema disappeared within several days when the arms were maintained in an elevated position. All the skin edge necroses and haematoma occurred on two patients, with one patient receiving an anticoagulant from a cardiologist after the first surgery day, to treat heart valve disease, while the other patient did not strictly control the movement of his arms.

No infection or shoulder movement limitation was observed. There was no keloid or atrophy of scars. Scars were flat in 45 axillae (72.6%) and hypertrophic in 15 axillae (24.2%). There was only one contractive scar.

Discussion

It is believed that the secretion of the apocrine glands and the activity of bacteria create the characteristic malodor of axillary osmidrosis [11]. The apocrine glands are found in connection with hair follicles and located at the junction of the dermis and subcutaneous fat. The surgical pattern designs for bromhidrosis are based on the location of apocrine glands. Therefore, any treatment methods that eliminate subcutaneous tissue are effective in the treatment of axillary bromhidrosis. Up to now, there are many invasive procedures have been proposed. Minimally invasive procedures include mechanical liposuction, curettage, scissors trimming, using small transverse incision, and combined techniques [2], [5], [12]. Many of which results in an inconspicuous scar, but the blind undermining that occurs during the operation increases damage to the skin edge and subdermal vascular plexus and the risk of haematoma and incomplete excision of apocrine glands. Besides, they depend a lot on the surgeon's experience. So an incision with eligible length can achieve full exposure during the operation and control hemostasis meticulously. Our method is a simple surgical procedure, and the glands can be easily excised under direct vision. Therefore, it is not surprising that as high as 90.3% of our patients achieved a good result regarding malodour elimination and 27/31 (87.1%) patient satisfied after treatment.

In our group patients, there was a strong predominance of females, which is similar to previous reports [2], [5], [6]. Most patients have family members who also have bromhidrosis in our study (74.4%). An autosomal dominant inheritance pattern has been proposed. Recently, some studies have found a strong relationship between bromhidrosis and wet ear wax associated with one single nucleotide polymorphism (SNP) 538G > A in exon 4 of the human ABCC11 gene [13], [14].

Axillary osmidrosis is often accompanied by axillary hyperhidrosis. In our study, all patients with a complication of axillary hyperhidrosis reported a reduction in sweating. Beer GM et al. recently reported that most of the eccrine and apocrine glands were found in the subcutaneous tissue near the border to the dermis and not in the dermis [15]. Therefore, our method was also effective in treating axillary hyperhidrosis, although the reduction in axillary sweating was not the primary objects.

Axillary osmidrosis is a distressing problem. Most sufferers limit their social activities because of embarrassment due to offensive axillary odour. The appropriate surgical technique should improve their quality of life. The Dermatology Life Quality Index is a reliable tool for measuring the impact of skin disease on the quality of life of patients and it has been applied to many common skin conditions. In our study, median DLQI score was 16.1 before the operation,

compared with 3.3 postoperatively. The difference is statistically significant ($p < 0.05$).

A haematoma is one of the severe complications after local osmidrosis surgery, the main reasons are uncontrolled bleeding meticulously and active movement of the arm in the early postoperative period. There is two cases of hematoma in our study, careful assessment of the history before the bleeding also revealed that one patient did not abide by the postoperative rest. Thus, doctor's recommendations also have an important role, and immediate evacuation of the large haematoma will lessen the dangers of skin-flap survival.

The ugly scar is also a problem that causes patients' anxiety after surgery. In our group of patients, there was a predominance of flat scars (72.6%), followed by hypertrophic scars (24.2%), with only one axilla with contractive scars (Figure 2). During the followed period, we found a phenomenon that the scars in the right axillary fossa were more conspicuous than those in the left side. This may be attributed to the increased strains in the right side due to relatively more movements. The case of contractive scars occurred on a patient with hematoma, but the contractive degree was slight and acceptable.

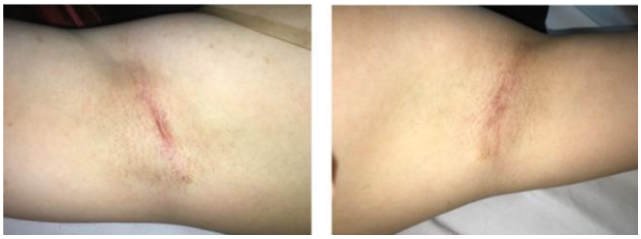

Figure 2: The scar in both side of patient's axillae 6 months postoperatively

In conclusion, our surgical technique for the treatment of axillary bromhidrosis is a simple surgical procedure and easy to perform, with low complications and effective elimination of malodour. The quality of life significantly improved after the operation.

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Clinical Science

Successful Treatment of Facial Atrophic Acne Scars by Fractional Radiofrequency Microneedle in Vietnamese Patients

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Keywords: facial atrophic acne scars; Radiofrequency; fractional RF microneedle

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Abstract

AIM: This study aimed to evaluate the effect of the fractional Radiofrequency microneedle treatment for facial atrophic acne scars.

METHODS: A group of 52 patients were recruited for the study. Goodman & Baron's acne scar grading system was used for assessment at their first visit and the end of 3 months after the last treatment session.

RESULTS: The results displayed that 73.1% of patients have the improvement of the Goodman scar level after four times of treatment. The Goodman and Baron scar point mean was reduced from 16 ± 7.6 to 5.6 ± 5.0 ($p < 0.01$). Post-inflammatory hyperpigmentation was experienced in 5 patients (9.6%).

CONCLUSION: The microneedle fractional Radiofrequency is an effective treatment method of facial atrophic acne scars, with minor side effects and a short downtime.

Introduction

Atrophic acne scars are dermal depressions commonly caused by the destruction of collagen after inflammatory acne [1].

Recently, fractional radiofrequency microneedle (FRM) technique has been shown to be clinically effective in managing acne scars and less post-inflammatory hyperpigmentation (PIH) [2], inducing collagen shrinkage, collagen neogenesis and stimulating remodelling [3].

This study aimed to evaluate the effect of the fractional Radiofrequency microneedle treatment for facial atrophic acne scars.

Material and Methods

The study was performed on 52 patients with acne scars and skin phototypes III–V. The average age is 26.7 ± 6.1 years (range 15-43 years old). Male and female ratios are roughly equal.

The observed scars were mainly rolling scars

and boxcar, and the ice pick was relatively low (19.5%). Patients with post-acne scars were mostly severely scarred, Goodman 4 (71.2%); Goodman 3 (28.8%) [4], [5].

All subjects were treated with two consecutive passes of an FRM (INTRAcel TM, Jeisys Medical, Seoul, Korea) with minimal or no overlapping. The subjects were treated for a total of four sessions at 1 month intervals.

Results

At the 3-month follow-up visit, the colour of the scar was significantly improved with 92.5% of normal skin colour and 3.8% of acne related post-inflammatory erythema (PIE) as shown in Figure 1. This improvement was statistically significant compared with pretreatment ($p < 0.05$).

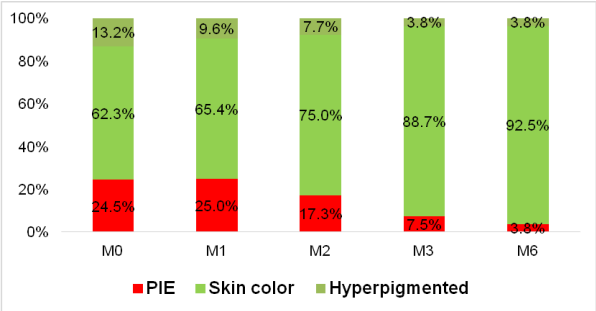

Figure 1: Improvement of the color of scars (PIE: Post-inflammatory erythema-M0: Baseline-M1: first month-M2: second month-M3: third month-M6: sixth month)

The improvement of scars according to Goodman and Baron qualitative scar grading began to be apparent only after 2 treatments. Grade 4 scars were decreased from 71.2% to 59.6%. The improvement was stronger after 3 treatments and 3 months after the end of treatment. Grade 4 showed a significant decrease from 71.2% to 38.5% and 25% ($p < 0.01$). There were 73.1% of patients who showed improvement by 1 grade. These were presented in Figure 2.

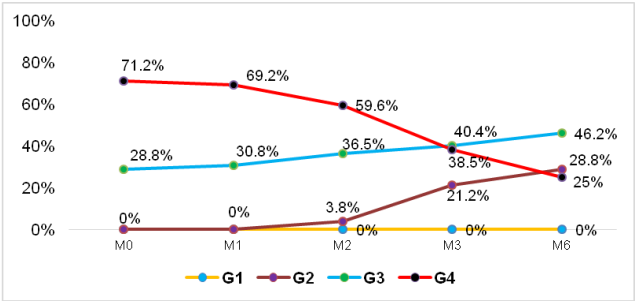

Figure 2: Improvement of Goodman's qualitative acne scar grading system. (M0: Baseline- M1: first month- M2: second month- M3: third month- M6: sixth month- G1: Grade 1-G2: Grade 2- G3: Grade 3- G4: Grade 4)

The acne scar scores improvement was almost negligible after one treatment. However, after 4 treatments, mean scars decreased from 16 ± 7.6 (before treatment) to 5.6 ± 5.0 ($t = 17.62$; $df = 51$; $p < 0.01$), Figure 3.

The treatment was generally well tolerated. Only five patients (9.6%) reported post-inflammatory hyperpigmentation and subsided spontaneously within 1 month without any recurrences after the remaining treatment sessions.

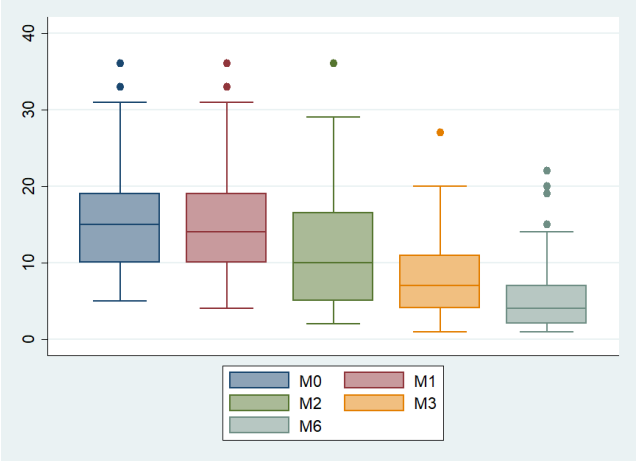

Figure 3: Improvement of Goodman and Baron's quantitative acne scar grading system (M0: Baseline-M1: first month-M2: second month-M3: third month-M6: sixth month)

Discussion

Scars can occur early in acne patients, about the severity of acne, duration of untreated acne and duration of acne.

At the 3-month follow-up visits, the colour of the scar was significantly improved with 92% of normal skin colour and 3.8% of acne-related post-inflammatory erythema (PIE).This improvement was statistically significant compared with pretreatment (p-value = 0.001 < 0.05).This was consistent with another study in the literature [6]. PIE is very common following inflammatory acne and is often cosmetically unacceptable to patients. FMR treatment could improve erythema by reducing inflammation and abnormal vessel proliferation, by inhibiting NF-κB expression and angiogenesis VEGF directly or indirectly [6].

The improvement was stronger after 3 treatments and 3 months after the end of treatment, showing a significantly decrease in the severity levels of the scars. Grade 4 scars were reduced from 71.2% to 38.5% and 25% ($p = 0.000 < 0.01$). 73.1% of patients showed improvement by 1 grade.

The median Goodman and Baron's global

scores for acne severity was significantly lower than baseline at the 3-month follow-up visit, from 16 ± 7.6 to 5.6 ± 5.0 ($t = 17.62$; $df = 51$; p-value = 0.00 < 0.01).

In conclusion, FRM treatment can be considered as an effective modality of treatment for acne scars in patients with an added advantage of minimal downtime and effective improvement. This method can be considered as a good solution for the treatment of atrophic acne scar in Asians with low post inflammatory hyperpigmentation.

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Improving Treatment Outcome of Pemphigus Vulgaris on Vietnamese Patients by Using Desmoglein Elisa Test

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Abstract

BACKGROUND: Pemphigus Vulgaris (PV) is a chronic disease, is characterized by the presence of flacid bullous in skin and mucosa. There are 2 main autoantibodies against desmoglein3 (Dsg3) and desmoglein1 (Dsg1).

AIM: The aims of this study were to evaluate the before and after treatment outcome with corticosteroid, using Desmoglein ELISA test.

METHOD: Forty patients with Pemphigus include 36 PV and 4 PF (28 women, 12 women) were enrolled. The titers of Dsg in pemphigus patients by using ELISA test were done before and 1-month treatment

RESULTS: Both anti-Dsg1 and anti-Dsg3 levels were significantly reduced after treatment ($P < 0.05$). The severity of skin lesions was correlated with anti-Dsg1 antibody level and the severity of oral lesions was significantly correlated with anti-Dsg 3 antibody levels ($p < 0.05$)

CONCLUSION: It is recommended that we can predict and improve the outcome of treatment by using Desmoglein ELISA test.

Introduction

Pemphigus is a group acquired autoimmune bullous skin disease, it is characterized by flaccid blisters on the skin and mucous membranes, caused by acantholysis phenomenon (Amagai.M, Ishii.K et al. 1997) [1]. There are 2 main subtypes: Pemphigus vulgaris (P.V) and Pemphigus foliaceus (P.F). The pathogenic of disease is characterized by the presence of autoantibodies against desmosomal glycoproteins, including desmoglein 3 (Dsg3) in P.V and desmoglein 1 (Dsg1) in P.F. ELISA is a quantitative method for measuring antibody levels and a useful test for the diagnosis of pemphigus.

We tried to find the value of Dsg 1,3 by ELISA to predict the severity and monitoring this disease before and after treatment.

Methods

Based on clinical presentation and histopathology, from July 2013 to September 2014, forty pemphigus patients (36 PV, 4 PF) were enrolled in this study, including 28 women and 12 men. Mean age of male was 40.1 ± 9.0 years and of females was

51.3 ± 14.0 years. Dsg ELISA testing was performed on the sera of 40 patients before and after 1-month treatment. Anti-desmoglein autoantibodies were detected by ELISA method (kits from Medical and Biological Laboratories Co Ltd. Nagoya, Japan) with 100-fold serum dilution. The index value of positive reactions was considered greater than 20 U/L.

SPSS 20.0 software was used to analyse the data. Paired t-test was used to determine the difference in the anti-Dsg index values before and after treatment. $P < 0.05$ was considered significant.

Results

Forty patients with pemphigus (12 men, 28 women) were enrolled. The mean ± SD age was 48.0 ± 13.6 years, with a range of 15 to 80 years. The most frequent phenotype was muco-cutaneous in 25/40 (62,5%) cases, mucosal dominant and cutaneous dominant phenotypes were seen in 1/40 (2,5%) and 14/40 (35%) cases, respectively.

Table 1: Distribution of anti-Dsg ELISA

Level	Cutaneous lesions	Dsg 1 positive	Dsg3 positive	Mucosal lesions	Dsg 1 positive	Dsg 3 positive
No lesion	1	0	1	14	13	7
Mild	5	3	4	13	11	11
Moderate	23	20	16	13	10	13
Severe	11	11	10	0	0	0

The changes of the mean anti-Dsg1 and anti-Dsg3 index values (± SD) before and after treatment are shown in Table 2. The decrease in the mean anti-Dsg1 and antiDsg3 index values was statistically significant with a p-value below 0.05.

Table 2: Anti-Dsg ELISA before and after 1- month treatment

Disease	Dsg 1 (U/L)		Dsg 3 (U/L)	
	Before	After	Before	After
PV	81. 5 ± 52.5	67.8 ± 53.4	91.2 ± 54.1	65.6 ± 53.3
PF	138.3 ± 38.3	94.7 ± 40.7	56.6 ± 23.3	28.2 ± 19.1
Total	87.2 ± 53.7	61.5 ± 53.0	87.7 ± 55.1	60.9 ± 53.1
p	< 0.05		< 0.05	

Discussion

There are many documents report about the relationship between desmoglein titer and the severity of pemphigus disease. Amagai et al., (1999) used ELISA test in serum pemphigus patients showed 97.9% of P.F patients were positive with anti-Dsg 1 and 97.5% of P.V patients were positive with anti-Dsg 3 (Lenz, Amagai et al. 1999) [2]. Harman et al (2000) showed that the sensitivity of the ELISA in diagnosing Pemphigus is above 98% and in those patients untreated, the sensitivity was 100% (Harman, Gratian et al. 2000) [3]. Daneshpazhooh et al (2007) found that the rate of positive is 76.1% with anti- Dsg1; with anti- Dsg 3 is 94.5% (Daneshpazhooh, Chams-Davatchi et al. 2007) [4]. In many other studies also showed anti-Dsg has generally higher, ranging from 80 to 100% depending on each author (Anand, Khandpur et al. 2012; Avgerinou, Papafragkaki et al. 2013; Bracke, Speeckaert et al. 2013) [5], [6], [7]. Many studies have shown that this technique is highly sensitive and high specificity and it can evaluate the correlation between antibody concentration and the degree of activity (Marinovic, Fabris et al. 2010; Schmidt, Dähnrich et al. 2010; Anand, Khandpur et al. 2012; Bracke, Speeckaert et al. 2013) [5], [7], [8], [9]. Recently, it using as a marker to diagnosing and monitoring the severity of a disease. It is believed that oral dominant pemphigus is characterized by the presence of anti-Dsg3, and anti-Dsg 1 is in cutaneous dominant (Aoyama, Tsujimura et al. 2000; Harman, Gratian et al. 2000; Abasq, Mouquet et al. 2009; Bracke, Speeckaert et al. 2013) [3], [7], [10], [11]. On the other hand, studies regarding the correlation between the severity of this disease and anti-Dsg levels as well as its value in monitoring the disease are. Our results also showed that anti-Dsg ELISA is a simple method and highly valuable in the diagnosis.

There was a statistically significant correlation was seen between Dsg1 index values and severity of skin involvement and direct statistically significant correlation was seen between Dsg3 index values and the severity of oral involvement. Mortazavi et al (2009) showed that: the degree of skin damages a significant increase with anti-Dsg1 concentrations, and there was a relationship between the level of mucosal lesions with anti-Dsg3 (Mortazavi, Shahdi et al. 2009) [12].

Both anti-Dsg1 and anti-Dsg3 levels were significantly reduced after 1-month treatment ($p < 0.05$). In some studies also concluded that there was significant decrease level of Dsg after treatment. (K.E.Harman, P.T.Seed et al. 2001; Kumar, Arora et al. 2006; Bracke, Speeckaert et al. 2013) [7], [13], [14], [15].

In conclusion, Dsg ELISA is not only a sensitive tool for diagnosis of PV, but also has a predictive means of its severity as well as for monitoring the activity and relapse of disease.

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Clinical Aspects and Treatment of Pityriasis Lichenoides Et Varioliformis Acuta: A Retrospective Vietnamese Study

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Abstract

BACKGROUND: Pityriasis lichenoides et varioliformis acuta (PLEVA) is an uncommon condition which presents acutely with papulo-vesicles that may develop necrotic, ulcerative, or hemorrhagic changes.

AIM: We studied clinical, and treatment characteristics of PLEVA hospitalised patients at our hospital from September 2009 to December 2014.

METHODS: The records of 15 PLEVA patients were retrospectively reviewed.

RESULTS: The median age of onset was 21.8 ± 18.81 (from 1 to 68), male to female ratio was 2/1. The common area of onset was trunk (60.0%) and extremities (33.3%). Clinical features were purpuric papules (100%), hemorrhagic crusted papules (46.7%), pustular purpuric papules (40%), and necrotic ulcerating lesions (13.3%).

CONCLUSION: All patients were received systemic antibiotics (macrolides: 53.3%, others: 46.7%), 2 patients were added immunosuppressive drugs. A 1-year-old patient died, others had a good response.

Introduction

Pityriasis lichenoides is a group of rare skin diseases, including Pityriasis lichenoides chronic (PLC) and Pityriasis lichenoides et varioliformis acuta (PLEVA) [1]. PLEVA may occur at any age, but most frequently occurs in children and young adults. The average age of disease in our study was 7.75 for children and 37.9 for adults. Survey of the gender distribution depicted that males had approximately 2 times more frequently than females; this data is similar to the study of Jandrei Rogério Markus [2].

Lesions can occur on any area of the body, except palms and soles, and are characterised by the sudden onset of red papules that quickly develop into scaling papules. The papules may erode into crusted red-brown spots and then turn into a central necrotic ulcer, leaving scars after healing — this condition responses well to erythromycin and UV therapy [3].

This study aims to describe the clinical features and treatment methods of PLEVA at National hospital of dermatology and Venereology (Vietnam).

Methods

A total of 15 patients were enrolled from September 2009 to December 2014. The age of onset

was 21.8 years (range: 1-68 years). The majority of patients were males (67.7%). The lesions located on many parts of the body, except palms and soles, but trunk and extremities were most frequently affected areas of onset, which accounted for 60%.

Results

Clinical features were purpuric papules (100%), hemorrhagic crusted papules (46.7%), pustular purpuric papules (40%), necrotic ulcerating lesions (13.3%). The treatment proposed was erythromycin or other macrolide antibiotics in 8 patients (53.3%) and not macrolide in 7 patients (46.7%); 1 patient was treated by phototherapy combined with erythromycin, and 2 patients have also received immunosuppressive drugs. A 1-year-old patient died, others had a good response as shown in Table 1.

Table 1: Patient demographics, clinical and treatment characteristics

Parameter	Value
Age (years), mean (SD), min/max	21.8 (18.8); 1/68
Children (n/age)	8/7.75 (3.2)
Adults (n/age)	7/37.9 (16.2)
Sex men, n (%)	10 (67.7)
Area of onset, n (%)	
Chest – Abdomen	8 (53.3)
Back – Buttocks	1 (6.7)
Upper limbs (except palms)	3 (20.0)
Lower limbs (except soles)	2 (13.3)
Armpits - Groin – Genitals	0 (0.0)
Scalp - Face – Neck	1 (6.7)
Rates of skin lesion, n (%)	
Purpuric papules	15 (100.0)
Hemorrhagic crusted papules	7 (46.7)
Pustular purpuric papules	6 (40.0)
Necrotic ulcerating lesions	2 (13.3)
Other symptoms	
Itching	8 (53.3)
Fever	7 (46.7)
Pneumonia	2 (13.3)
Anaemia	3 (20.0)
Leucocytosis	7 (46.7)
Dead	1 (6.7)
Oral drugs	
Erythromycin	6 (40.0)
Other Macrolide antibiotics	2 (13.3)
Other antibiotics	7 (46.7)
Phototherapy	1 (6.7)
Immunosuppressive drugs	2 (13.3)

N = 15.

Discussion

In our study, trunk area and extremities accounted for 60.0% and 33.3% respectively. These data are constant to other studies in the literature [3], [4]. The skin lesions are divided into 4 types: purpuric papules (100%), hemorrhagic crusted papules (46.7%), pustular purpuric papules (40%), necrotic ulcerating lesions (13.3%). According to Pradeen et al., [5], 100% PLEVA patients had purpuric papules while the necrotic ulcerating lesions were quite rare than demonstrated Wahie S et al., (24.6%) [3].

Patients with PLEVA may have a fever which can be considered as a sign of infection. In this study, fever and infections occurred in 46.7% and 20.0% of patients, respectively. Two patients suffered from pneumonia. In literature, it was reported that internal organs could be involved in many cases with abdominal or joint pain and even central nervous system could be damaged [6]. In our study, all patients received oral antibiotics (erythromycin: 40%), immunosuppressive drugs (methotrexate, corticosteroids) were given in severe cases and a single case using phototherapy (PUVA). A 1-year-old patient died. She was hospitalised for high fever, widespread hemorrhagic crusted papules and necrotic ulcerating lesions, pneumonia, anemia, leukocytosis and diagnosed with Febrile Ulceronecrotic Mucha-Habermann disease (a severe form of PLEVA). Other patients had good response.

The experience in National Hospital of Dermatology and Venereology (Vietnam) from September 2009 to December 2014 demonstrated that PLEVA occurred at any age but was most common in children and young adults, clinical manifestations were acute, diverse and most patients had good response to treatment with macrolide. Only one patient died for Ulceronecrotic Mucha-Habermann disease.

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Efficacy and Safety of Methotrexate in Combination with Mini Pulse Doses of Methylprednisolone in Severe Alopecia Areata. The Vietnamese Experience

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Keywords: Alopecia areata; Methotrexate; Mini-pulse dose; Alopecia areata totalis; Alopecia areata universalis

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Abstract

BACKGROUND: Treatment of severe alopecia areata remains very difficult, especially in alopecia areata totalis and alopecia areata universalis. Methotrexate is known to be effective in the treatment of severe and chronic autoimmune disorders.

OBJECTIVE: To assess the effectiveness and safety of MTX in combination with mini pulse dose of methylprednisolone in the treatment of severe alopecia areata.

PATIENTS AND METHODS: The open, uncontrolled study compared pre-treatment and after-treatment. Thirty-eight patients (age 16-64) with severity AA (SALT score > 50 %) visiting National hospital of Dermatology and Venereology from April-2004 to September-2015 were enrolled. All patients received oral methylprednisolone 24mg/day for 3 consecutive days of a week in combination with oral MTX 7,5 mg weekly. This regimen is maintained up to 12 weeks and follow-up until to 6 months.

RESULTS: After 6 months, 60.5% of patients show complete hair growth (good response) and 18.4% shows the medium response. There is a significant SALT score reduction: mean baseline SALT score 84.39 ± 17.03 compared to mean post-treatment SALT score 24.19 ± 29.42. Good clinical improvement noted in after 3 months. We do not observe any side- effects related to oral MTX and oral methylprednisolone, and no patients had to withdrawal treatment due to side- effects.

CONCLUSION: Combination Methotrexate and mini pulse dose of methylprednisolone are effective and safe in treatment severity alopecia areata.

Introduction

Alopecia areata (AA) is one of the most common diseases of hair loss, the pathogenesis of the disease is still unknown but recently, it is considered an autoimmune disease [1], [2], [3], [4]. It is characterised by recurrent non-cicatricial hair loss that can affect any hair-bearing area such as the scalp, beard, eyelashes, and eyebrows. Patients usually start silently, develop persistently and relapse [5]. Although it is a benign condition and most patients are asymptomatic, but it can cause emotional and psychosocial distress. Incidence varies according to race and geography. In the United States, an estimated 4.5 million people are infected. It accounts for 0.1 to 0.2% of the world population [6], [7]. The disease can occur at any ages and in both sexes, but predominantly in young people aged 15-45, rarely seen in older adults and young children. Male and females are affected equally, and the prevalence is almost the same for all ethnic groups [8], [9]. Some factors related to this disease included family, allergic, immunological, endocrine, psychological trauma or

infection.

Treatment of severe alopecia areata remains very difficult, especially in alopecia areata totalis and alopecia areata universalis [10], [11], [12], [13]. Corticosteroids are the most commonly used agents in the treatment of AA, especially in the extensive forms, but the success of these agents is controversial [4], [12], [14]. In several studies, they are reported that alone corticosteroid treatment is not effective and the relapse rate is still very high [12], [13], [15]. Methotrexate is known to be effective in the treatment of severe and chronic autoimmune disorders, and it is a safe and effective corticosteroid-sparing agent [16]. Recently, MTX combination with oral corticosteroid has been reported effect and safe in severe AA [17], [18], [19], [20]. So we want to assess the effectiveness and safety of MTX in combination with mini pulse dose of methylprednisolone in the treatment severe alopecia areata.

Materials and Methods

Study design and design: Thirty-eight patients (age 16 -64) with severity AA (SLAT > 50 %) visiting NHDV from April-2004 to September-2015 were enrolled. The diagnosis of alopecia areata was based on clinical criteria. Severity alopecia areata patients were identified when SALT scores from 50% to 95% of the scalp area. Alopecia areata totalis (AT) is when hair loss from 95 to 100% of scalp area without hair loss in the body. Alopecia areata universalis (AU) means hair loss all of the scalp and in the body.

Treatment regimen: The regimen included oral methylprednisolone 24 mg/day for 3 consecutive days of a week in combination with oral MTX 7,5mg/ week. This regimen is maintained up to 12 weeks and follow-up until to 6 months.

Follow-up and outcome assessment: The degree of hair loss was assessed by SALT (Severity of Alopecia Tool) score in before treatment and monthly (every 4 weeks) after treatment. Transaminase levels (AST, ALT) and complete blood count were performed before treatment and after 3 months of treatment (12 weeks). Photographs of hair loss area were taken for each visit and recorded in files. Evaluation of the efficacy treatment used SALT score and patient satisfaction.

- Good response: Hair grows well, thick, black, covering the area of scalp and body, patients are satisfied.

- Moderate response: hair grows thin, brown or white, partially covered, patients are satisfied.

- Poor response: hair does not grow, patients are not satisfied.

Follow the side effects: acne, hypertension, stomach pain, headache, nausea, elevation of transaminase levels, count blood cell.

Exclusion criteria included the patient who has SALT score < 50%, patients are contraindicated for MTX, steroids and the patient who has pregnant women or intended pregnancy and breastfeeding.

Statistical analysis

The data were analysed by SPSS20.0 version. Results were reported as the mean ± standard deviation (SD) for the quantitative variables and percentages for the categorical variables. Analyses for normal distribution fitness were performed. Student t-test was used for intergroup comparison. Chi-square test was applied for the analysis of categorical variables. *P* values < 0.05 were considered to be statistically significant.

Results

A total of 38 patients had severe alopecia areata, including 31 (82%) female and 7 (18%) males were enrolled in this study. The mean age of the patients was 29.61 ± 12.07 and the meandiseasedurationwas 26.47 ± 30.1 months. Eighteen patients (47.4%) had severe AA, and 9 patients (23.7%) had AT and11 patients (28.9%) had AU.

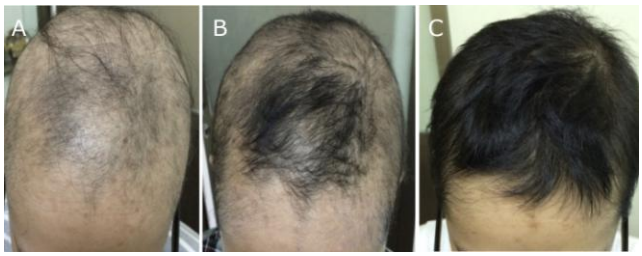

Figure 1: The effectiveness of treatment: patient at baseline (A); after one month of treatment (B); after 6 months of treatment (C)

Follow-up after 1 month of treatment showed that only 3 patients (7.9%) had a good response, 18 patients (47.4%) had a medium response, and 17 (44.7%) patients had a poor response.

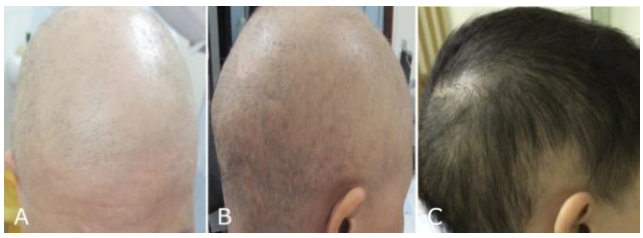

Figure 2: The effectiveness of treatment: patient at baseline (A); after one month of treatment (B); after 6 months of treatment (C)

However, at the end of 3 months of treatment, 22 patients (57.9%) had hair re-growth completely, 9 patients (23.7%) had hair re-growth partially, and 7 patients (18.4%) had still a poor response.

After 6 months of follow-up in this study, we found 23 patients (60.5%) had a good response and 9 patients (23.7%) had a medium response, and in those patients had no new patch or recurrent after stopping treatment as presented in Table 1.

Table 1: The efficacy of treatment every month

Responses	1-month treatment	2-months treatment	3-months treatment	6-months treatment
Good response	7.9 (3/38)	47.4 (18/38)	57.9 (22/38)	60.5 (23/38)
Medium response	47.4 (18/38)	28.9 (11/38)	23.7 (9/38)	23.7 (9/38)
Poor Response	44.7 (17/38)	23.7 (9/38)	18.4 (7/38)	15.8 (6/38)
Total	38	38	38	38

The area of hair loss decreases in each visited, SALT score in before treatment was 84.39 ± 17.03%, after 1-month treatment reduced to 65.10 ± 26.29%, and decreased dramatically after 2-months treatment was 45.67 ± 28.21% after 3-months treatment was 29.97 ± 29.67%. At the end of the study, the area of hair loss according to SALT was 24.19 ± 29.42% as shown in Table 2. No patients in our study had side effected related to oral corticosteroid and MTX.

Table 2: The SALT score in every month follow-up

SALT Score	Mean ± SD	P (before- after)
Before treatment	84.39 ± 17.03	$p < 0.05$
After 1 month	65.10 ± 26.29	
After 2 months	45.67 ± 28.21	
After 3 months	29.97 ± 29.67	
After 6 months	24.19 ± 29.42	

Discussion

This study shows that there is a significant clinical improvement when using a combination of methotrexate and mini pulse dose of methylprednisolone in treating alopecia areata, especially in the severe cases.

Over the past several years, the treatment of alopecia areata is very difficult; no therapy has long-term effects, the rate of recurrence is still high. Systemic corticosteroid was used in the treatment of hair loss in many years [21], [22]. This drug is effective, but the use of long-term drug causes many side effects [10], [14], [23], [24]. Joly (2006) was treated 22 patients had severe AA by using MTX and corticosteroid. These patients were treated with MTX alone (6 patients) or in combination with low dose oral prednisolone (16 patients). The dose of MTX varies from 15-25 mg/week; the dose of prednisolone varies from 10-20 mg/day. Results showed that the number of patients with hair grows completely were 14/22 patients (64%). No side effects have been reported. A reported by Chateaux and colleagues (2010) found that using corticosteroids in combination with MTX resulted in hair growth in 63% of patients. The dosage of MTX is 15-25 mg/week; the average duration of treatment is 3 months [18]. Royer et al., study (2011), 14 children (eight girls and six boys) aged between 8 and 18 years (mean 14.7) treated with MTX. The mean maximal dose was 18.9 mg weekly (range 15-25 mg/week), and the mean duration of treatment was 14.2 months (range 1 to 31 months). MTX was considered as successful (regrowth > 50% of hair) for five of them [19]. Comparison with other authors' studies also suggests that response rates for combination therapy are very high [20]. These studies have shown MTX to be effective in treated severe AA, with good response rates from 57 to 64% [24]. Thus our study used this regimen for a better outcome. It also helps to reduce the side effects of daily corticosteroids and to prevent recurrence of hair loss after stopping the drug. The results of recent studies suggest that alopecia areata are more related to immune dysfunction due to the presence of TCD4 and TCD8-active lymphocytes around the progressive hair follicles. Therefore, treatment of hair loss by using immunosuppressive drugs has been shown to be effective [23], [25], [26], [27], [28].

In conclusion, our study showed that no patient had severe side-effected had to stop treatment, only 2/38 (0.05%) patients had a headache, 3/38 (0.07%) patients had to feel vomiting. The results of this study were suitable for different research. After 3 months, we stopped these drug and follow-up the patients in 3 months next, but in the patients who responded, no patients had recurred. Compared with other single steroid studies, the relapse rate was relatively high, maybe over 50% of cases [10], [14]. The recurrence rate in our study was much lower than that reported by Joly [17]. Thus, we think this may be a good approach that can be applied clinically as it is effective, especially in patients who do not respond to other methods.

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Clinical Science

Using Patch Testing to Improve Therapeutic Outcome in the Treatment of Hand Eczema in Vietnamese Patients

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Keywords: Hand eczema; Allergic contact dermatitis; Atopic dermatitis

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Abstract

BACKGROUND: Hand eczema is a common chronic and relapsing skin disease with various clinical features. Hand eczema aetiology can be allergic contact dermatitis (ACD), irritant contact dermatitis (ICD), atopic dermatitis (AD) and unknown or combination causes. If the causative agents are not detected treatment of hand eczema will be a failure. A patch test can be useful to detect causative agents in suspected allergic contact hand eczema. Then patients will avoid contacting them. This results in the improvement of hand eczema. In Vietnam, patch test has not been used before, so we conduct this study.

AIM: To identify causative allergens by using patch test with 28 standard allergens in consecutive patients.

METHODS: A group of 300 HE patients from the National Hospital of Dermatology and Venereology (NHDV) in Vietnam were enrolled in this study. They were divided into 4 groups-ACD, ICD, AD and unknown aetiology. The patient was patch tested with 28 standard allergens to identify the causative agents.

RESULTS: Among the 300 HE enrolled patients, ACD accounted for 72.7%, AD and ICD had the same rate of 12.7%. 39.3% of the patients had a positive patch test. Reaction to nickel sulfate was the most common (10.3%), followed by potassium dichromate (9.7%), cobalt (4%) and fragrance mix (3.1%). About one-third of the cases had relevant clinical reactions correlated with the contact agents and clinical history. Males reacted to cement, thiuram mix and formaldehyde more than females, while females reacted to a nickel more than males.

CONCLUSIONS: Hand eczema has variable clinical features and diverse aetiology. ACD is an important cause of hand eczema that can be managed with a patch test to detect causative allergens. Nearly 40% of HE cases had positive patch test. Relevant patch test reactions were seen in one-third of the patients. We propose using patch test detect causative agents in suspected allergic contact hand eczema. Then patients will avoid contacting them. This results in the improvement of hand eczema.

Introduction

Hand eczema (HE) is a common chronic dermatitis that affects a significant proportion of population all over the world (2-4%). HE often relapses and negatively impacts the patient's quality of life [1]. As HE is multifactorial disease [2], [3], treatment often leads to failure. Patch test has been used for years to detect causative allergen in ACD [4], [5]. A patch test is also proposed to determine causative reasons for HE, particularly in a group of allergic contact HE patients. Boonstra et al., studied 1571 hand eczema patients, reporting more than 50% of cases with positive patch test [6]. Agner et al., patch tested 416 HE patients showing 63% with positive patch test results [7]. However, in Vietnam, patch test has not been used before so conducted this study to explore patch test results with 28 standard allergens and common causative allergens in consecutive patients. Thus, we can provide patients with an effective treatment and prevention.

This study aimed to identify causative allergens by using patch test with 28 standard allergens in consecutive patients.

Materials and methods

In this study, 300 HE adult patients were enrolled from November 2015 to May 2017 at the NHDV, Vietnam. The diagnosis of HE was made based on the medical examination and record findings according to the criteria set by the Danish Contact Dermatitis Group (DCDG). We chose the ICD 10 classification to divide our patients into 4 groups-ACD, ICD, AD and unknown. We performed a patch test using TROLAB baseline series (28 standard allergens), Germany (See Table 1). The patch tests were applied to the upper back of patients for 72 hours occlusion as shown in Figure 1.

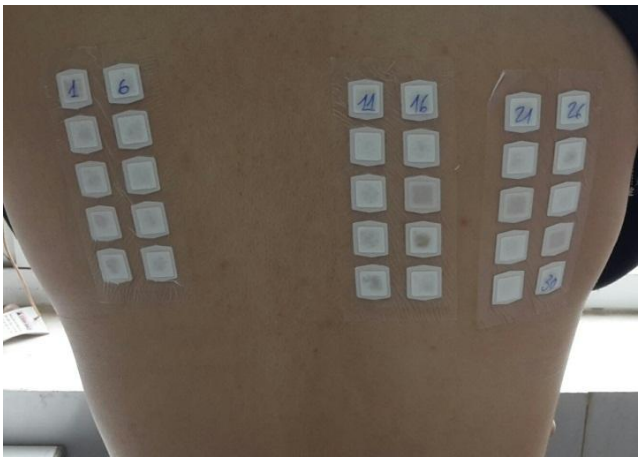

Figure 1: Finn chamber containing allergies on the patient's upper back

They were instructed to keep the test intact until their revisit at day 3 of the study. Patch test results were read after 72 hours. A positive reaction was noted if there were erythema and infiltration develops within the test area as shown in Figure 2.

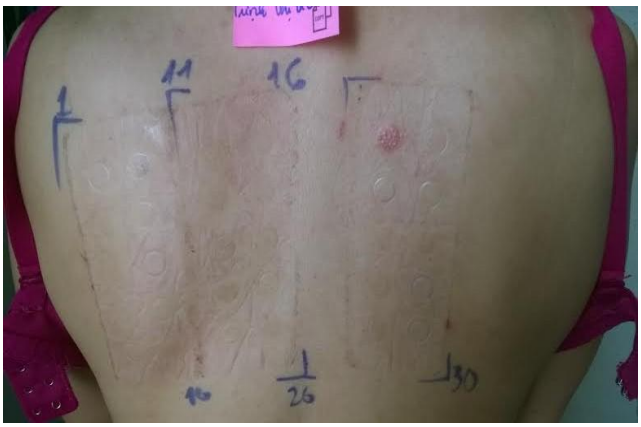

Figure 2: Positive reactions

Double reactions were retested and categorised as negative or positive depending on results. The Patch test results were read based on the guidelines of the International Contact Dermatitis Group. In cases where the results did not meet standard quality, such as loss of tested film chamber was lost or film peeling off before 72 hours, the patch test was redone. Patients taking oral or topical steroid were excluded from the study. Based on the patch test results, patients were provided with relevant management for their HE.

Statistics

Data analysis was performed with SPSS 16.0. Data are presented as absolute numbers and percentages for categorised variables. We used Chi-square test for comparison between groups. Fisher's exact test was used when the data was small to do Chi-square test. A t-test was applied for comparison of continuous variables. Odd ratio (OR) were calculated to see the influence of gender on patch test results.

Results

Patch test results

Positive patch test reaction was seen in 39.3% patients. Reactions to one, two and three allergens were reported at 25%, 9%, and 5.3%, respectively as shown in Figure 3.

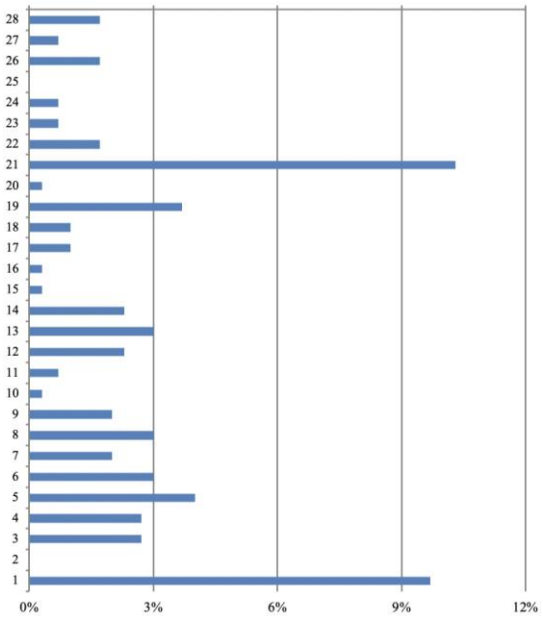

Figure 3: Rate of positive patch test reactions of 28 standard allergens

Around 27.7% of patients had clinically relevant reactions showing HE secondary to contact

allergy with nickel, cobalt in domestic goods, cement, fragrance mix, hair dyes, rubbers and synthetic plastic on the environment. Allergens number 10, 11, 15, 16, 24, 26, 27 and 28 showed positive patch test results but were not clinically relevant as presented in Table 2.

Table 1: List of 28 allergens

No	Allergens	Concentration
1	Potassium dichromate	0.5%
2	Neomycin sulfate	20%
3	Thiuram mix	1%
4	Fragrance mix II	14%
5	Cobalt chloride 6H20	1%
6	Paraphenylenediamine free base	1%
7	Benzocaine	5%
8	Formaldehyde (in water)	1%
9	Colophony	20%
10	Clioquinol	5%
11	Balsam of Peru	25%
12	N-Isopropyl-N'-phenylParaphenylenediamine	0.1%
13	Wood alcohols	30%
14	Epoxy resin	1%
15	Mercapto mix	1%
16	Budesonide	0.1%
17	Paraben mix	16%
18	Paratertiarybultyl phenol formaldehyde resin	1%
19	Fragrance mix	8%
20	Quaternium-15	1%
21	Nickel sulfate 6H20	5%
22	5-chloro-2-methyl-4-isothiazoline-3-one + 2-methyl-4-isothiazoline-3-one	0.01%
23	Mercaptobenzothiazole	2%
24	Sesquiterpene lactone mix	0.1%
25	Tixocortol pivalate	1%
26	Dibromodicyanobutane	0.3%
27	Hydroxymethylpentylcyclohexene-carboxyladehyde	5%
28	Primine	0.01%

Positive patch test reaction seen in males was 1.72 higher than females ($p < 0.05$, test $\chi 2$). Males react to potassium, thiuram mix and formaldehyde more often than females, while females react to a nickel more than males as shown in Table 3.

Table 2: Relevant patch test results

	Positive reaction	Clinical relevant reaction
	N =118	N = 83 (27.7%)
Potassium dichromate (1)	29	18 (62.1)
Thiuram mix (3)	8	4 (50)
Fragrance mix II (4)	8	5 (62.5)
Cobalt chloride 6H20 (5)	12	6 (50)
Paraphenylenediamine free base (6)	9	4 (44.4)
Benzocain (7)	6	2 (33.3)
Formaldehyde (8)	9	4 (44.4)
Colophony (9)	6	2 (33.3)
N-Isopropyl-N'-phenyl-Paraphenylenediamine (12)	7	3 (42.8)
Wood alcohols (13)	9	4 (44.4)
Epoxy resin (14)	7	3 (42.8)
Paraben mix (17)	3	1 (33.3)
Paratertiarybultyl phenol formaldedyde resin (18)	3	1 (33.3)
Fragrance mix (19)	11	5 (45.4)
Nickel sulfate 6H20 (21)	31	18 (58.1)
5-chloro-2-methyl-4-isothiazoline-3-one + 2-methyl-4-isothiazoline-3-one (soluted 3:1 in water) (22)	5	2 (40)
Mercaptobenzothiazole (23)	2	1 (50)

Regarding history of atopy, there was no difference between patch test reaction between atopy group versus non-atopy group (p ($\chi 2$): 0.228; CI: 1.34 (0.83-2.15).

Table 3: Patch test results in genders

	Potassium dichromate	Thiuram mix	Formaldehyde	Nickel sulfate
	n=58	n=16	n=18	n=62
Male	28 (23.1)	7 (5.8)	7 (5.8)	4 (3.3)
Female	1 (0.6)	1 (0.6)	2 (1.1)	27 (15.1)
Total	29 (9.7)	8 (2.7)	9 (3)	31 (10.3)
p (χ^2)	0.0001	0.006*	0.02*	0.001
OR	53.6	10.9	5.4	0.2
(CI95%)	(8.5-2202.9)	(1.4-495.2)	(1.0-54.2)	(0.05-0.58)

*Fisher's exact test.

Discussion

The rate of reacted patch test reported in our study was 39.3%. This number is consistent with others studies reporting positive patch test results ranging between 15% and 62.3%. Studies reporting a higher rate of positive patch test was typically done in such that the results were read in 3 separated time points-2, 3, and 7 days. By doing it this way, we would not miss the delayed response that has been documented to be as high as 20% [3]. Studies using additional allergens also reported a higher rate of a positive result because these allergens are more specific to patients' conditions than standard allergens.

Fall and Sabatini et al., conducted patch test studies, reporting a declined trend in patch test results to nickel sulfate, cobalt chloride, colophony and methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI), while an upward trend to p-phenylenediamine and fragrance mix. The explanation can be that the general public has become increasingly aware that offended agents such as nickel sulfate and cobalt chloride are to be avoided. In contrast, there are far more cosmetic, and odour products used in our daily life, that is making us have more reactive to these allergens [8], [9].

Among agents, nickel sulfate, potassium dichromate, cobalt, fragrance mix, paraphenylenediamine, formaldehyde, wood lanolin, and colophony was mostly registered as the suspected agents [10]. This trend was also observed in our studies.

Clinical relevant patch test reaction is a positive reaction that suitable with clinical situation. The rate of clinical relevant patch test reactions in our study was about 28%. Clinical relevant reacted allergens include potassium dichromate (62.1%), nickel sulfate (58%), cobalt (50%), fragrance mix, epoxy resin, paraphenylenediamine free base, etc. In comparison to other similar studies using additional series of allergens; the rate of relevant patch test with a standard allergen is often lower because they may be not specific to patient's contact history. As a result, a patch test with standard allergens can be considered as an initial screening test to detect potential sensitive allergens in patients with sensitive skin. After a follow of 3 months after the consultation to avoid offended allergens, hand eczema condition of the patients has been improved remarkably

In our study, males reacted to potassium, thiuram mix and formaldehyde more than females while females reacted to a nickel more than males. This observation was consistent with other studies. There are recent changes in reaction trends seen in both genders. Ertam at al. showed that nickel sulfate was the most common reacted allergen in female, particularly young ones under 35-year olds [10]. Also,

reaction to potassium dichromate increases in young women because of their higher participation in construction works [8]. Besides, reaction to fragrance mix increases in males because they contact to odour products more and more [8], [9], [11].

We found that recurrent vesicular HE brought in a higher rate of positive patch test while hyperkeratotic HE is less reactive to any allergens. This suggests that recurrent vesicular might be induced by contact allergy while other types (such as hyperkeratosis) are not. The types of chronic fissure also have underlying aetiology with regards to contact allergy because there were more than one-third of cases with positive patch test [6]. These findings were in agreement with prior studies by Johansen and Diepgen et al., [12], [13], [14], [15].

In summary, we have demonstrated that patch test was particularly useful in certain population subgroups, highlighting the causal relationship between HE and common offended allergens. The result of the patch test studies was helpful in guiding patient treatment and disease prevention.

In conclusion, hand eczema has variable clinical features and a complex aetiology. Allergic contact dermatitis is an important cause of hand eczema, which can be managed with a patch test to detect causative allergens. Nearly 40% of hand eczema cases have a positive patch test. Relevant patch test reactions were seen in one-third of the patients in our study. We propose that patch test should be used to improve therapeutic outcome in the treatment of relapsing or stubborn hand eczema.

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Anatomical Evaluation for Successful Dye Laser Treatment of Port Wine Stain in Vietnamese Patients

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Keywords: Port wine stain; Capillary malformation; Nevus flammeus; Vbeam perfecta; Pulsed dye laser

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Abstract

AIM: To assess the efficacy in the treatment of port wine stain in the head and neck by using (Vbeam perfecta®).

METHODS: Forty-two port wine stain patients were recruited at the National Hospital of Dermatology and Venereology, Hanoi, Vietnam.

RESULTS: We reported an excellent response (43.8%) (76%-100% lightening), a good response (18.8%) (51%-75% lightening), fair improvement (18.8%) (26%-50% lightening), and no response (18.8%) (0%-25% lightening).

CONCLUSION: In conclusion, pulsed dye laser is an excellent technique to remove port wine stains on the face and neck.

Introduction

Port wine stain (PWS) is also called capillary malformation or nevus flammeus. PWS occurs in 0.1 – 0.2% of newborns in the world, but there are no reports about the frequency in the Vietnamese population. PWS appears at birth as a pale pink to red well-defined patches and grows in size commensurate with patient's growth. They are typically seen in the head and neck area although they can occur anywhere on the skin and mucous membrane. If not treated, the disease can be disfigured in adults, with papular nodules on the PWS surface. As the patient aged, the colour changes from pink to red to purple from childhood to adulthood, and this appears to be correlated with the wider vessel in older patients.

Pulsed dye laser **(**PDL) is considered one of the possible therapeutic choices for the treatment of vascular malformations and PWS [1].

Material and Methods

In this study, we access the utility of using pulsed dye laser (Vbeam perfecta®) in the treatment of forty-two Vietnamese patients with congenital PWS

at the National Hospital of Dermatology & Venereology, from 2011 to 2014.

Every patient had 4 test patches with different fluences (11; 11.5; 12; and 12.5 J/cm^2), but the same pulse duration (1.5 mms) and spot size (7 mm). After 8 weeks, the test area showed the best response was used as the set up for the next treatment. The results were evaluated by comparing pre and post photographs taken before and after each treatment using the Physician Global Assessment.

Results

Patients older than 18 years old achieved a better outcome than less than 18-year-old-patients (30% vs 18.2%, respectively) as shown in Table 1.

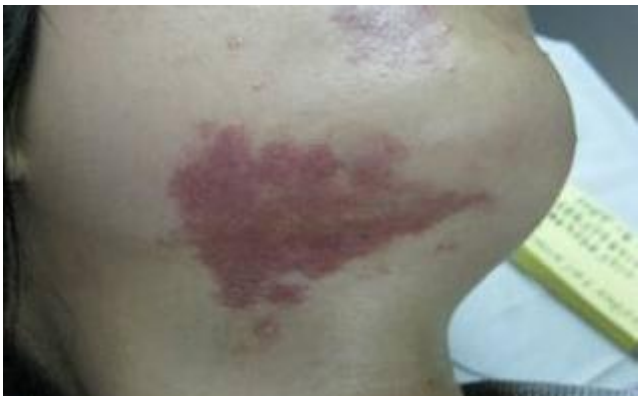

Figure 1: PWS under the chin

We found that there were no differences in responding rates according to age (≥ 19-year-old vs ≤ 18-year-old), p > 0.05.

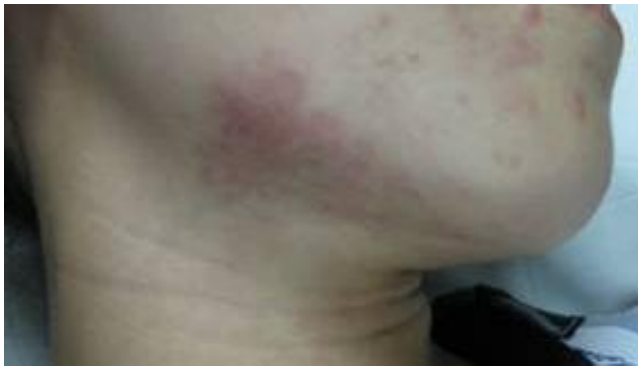

Figure 2: After 3 times treatment by using Vbeam perfecta

In our study, patients having purple or red plaques showed greater improvement than pink plaques (91.7% and 87.5% response rate compared to 50%, respectively) as presented in Table1.

Table 1: Correlation between results with age and some lesion's manifestations

Results of treatment		Respond rate to treatment		p
Features		Respond rate	No, respond rate	
Age	≤ 18 years old	70.0%	30.0%	0.369
	> 18 years old	81.8%	18.2%	
Color	Purple	91.7%	8.3%	0.018
	Red	87.5%	12.5%	
	Pink	50.0%	50.0%	
Size	< 20 cm^2	75.0%	25.0%	0.560
	≥ 20 cm^2	78.6%	21.4%	
Surface	Flat	69.7%	30.3%	0.058
	Elevated	100%	0%	

Regarding the lesion size, there was no statistical difference between lesions with greater or smaller 20 cm^2, p > 0.005 (as shown in Table 1).

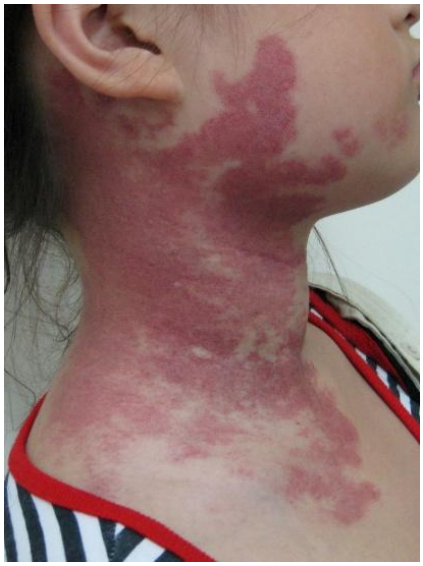

Figure 3: PWS on the cheek, and neck

All patients had elevated surface (hypertrophic) lesions respond to treatment, while only 69.7% of patients with flat surface lesion responded to treatment, as presented in Table 1. However, this difference is not different statistically, but we would need a larger sample size to confirm this conclusion.

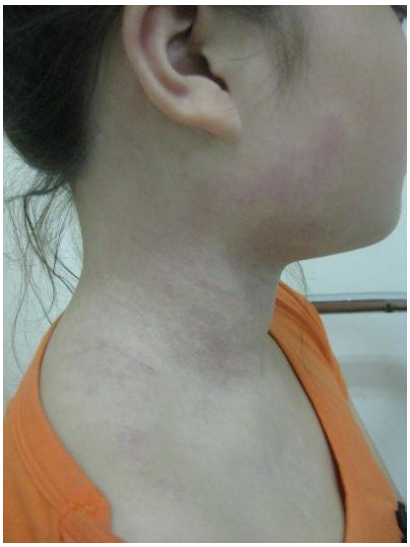

Figure 4: After 10 times treatment

We also analysed the anatomical distribution of the lesion and found that perioral regions including the lips had the highest rate of failure (Table 2).

Table 2: Correlation between results with lesion's distribution

Results/Distribution	Respond		No respond		Total
	Patients	Percentage (%)	Patients	Percentage (%)	
Cheeks	24	72.7	9	27.3	33
Perioral	8	61.5	5	38.5	13
Neck	8	100	0	0	8
Periorbital	4	80	1	20	5
Chin	3	100	0	0	3
Forehead	2	100	0	0	2
Nose	1	100	0	0	1
Ears	1	100	0	0	1

Discussion

Our study did not support the theory that PWS should be treated as soon as possible, to avoid developing hypertrophic and nodular lesions at middle age [2], [3]. The reason explains why PWS on the neck is improving better than lip and cheek is that neck skin is thinner than cheek and lip skin, by Richard et al., [4].

Red or purple PWS has superficial location whereas pink PWS, due to the small vessel size and deeper location, predict a poor response [4], [5]. Our study was in support of this theory.

The side effects as hyperpigmentation, hypopigmentation, blistering and crusting were not severe and improved with times, in according to other studies in the literature [6], [7], [8].

In conclusion, this is the first report of the utility of the 595 nm pulsed dye laser (Vbeam perfecta®) for PWS in Vietnamese patients, confirming the efficacy in treatment without considerable side effects.

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Efficacy of Surgical Excision for Nevus Sebaceous - Vietnamese Experience

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Abstract

BACKGROUND: Nevus Sebaceous (NS) is hamartoma predominantly composed of sebaceous glands and is classified as a type of epidermal nevus. In most case, clinical manifestation of NS is typical, so histopathology examination is important only in atypical lesions for its risk of malignancy. Clinical symptoms are plaques or papules (100%), appearing in the head area (100%) with smooth surface (65.8%), usually with hair loss (60.7%). The histopathology is mostly characterized by the image of sebaceous gland hyperplasia (100%), no hair follicles (60.7%) or immature follicles (14.3%).

AIM: The aim of our study is describing clinical and histopathological manifestation, make diagnosis and evaluate the best therapy.

METHODS: Our study recruited 38 patients with NS, 3 patients (7.9%) with atypical aspects. All patients were treated by surgical excision.

RESULTS: Complications as hair loss and infections were reported in 36.8% patients. No patients had recurrence after one year of treatment.

CONCLUSION: Based upon our experience, surgery is cheap, simple, associated with high aesthetics effectiveness and low recurrence rate, proposing as the first choice for treatment of NS.

Introduction

Nevus Sebaceous (or Nevus of Jadassohn) is hamartoma, predominantly composed of sebaceous glands. It was classified as a type of epidermal nevus and was described firstly in 1895 by Jadassohn. NS occurs with equal sex and race frequency. Etiology and pathophysiology are still unclear. Recently, some studies showed that NS may relate to RAS mutation [1] and human papillomavirus [2].

NS often occurs at birth, with newborn incidence of 0.3% [3], or in early childhood. Rarely, NS can combine with disorders of the central nervous system, skeletal deformities, ocular lesions to make nevus sebaceous syndrome [4]. Risk of malignancy with NS is relatively low, as reported in literature, most associated with basal cell carcinoma (BCC), trichoblastoma, trichilemmoma [5].

The aim of our study is describing clinical and histopathological manifestation, make diagnosis and evaluate the best therapy.

Methods

A group of 38 patients was diagnosed with NS by clinical and histopathology manifestations from September 2016 to July 2017 at National hospital

dermatology and venereology in Vietnam.

All 38 patients were treated by surgery. One-year follow up evaluated lesions clearance, complications, scars and possible recurrence.

Almost all patients were visited to our hospital because of aesthetics reasons (57.9%). Complications were found in 47.4% patients, such as itchiness (23.7%), bleeding (2.6%) or both (21.1%).

Results

Every NS affected cephalic area, with most typical clinical signs as shiny smooth surface (65.8%) and hair loss (60.7%) as presented in Table 1.

Table 1: Clinical manifestations of NS

Clinical manifestations		Patients (n = 38)	Percentage (%)
Located	Scalp	28	73.7
	Face	8	21.1
	Neck	2	5.3
	Others	0	0
Surface	Smooth	25	65.8
	Rough	13	34.2
Hairs on lesion	Loss	17	60.7
	Less	11	39.3
Tumor on primary lesion		1	2.6

We noted that 80% of lesions located in hair-bearing area had an oval shape, while 80.7% lesions located in others site (face and neck) had a linear shape.

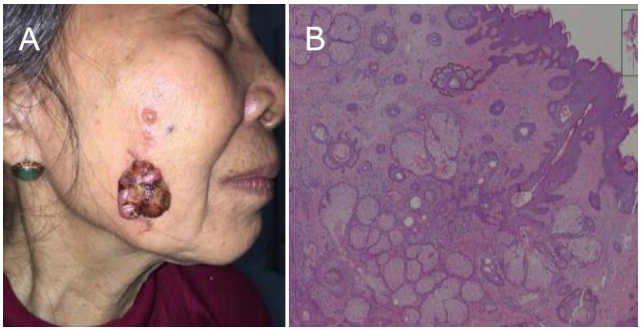

Figure 1: a) A tumor developed on sebaceous nevus; b) Histopathology showed sebaceous nevus

Only 1 patient presented clinically with BCC on NS (Figure 1) but histopathology confirmed that 3 more patients had neoplastic involvement, such as trichilemmoma, hidradenoma papilliferum and benign hyperplastic squamous epithelium. Prior to 2000, the rate of BCC on NS was quite high, although in 21% of cases it could be trichoblastoma misdiagnosis. Recent studies showed an incidence lesser than 7.1%, which is similar to our results [5]. Other histopathological signs of nevus sebaceous are listed in Table 2.

Because of the small size of lesions (mean area 7.2 cm^2), 86.8% patients were treated by surgery and direct closure. The remaining five patients required reconstruction with skin flap.

Table 2: Histopathology manifestations of NS

Histopathology manifestations		Patients (n = 38)	Percentage (%)
Sebaceous gland hyperplasia		38	100
Sebaceous gland associated with epidermis		29	76.3
Papillomatosis		27	71.1
Hair follicles	Absent	17	60.7
	Immature	4	14.3
	Mature	7	25.0
Tumor on histopathology		3	7.9

BBCs were treated with MOHS surgery. Hair loss in scalp lesions improves after surgery ($p = 0.036$). 100% patient presented flat scar at 3 months follow up, as shown in Figure 2. No patient suffered from hypertrophic scar, keloid scar or ugly scar after surgery. No recurrence was reported after 1 year of follow-up. Based upon our experience, surgery is the first choice of treatment. Other methods include photodynamic therapy (PDT), laser CO_2 or dermabrasion but presents higher recurrence rate [6], [7], [8] and are suggested only for no hair areas (face, neck, extremities and trunk).

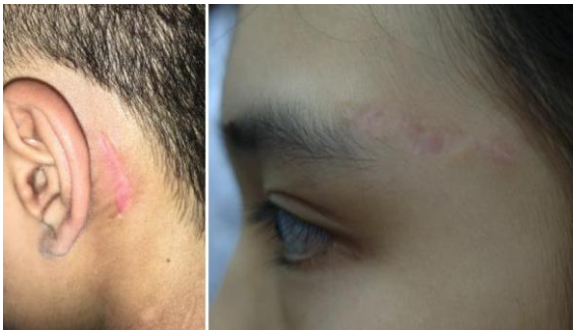

Figure 2: Flat scar at 3 months after NS removal

Discussion

Diagnosis of NS depends on clinical manifestation but histopathology is useful to confirm the diagnosis and to rule out malignant involvement.

Based upon our experience, surgery is cheap, simple, associated with high aesthetics effectiveness and low recurrence rate, proposing as the first choice for treatment of NS.

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Clinical Science

Early Treatment with Imiquimod 5% Cream of Periungual Warts in Vietnam: The Poorer, the Better

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Keywords: Imiquimod; Periungual warts

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Abstract

AIM: To evaluate the efficacy of imiquimod 5% in periungual wart treatment.

MATERIAL AND METHODS: A group of 40 patients were recruited to apply imiquimod 5 % cream once daily for 5 consecutive days per week in 8 weeks. They were classified into 3 levels: Mild (the total lesion area ≤ 25 mm^2), moderate (25 mm^2 <total lesion area ≤ 50 mm^2), severe (total lesion area > 50 mm^2). The outcome was evaluated at the 4th and the 8th week. The result was graded as excellent (complete clearance), good (≥ 50% clearance) and poor (< 50% clearance).

RESULTS: The total area of the wart lesion got decreased significantly from the beginning to the 4th and the 8th week (36.7 mm^2 vs 16.8 mm^2, p = 0.0001 and 16.8 mm^2 vs 8.8 mm^2, p = 0.01). The complete clearance rate at the 4th week was lower than that at the 8th week significantly (22.5% vs 72.5%, p = 0.04). The clearance rate of patients suffering severe warts was lower significantly than that of mild/ moderate patients (82.8% vs 45.5%, p = 0.03). The duration of the disease in people who responded completely to imiquimod was shorter than that of patients partially responded (10.2 ± 14.1 months vs 22.3 ± 14.3 months, p = 0.02). Adverse effects were not common, mild and local only. Recurrence rate after 6 months of follow up was 3.5%.

CONCLUSION: In conclusion, Imiquimod 5% cream is a safe and effective drug in the treatment of periungual warts.

Introduction

Periungual warts a common skin disease and can interfere with nails development, mainly in immunosuppressed patients [1], [2].

Tissue destruction therapy is painful, and the recurrence is frequent. Imiquimod is a topical immunosuppressive agent, which stimulates the production of inflammatory cytokines that activate and maintain cell-mediated immune response [3].

This study aimed to evaluate the efficacy of imiquimod 5%, once daily for 5 consecutive days per week, in periungual wart treatment in 40 Vietnamese patients, including 19 females (aged 20.4 ± 13.8) and 21 males (aged 27.3 ± 13.5) patients.

Material and Methods

A group of 40 patients were recruited to apply imiquimod 5 % cream once daily for 5 consecutive days per week in 8 weeks. They were classified into 3 levels: Mild (the total lesion area ≤ 25 mm^2), moderate (25 mm^2 <total lesion area ≤ 50 mm^2), severe (total lesion area > 50 mm^2).

The outcome was evaluated at the 4th and the 8th week.

The result was graded as excellent (complete clearance), good (≥ 50% clearance) and poor (< 50% clearance).

Results

The warts condition before the treatment was mild in 21 patients (52.5%) (the total lesion area ≤ 25 mm^2), moderate in 8 patients (20.0%) (25 mm^2 <total lesion area ≤ 50 mm^2) and severe in 11 patients (27.5%) (total lesion area > 50 mm^2). The duration of disease was 13.5 ± 15.0 months.

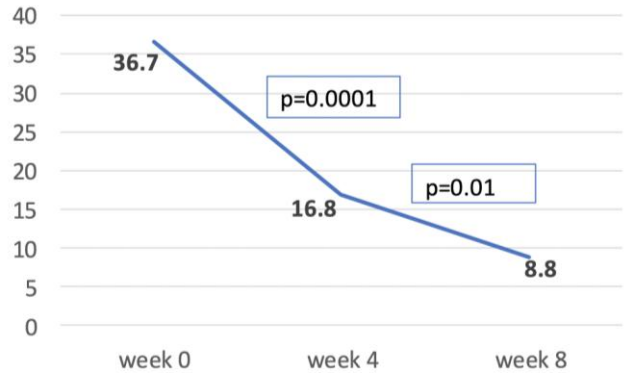

Figure 1: Wart area (in mm^2) change by the time

The total area of warts got decreased significantly from 36.7mm^2 at week 0 to 16.8 mm^2 at the 4th week and 8.8 mm^2 at the 8th week ($p < 0.05$) as shown in Figure 1. The excellent outcome at the 8th week was higher than that at the week 4th significantly (72.5% vs 22.5%, p = 0.04). The complete clearing rate at the 8th week was significantly higher than that at the 4th week due to the slow effect of imiquimod in stimulating immune cells.

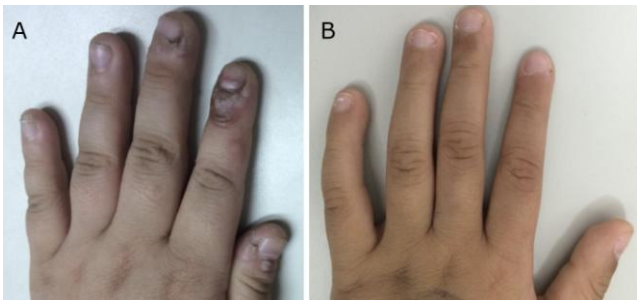

Figure 2: Periungual warts before (A) and after (B) treatment with imiquimod 5 % cream

An excellent outcome was seen in 68.2% of people who had got treated by other modalities before applying imiquimod and 77.8% of naïve patients, the difference was not significant (p = 0.37, Fisher exact test) (Table 1).

Table 1: Treatment outcomes and related factors

Outcomes	N	Wart duration (m ± SD)	P	Wart severity at the beginning				P	Treatment before imiquimod				P
				Severe		Mild/ moderate			Yes		No		
				N	%	N	%		N	%	N	%	
Excellent	29	10.2 ± 14.1	0.02	5	45.5	24	82.8	0.03	15	68.2	14	77.8	0.37*
Good/poor	11	22.3 ± 14.3		6	54.5	5	17.2		7	31.8	4	22.2	

*: Fisher's exact test.

No systemic side effects have been reported. Local side effects had been seen in 37.5% patients, but 73.33% of the side effect was mild.

After 6 months of follow-up, there was only one relapse case (3.5%) after 3 months.

Discussion

Excellent results in a group of patients suffering mild/moderate wart were higher than that of the group having severe wart (82.8% vs 45.5%, p = 0.03). So longer the duration of disease was, the less effective the treatment modality was [4], [5], [6].

There was only one relapse case after 3 months. It could be explained by the ability of imiquimod cream that can start and maintain HPV specific cell-mediated immunity [7], [8], [9], [10].

In conclusions, Imiquimod 5% cream is safe and effective drug in the treatment of periungual warts. Early treatment leads to better results.

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Efficacy of Oral Isotretinoin in Combination with Desloratadine in the Treatment of Common Vulgaris Acne in Vietnamese Patients

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Keywords: Common acne; Isotretinoin; Desloratadine

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Abstract

AIM: To evaluate the efficacy of oral isotretinoin used alone and in combination with desloratadine in the treatment of moderate acne vulgaris.

METHODS: A comparative clinical trial was undertaken to evaluate the efficacy of oral isotretinoin alone and in combination with desloratadine in the treatment of 62 moderate acne vulgaris patients. Patients were randomised into two groups with 31 patients in each group. Each studied group's patient took 20 mg isotretinoin and 5 mg desloratadine per day. In the control group, patients took only 20 mg isotretinoin per day. The treatment time was 16 weeks. The evaluation and follow-up were done at week 2, 4, 8, 12 and 16 of the treatment.

RESULTS: The studied group had a better curative rate than the control group (45.2% versus 22.6%). The average number of inflammatory lesions in the studied group was significantly lower than the control group (0.19 versus 0.94). The mean GAGS score of the studied group was significantly lower than the control group (3.71 versus 6.52). Acne outbreaks rate of the studied group was lower than the control group (in week 2: 22.6% versus 45.2% and in week 4: 16.1% versus 38.7%, respectively). The rate of itchy was lower in the studied group.

CONCLUSION: In the treatment of moderate acne vulgaris, oral isotretinoin in combination with desloratadine is more effective and has fewer side effects than using isotretinoin alone.

Introduction

Acne is a common skin disease, affecting approximately 85% of adults. The increased secretion of sebum, the follicular hyperkeratosis, the presence of *Propionibacterium acnes* and inflammatory response are the four major factors in the acne pathogenesis [1]. Currently, isotretinoin is the only drug that targets all the causative factors of acne. This medicament is also effective in acne cases unsuccessfully treated with other therapeutic agents. However, isotretinoin results in some side effects including dry skin cracked lips, erythema and rashes.

Antihistamines H1 have been used for a long time to treat pruritus and allergic conditions. Recently, they have also been used in acne treatment because of their ability to reduce sebum and side effects created by isotretinoin [2]. Some studies also mention the effect of antihistamines in reducing inflammation and preventing acne scars.

In Vietnam, there has been no evaluation study done on the use of antihistamines in acne

treatment.

This study aimed to evaluate the efficacy of oral isotretinoin used alone and in combination with desloratadine in the treatment of moderate acne vulgaris.

Methods

A comparative clinical trial on 62 moderate acne vulgaris patients was conducted at the National Hospital of Dermatology and Venereology, from August 2017 to August 2018.

A group of 62 patients were randomised into 2 equal groups: studied group and control group.

Both groups were treated with isotretinoin 20mg per day in 16 weeks. The combined treatment was 5mg desloratadine daily in 16 weeks for the studied group.

For the evaluation, we counted the number of acne lesions, scoring GAGS (Global Acne Grading System), recording unwanted effects after 2, 4, 8, 12 and 16 weeks of treatment.

Evaluation of acne outbreak during treatment was based on the appearance of new nodules at each re-examination. We used a scale of no outbreak (no new lesion), mild outbreak (< 5 nodules), moderate outbreak (5-10 nodules) and severe outbreak (≥ 10 nodules).

The evaluation of clinical efficacy after 16 weeks of treatment was scaled of:

- Excellent: no inflammation and non-inflammation lesions.

- Good: reduced by ≥ 90% of the number of lesions.

- Fair: reduced by ≥ 75-90% of the number of lesions.

- Moderate: reduced by ≥ 50-75% of the number of lesions.

- Poor: reduced by <50% of the number of lesions.

Results

General characteristics of the included objects

At the initiation time of treatment, the two groups had similar characteristics regarding patient gender, age, average illness duration, number of lesions, illness severity and isotretinoin dose, as presented in Table 1.

Table 1: Characteristics of patients in both groups before treatment

Indicator		Studied group (n = 31)	Control group (n = 31)	p
Sex	Male (n)	11	12	p = 0,074
	Female (n)	20	19	
Mean age (years)		21,90 ± 4,1	22.06 ± 4.20	p = 0.88
Mean duration of disease (months)		38,74 ± 34,44	43.16 ± 26.62	p = 0.55
Mean weight (kg)		52,32 ± 8,56	57.61 ± 9.90	p = 0.186
The number of inflammatory lesion		20,29 ± 1,94	19.58 ± 8.60	p = 0.172
The number of non-inflammatory lesion		48,90 ± 29,36	47.87 ± 25.44	p = 0.345
Total no of lesions		68,87 ± 35,86	68.45 ± 28.95	P = 0.182
Mean GAGS score		22,90 ± 3,11	22.77 ± 3.03	p = 0.869

Treatment results

Change in the number of inflammatory lesions

In the studied group, the number of inflammatory lesions was significantly lower than that in the control group, with p < 0.025 as shown in Figure 1.

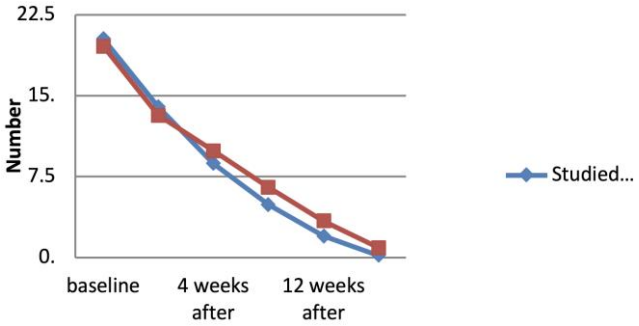

Figure 1: The numbers of inflammatory lesions

Change in the illness severity score

An illness severity score of the studied group was significantly lower than that in the control group from week 4 onwards with p < 0.05 as shown in Table 2.

Table 2: Change in the illness severity score

Time	Studied group	Control group	p
Week 0	22.9 ± 3.11	22.77 ± 3.03	0.869
Week 2	20.5 ± 4.22	21.45 ± 4.31	0.388
Week 4	17.11 ± 4.22	19.35 ± 4.70	0.06
Week 8	13.78 ± 5.48	15.03 ± 4.11	0.025
Week 12	8.44 ± 5.40	12.03 ± 4.27	0.007
Week 16	3.71 ± 3.81	6.52 ± 4.35	0.015

Treatment efficacy after 16 weeks

The studied group had 45.2% of acne resolved, higher than that in the control group: 22.6%, with p < 0.05 as shown in Figure 2.

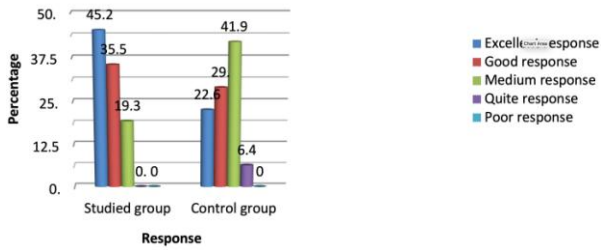

Figure 2: Treatment efficacy after 16 weeks

Unwanted effects

Acne outbreak

The studied group had a significantly lower outbreak rate than that in the control group with $p < 0.05$ at week 2 and 4. At week 16, both groups had no outbreaks.

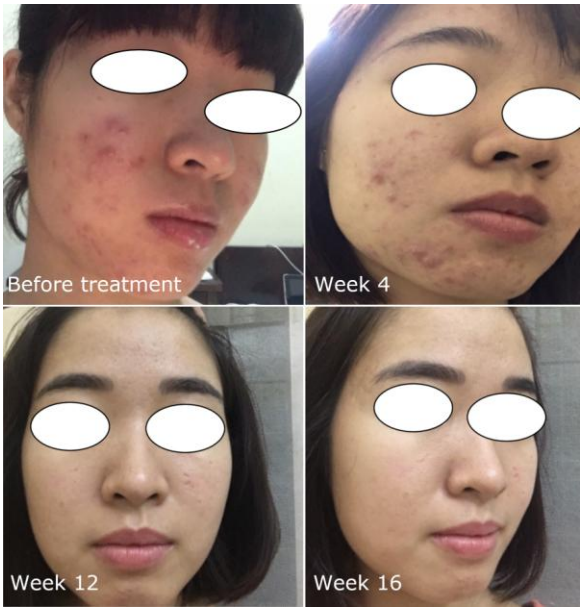

Figure 3: 26 years old female from the studied group (Isotretinoin + Desloratadine)

Other unwanted effects

At the time of follow-up, both groups experienced side effects such as dried skin, dried lips, itching. In the studied group, the rate of itching was significantly lower than the control group (week 2: 12.9%; week 4: 6.2% versus 64.5% in week 2 and 71% in week 4). There was no difference between the two groups regarding side effects such as dried lips, dried skin, flaking and blushing.

Discussion

Studies have shown that inflammation in acne starts very early, even before the appearance of the lesion and continues at all stages of acne lesion development [3]. Acne inflammation response is due to the release of inflammatory mediators such as histamine and leukotrienes. Therefore, the use of antihistamines can effectively prevent the formation of new acne lesions and have a significant impact on resolving the old acne lesions. In our study, the average number of inflammatory lesions in the studied group was significantly lower than that in the group using only isotretinoin. The reason probably is the combination of anti-inflammatory effects of both retinoids and antihistamines. However, we did not find any difference in the reduction of non-inflammatory lesions between the two groups.

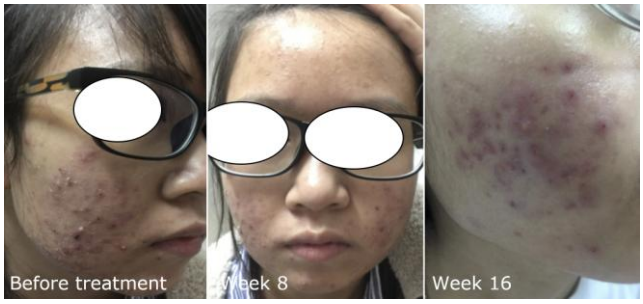

Figure 4: 24 years-old female from the control group (Isotretinoin)

After 16 weeks, the mean GAGS score in the studied group was lower than in the control group (3.71 ± 3.81 vs 6.52 ± 4.35), with $p = 0.015$. In Lee's study, the reduction of GAGS scores in the studied group was seen from week 2. However, the significant difference was just from week 4 onwards [2]. Yosef's study showed similar results [4].

After 16 weeks of treatment, both groups had good outputs: the studied group achieved 45.2% excellent, 35.5% good, and remaining 19.3% fair; the results in the control group were 22.6%, 29%, and 49.1% average response, respectively. However, our results showed that the desloratadine group was better ($p < 0.05$). Experimental studies have shown that desloratadine inhibits inflammatory mediators including IL-4, IL-6, IL-8, IL-13, prostaglandins, leukotriene, tryptase and histamine [5]. Thus, desloratadine acts as an anti-inflammatory role. Also, desloratadine also reduces the formation of squalene, an important component of the sebum [6], [7]. In Lee's study, the studied group had 40% of cases clear, 50% improvement while the control group had 20% of patients clear, 40% improvement [2]. Studies by Dhaher SA and Jasim ZM showed the same results of 50% excellent result, 39.5% good results in the studied group while control group were 31.6% excellent, 34.2% good, 26.3% average and 7.9% poor [8].

Acne outbreaks are common side effects after starting treatment with isotretinoin for 2-4 weeks. The mechanism of the outbreak is unclear, but it is related to the release of *P. acnes and sebaceous gland* antigens, enhancing the inflammatory response [9]. In

our study, the anti-inflammatory effect of antihistamines may have resulted in mild outbreak rate of the studied group: 22.6% at week 2, 16.1 % at week 4, that were lower than those in control group (45.2% and 38.7%, respectively). Similar results were seen in Lee's study [2].

In our study, the itching was less common in the studied group, attributed to the effects of desloratadine.

In conclusion, treating moderate acne vulgaris with oral isotretinoin in combination with antihistamines enhances the curative effectiveness and reduces side effects of itching and acne outbreaks, that is linked with oral isotretinoin intake.

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The Effectiveness of Narrow Band Uvb (Nb-Uvb) In the Treatment of Pityriasis Lichenoides Chronica (PLC) In Vietnam

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Keywords: Phototherapy; NB-UVB; Pityriasis lichenoides chronica; Effectiveness; Safety

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Abstract

AIM: This prospective clinical study presents the experiences with NB-UVB monotherapy in the treatment of PLC on Vietnamese patients.

METHODS: We enrolled at National Hospital of Dermatology and Venereology (NHDV), Vietnam, 29 PLC patients with generalised disease involving at least 60% of the total body surface (based on Nine's Rule) and/or failed to respond to other modalities of treatment. Patients were treated with NB-UVB followed the guideline of the psoriatic treatment of AAD-2010, three times weekly.

RESULTS: A complete response (CR) was seen in 24 out of 29 PLC patients (82.8%) with a mean cumulative dose of 9760.5 mJ/cm^2 after a mean treatment period of 4.6 weeks (13.8 ± 7.4 exposures). Mild side effects were observed: 69% erythema minimum, 55.2% irritation related to dry skin. No severe side effects were seen during the study. No relapses occurred in 24 CR patients within a mean period of 3 months after the last treatment.

CONCLUSION: NB-UVB therapy is an effective and safe option for the treatment and management of PLC.

Introduction

Pityriasis lichenoides chronica (PLC) is a chronic papulosquamous disorder of unknown aetiology with remissions and exacerbations. Although being a self-limited condition, therapeutic approach is required based on cosmetic and symptomatic concerns. Many treatment options including topical or systemic corticosteroids, oral tetracycline, topical calcineurin inhibitors such as tacrolimus, and methotrexate have been used with different success rates. NB-UVB phototherapy has recently demonstrated high levels of efficacy and tolerability in the treatment of patients with PL. Despite the variety of reports in the literature, no studies have been conducted to primarily evaluate the efficacy of such modality in PLC case series treatment.

This prospective clinical study presents the experiences with NB-UVB monotherapy in the treatment of PLC on Vietnamese patients.

Methods

Twenty-nine Vietnamese patients, aged 3 to 75 years old (11 males, 18 females, the initial mean

age of disease 25 ± 16.8 years old) were treated with NB-UVB mono-therapy. Treatment with NB-UVB (311 nm) was given three times weekly in a Daavlin cabinet (Daavlin, CA, USA) equipped with Philips TL-01/100 W fluorescent lamps (Philips Company, Eindhoven, the Netherlands). The initial and increasing treatment dose of NB-UVB in every treatment session depended on patients' skin type classified by Fitzpatrick (AAD-2010 guidelines). In the case of mild side-effects including mild to moderate erythema, burning sensation, the dose of NB-UVB was decreased by 20%. In case of severe side-effects such as severe erythema, burning or photosensitivity, the treatment was stopped, and the patient was applied topical corticosteroids with an oral non-steroidal anti-inflammatory drug (NSAID). If one to three sessions were missed, the dose was unchanged, and if more than four sessions were missed, the dose was decreased by 25% (within 7 sessions), 50% (from 8 to 11 sessions) or began again (over 12 sessions).

Complete response (CR) was defined as more than 90% resolution in skin lesions (papulosquamous and plaque lesions). Partial response (PR) was defined as the resolution of 50-90% in skin lesions. Poor response (NR) was taken as less than 50% reduction in lesions. Patients were assessed every 6 sessions until they cleared skin lesions or after completed 36 sessions. If the patient's skin lesions cleared before completing 36 treatment sessions, they were observed for at least 3 months to determine any recurrence. Detection of more than 10 new lesions was defined as recurrence.

Both thickness and scaling scores were assessed at the initial and at the end of treatment (PASI score). Patients also fulfilled a self-evaluation satisfaction questionnaire.

Results

After one month treatment (4.6 weeks), 82.8% complete response was achieved with the mean number of treatment sessions was 13.8 (range: 4-30 sessions). The mean number of sessions required to achieve the first clinical response was 6.4 (range: 3-14 sessions).

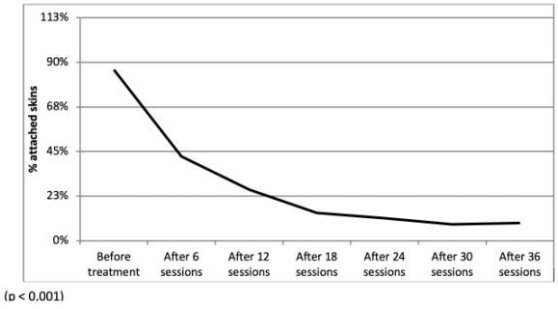

Figure 1: Improvement of the total body surface in skin lesions

Most patients had reduced the total body surface area (BSA) after 6 sessions ($p < 0.001$). The improvement of skin had seen and maintained after 12 sessions ($p < 0.001$) as shown in Figure 1.

Thickness, scale and pruritus of skin lesions had good improvement after the last session by NB-UVB mono-therapy ($p < 0.001$) as shown in Figure 2.

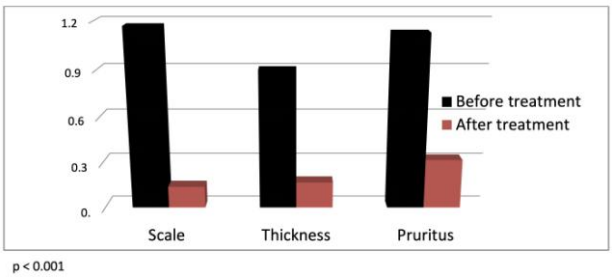

Figure 2: Improvement of thickness and scale of skin lesions

The mean cumulative dose was 9760.5 mJ/cm^2. All patients have remained relapse-free for at least 3 months.

A group of 27/29 patients treated with phototherapy reported minimal erythema (69%) and itchy (55.2%). These side effects have resolved quickly after topical emollients and irradiation dose reduction. None of the patients discontinued treatment as a result of side effects.

All patients were satisfied with the treatment; more than 80% of the patients would recommend the procedure.

Discussion

In National Hospital of Dermatology and Venereology (NHDV), 29 patients with PLC (11 males and 18 females) with the initial mean age of disease was 25 ± 16,8 years and mean disease duration was 39,9 ± 57,9 months. This is convenient with criteria chronic and most commonly occurs in children and young adults of PLC. Responses to various treatment modalities, such as topical corticosteroids and oral antibiotics were extremely poor despite diffuse skin lesions. Topical corticosteroids are unable to affect the course of disease whereas systemic antibiotics, including erythromycin and tetracycline, have been used for their anti-inflammatory rather than antibiotic effects [1], [2].

The exact mechanism of NB-UVB for a phototherapeutic treatment modality for PL, including PLC is unknown. In the previous studies, NB-UVB has been shown to be the safe and effective treatment option for several inflammatory and neoplastic skin diseases characterised by epithelial and dermal infiltrates rich in T lymphocytes. In chronic plaque

psoriasis, NB-UVB mono-therapy could reduce the number of activated T cells by inducing T cells apoptosis [3]. Recent studies have revealed that UVB suppresses the all activating and antigen-presenting capacity of epidermal Langerhans cells and therefore UVB modulates the circulating cytokines accounts, such as IL-1, IL-6, IL-8, IL-12 and TNF-α production by human keratinocytes due to immunosuppression [4]. The expression of ICAM-1 has been suppressed in cultured human keratinocytes, and decreases the release of histamine from mast cells by systemic UVB-induced, in turn, decrease the itch response of skin lesions [5]. In the present study, 29 PLC patients were treated with NB-UVB monotherapy. 82.8% of patients achieved a CR within 13.8 ± 7.4 sessions (4, 6 weeks) of their first therapy session. Thickness, scale and pruritus of skin lesions were reported reducing after finished treatment. No patients relapsed during the follow-up (for at least 3 months after the last treatment). These results, compared with the published data, demonstrated that NB-UVB therapy should be highly recommended for PLC treatment.

Similarly, several studies demonstrated the efficacy of NB-UVB phototherapy in PLC treatment. Farnaghi et al. described their experience with NB-UVB in eight PLC patients. CR was achieved by 87.5% (7/8) of the patients within a mean number of 37 ± 11 treatments [6]. Fernandez at al. has reported on 8 adults diffuse PLC patients whose disease showed no response to topical therapy. A CR rate of 88% in a mean of 23 sessions (cumulative dose 16,99 J/cm^2) was obtained [7]. Ersoy et al. reported on 25 PLC patients (14 male, 11 female). CR was achieved in 48% of the patients after 25 sessions (8 weeks) of the median number treatment [8]. Although the relapse-free rates after NB-UVB monotherapy varied from 42 to 73% in the literature, the discrepancy in relapse rates between previous studies and the present study may reflex differences both in the length of follow-up periods and in the choice of the initial and increasing dose in every session treatment. In the current study, NB-UVB phototherapy proved to be safe modality in the treatment of PLC patients. Short-term adverse effects showed minimal erythema and itch in most patients which could be quickly resolved while long-term adverse effects were unavailable.

In conclusion, NB-UVB therapy is an effective and safe option for the treatment and management of PLC. It also has several advantages over treatment with BB-UVB and PUVA. So NB-UVB should be considered as the first line in generalised cases interested in treatment.

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Efficacy of Oral Itraconazole in the Treatment of Seborrheic Dermatitis in Vietnamese Adults Patients

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Keywords: Seborrheic dermatitis; Oral itraconazole

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Abstract

AIM: This longitudinal study aims to evaluate the efficacy of oral itraconazole in the treatment of seborrheic dermatitis in Vietnamese patients.

METHODS: Thirty patients were enrolled at National Hospital of Dermatology and Venereology, Hanoi, Vietnam and were treated with oral itraconazole (200 mg daily in 14 days followed by 200 mg weekly in 4 weeks). The clinical severity was assessed by a four-parameter scoring system. All patients completed the six-week regimen with good adherence.

RESULTS: At the week 2nd, 70% of the patients had moderate to severe diseases. At the week 6th, 63.4% of the patients achieve clearance of the lesions, and none had severe disease. No side effects were reported.

CONCLUSION: Oral itraconazole can be an option for seborrheic dermatitis because of good efficacy, safety profile and adherence.

Introduction

Seborrheic dermatitis (SD) is a chronic skin condition characterised by erythema and greasy scales in oily areas. It is considered multifactorial, but *Malassezia furfur* has been proved to play a role in the pathogenesis [1]. SD is not curable and tends to persist and relapse. Skin lesions, especially in the face, can affect a patient's quality of life at different degrees. Treatment of SD includes topical corticoid, topical or systemic antimycotic, vitamin A acid, and other agents [2]. The antifungal regimens have shown efficacy in the management of SD, reducing *Malassezia* proliferation and inflammation. Some studies have reported the benefit of topical ketoconazole or topical corticoid [3], but the evidence of oral itraconazole is weak. Therefore, we conducted this study to evaluate the efficacy of oral itraconazole in Vietnamese SD patients.

Methods

We conducted a longitudinal study at the National Hospital of Dermatology and Venereology on 30 seborrheic dermatitis patients who was 18-60 years old and treated with oral itraconazole (Table 1).

Table 1: Patient characteristics

Age (year), mean ± SD	36.90 ± 10.73
Male-to-female ratio	1.5
Age of onset (year), mean ± SD	34.13 ± 12.42

We excluded pregnant or lactating women and patients with hepatic, renal or cardiovascular diseases, hyperlipidemia, acute infection, malignant diseases, HIV, or ≥ 5 *Demodex* in one slide.

The standard oral itraconazole regimen was 200 mg/day in 14 days followed by a single weekly dose of 200 mg in 4 weeks. Patients were asked to return for follow-up after two, four, and six weeks. In all follow-up visits, the severity of SD was assessed by a scoring system including four parameters: pruritus, burning, erythema, and scaling-each of which is given a score from 0 to 3, corresponding to the absence or a mild, moderate, or severe presentation [4]. A total score of 0, 1-2, 3-4, and ≥ 5 was considered cure, or good, moderate, or severe disease. We also recorded side effects of oral itraconazole, including rash, nausea, vomiting, constipation, headache, and dizziness.

Results

All patients completed six-week follow-up and reported to adhere to the regimen. Changes in the severity at each follow-up visits were shown in Figure 1.

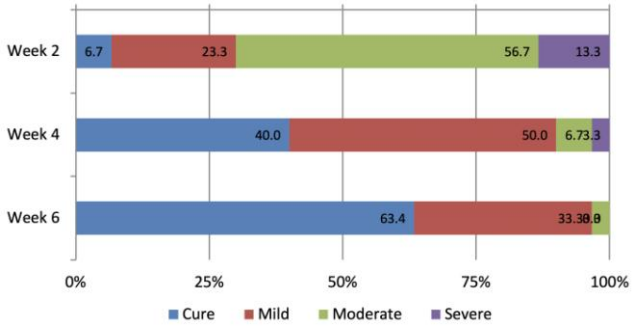

Figure 1: Changes of severity after treatment

After two weeks, 70% of the patients still had moderate to severe disease, and only 6.7% had a clearance of lesions. However, the proportion of patients with clearance of lesions consistently increased after four and six weeks. After completing the regimen, 63.4% of the patients achieved clearance and none had severe disease.

During 6 weeks of treatment, no side effect was observed in all patients.

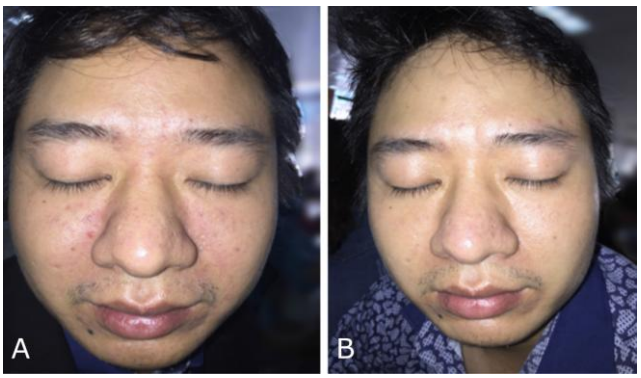

Figure 2: A) Clinical presentation at baseline; B) Clinical presentation after 6 weeks of treatment

Discussions

In this study, we evaluated the patient's response to oral itraconazole in the treatment of seborrheic dermatitis. After four weeks, less than half of the patients achieved clearance while previous studies on topical antifungals reported a high rate of clearance within 2-4 weeks [3].

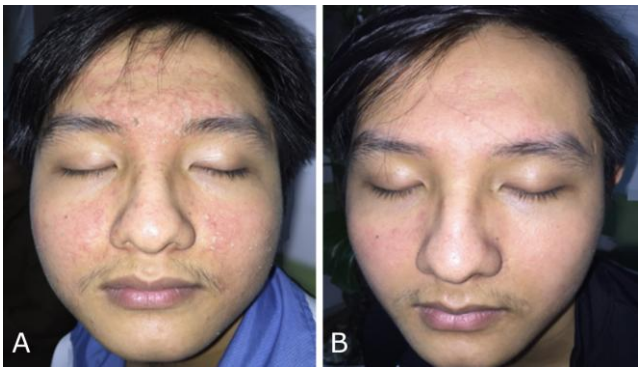

Figure 3: A) Clinical presentation at baseline; B) Clinical presentation after 6 weeks of treatment

This can be explained by the direct action of topical antifungals on the yeasts in skin lesions. Oral itraconazole is absorbed through the gastrointestinal tract, metabolised at the liver, and eventually distributed to the skin; thus, takes a longer time to exert its fungicidal activity.

Other studies reported clinical response within the first month and their effectiveness was maintained over 3-14 months [5]. Meanwhile, topical agents are also known for their high recurrence rate: patients treated with topical antifungals relapsed after 2-4 weeks [3].

Adherence is a problem in the treatment of any chronic conditions. Applying topical agents daily for months might be challenging for patients. Kruk et al., (2006) compared doses intermittently and daily and found better adherence when patients took the

intermittently dosed [6], [7]. Therefore, the current dosing regimen of oral itraconazole can benefit patients, especially those who require long-term treatment or tend to poorly adhere to therapy.

We did not record any side effects of oral itraconazole, and neither previous studies had reported any [5]. This can be a strength of oral itraconazole compared with other oral agents since adverse effects have been reported in the studies of oral terbinafine, fluconazole, and ketoconazole [5].

In conclusion, in our study oral itraconazole appears to be effective in the treatment of seborrheic dermatitis with a good safety profile and good adherence in Vietnamese patients.

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Efficacy of Narrow - Band UVB Phototherapy versus PUVA Chemophototherapy for Psoriasis in Vietnamese Patients

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Abstract

BACKGROUND: Psoralen UVA (PUVA) and narrow-band UVB (NBUVB) chemophototherapy are treatment options for psoriasis.

AIM: To compare the effectiveness of NBUVB with PUVA in Vietnamese psoriasis patients.

METHODS: We conducted a non-randomized trial on 60 patients with plaque-type psoriasis (30 NBUVB, 30 PUVA). Both regimens were thrice-weekly. The extent of lesion was assessed by the Psoriasis Area Severity Index (PASI). Clearance was defined as a ≥ 75% reduction in a follow-up PASI score from baseline. Patients with clearance were followed-up until 6 months after stopping treatment. Relapse was defined as 50% or more of the original extent.

RESULTS: The proportion of patients achieving PASI75 was comparable (76.7% in NBUVB versus 80% in PUVA; $p > 0.05$). Patients in both groups had a similar number of sessions to achieve clearance but patients in the PUVA group exposed to a significantly higher cumulative UV dose. After six months, the relapse rate was higher in the NBUVB group compared with in the PUVA group ($p > 0.05$).

CONCLUSION: Thrice weekly NBUVB is as effective as thrice weekly PUVA in treating psoriasis for Vietnamese patients.

Introduction

Psoralen UVA (PUVA) chemophototherapy is a well-established and effective treatment for psoriasis. The main concern with PUVA is the risk of non-melanoma skin cancers as well as melanoma [1].

Compared with PUVA, narrowband UVB (NBUVB) has some advantages: it does not require psoralen, is more accessible and less phototoxic or carcinogenic [2], [3]. Moreover, NBUVB did not have harmful effects on pregnant women [4] and Asian children [5].

Despite these advantages, systemic PUVA is superior to NBUVB regarding the proportion of patients achieving clearance [6] and exhibited a longer duration of remission [7].

Given the controversy in the indication of NBUVB and PUVA, we conducted a prospective trial to examine the effectiveness of NBUVB in treating psoriasis in comparison with PUVA in Vietnamese patients.

Methods

Study design

We conducted a non-randomized controlled trial on adults with chronic plaque-type psoriasis of moderate to a severe extent. Patients with Fitzpatrick's skin types III and IV were selected because they represented the local population. The decision to administer NBUVB or PUVA was based on the day of the week when patients were admitted (NBUVB on Monday, Wednesday, and Friday, and PUVA on Tuesday, Thursday, and Saturday); this allocation was done due to local logistic requirements. We excluded patients aged < 18 years and who had a history of skin cancer or solar keratoses, phototherapy, PUVA, or systemic therapy for psoriasis within the preceding three months.

Study procedures

Patients in the NBUVB group were treated three times weekly with a starting dose of 500 mJ/cm^2. Next dose was increased by 20% of the previous, to a maximum of 2000 mJ/cm^2. Patients underwent up to 25 sessions. The dosage was adjusted if patients developed erythema.

Patients in the PUVA group were treated three times weekly with a starting dose of 2 J/cm^2, increasing by 20% each session, to a maximum of 15 J/cm^2 per dose. Patients underwent up to 25 sessions. The dosage was adjusted if patients developed erythema. Oral methoxsalen tablets (10 mg of Meladinine 10 mg tablet produced by CLS Pharma from French) at a dose of 0.6 mg/kg rounded up to the nearest 10 mg were taken 2 hours before treatment. Patients wore UV-A protective spectacles for 24 hours after treatment.

We assessed the extent of lesions by the Psoriasis Area Severity Index (PASI). Clearance is defined as a 75% reduction in a follow-up PASI score from baseline (PASI75). PASI was measured by a clinician at recruitment (baseline) and repeated after every eight treatments (or earlier if study staff deemed patients had achieved PASI75). Patients who did not reach PASI75 would be managed according to local guidelines.

We also monitored adverse effects of the therapy: erythema in both groups and symptoms after taking psoralen in patients treated with PUVA. The severity of erythema was divided into three grades: grade 1 (minimally perceptible erythema); grade 2 (well-defined asymptomatic erythema) and grade 3 (painful erythema persisting for more than 24 hours).

We continued to follow up patients every month over six months after completing therapy. Relapse was defined as 50% or more of the original PASI index.

Materials

UV machine: Medisun 2800, whole body exposure units fitted with 22 fluorescent lamps (Philips TL100W/01), intensity (3.1 mW/cm^2) was measured monthly.

UVA machine: Houva II, whole body exposure units fitted with 24 UVA lamps, intensity (11.1 mW/cm^2) was measured monthly.

Psoralene: Meladinine 10 mg tablet produced by CLS Pharma from French.

Data collection and analysis

Demographic and clinical data were recorded in a case report form. All data were entered into an electronic database and analysed with SPSS 20.0 (IBM Corporation, USA). Descriptive data were described in proportion or mean (standard deviation). We used the Student's *t*-test and the chi-square test to test for difference between continuous and categorical variables, respectively. The Kaplan-Meier curve and the Cox proportional hazard regression were used to compare the relapse rate between the two groups.

Ethics

The study was approved by the institutional review board of the National Hospital of Dermatology and Venereology, Vietnam. Informed consent was obtained from all patients.

Results

Between March 2014 and September 2015, we recruited 30 patients to the NBUVB group and 30 to the PUVA group. The baseline characteristics of the two groups, with no significant difference, were presented in Table 1.

Table 1: Baseline characteristics

	NBUVB (n = 30)	PUVA (n = 30)
Male, n (%)	18 (60)	20 (66.7)
Age, mean ± SD	35.8 ± 13.9	37.53 ± 15.19
Duration, mean ± SD	7.8 ± 5.8	10.7 ± 8.4
Itching, n (%)	24 (80)	23 (76.7)
Skin type, n (%)		
III	2 (6.7)	4 (13.3)
IV	28 (93.3)	26 (86.7)
PASI score, mean ± SD	19.2 ± 7.7	19.5 ± 7.7

SD: standard deviation.

Forty-seven patients achieved clearance after the intervention, and the proportion was comparable between the two groups (73.3% in the NBUVB group versus 80% in the PUVA group, p > 0.05) as shown in Table 2.

Table 2: Treatment outcomes

	NBUVB	PUVA	*p*
Clearance, n (%)	22 (73.3)	24 (80%)	> 0.05
Number of sessions to clearance	19.7 ± 4.7	19.8 ± 4.8	> 0.05
Cumulative dose to clearance(j/cm^2)	26.2 ± 9.4	191.8 ± 79.7	< 0.01

The number of sessions needed to achieve clearance was not different between the two groups; however, patients in the NBUVB exposed to a significantly lower cumulative UV dose.

We followed up patients with clearance for six months. A slightly higher relapse rate in the NBUVB group, but Cox regression did not show any significant difference (p = 0.03) as presented in Figure 1.

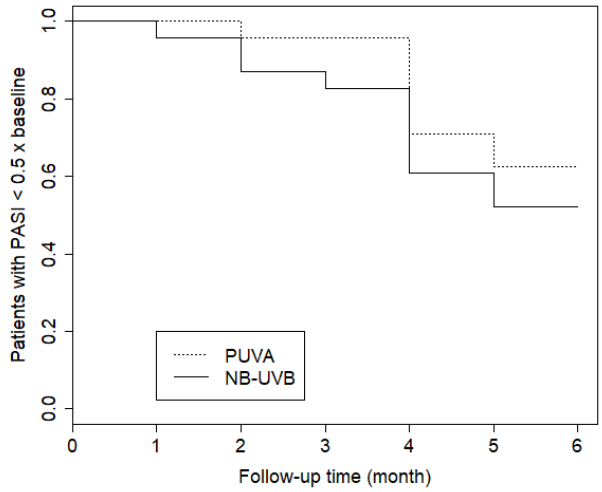

Figure 1: Kaplan-Meier's curve of relapse after therapy

Seven patients in the NBUVB group had grade 1 erythema after intervention while in the PUVA group, 3, 3, and 1 patient had grade 1, 2, and 3 erythema, respectively. Nine patients had gastrointestinal complaints including nausea, emesis, and abdominal pain following meladinine administration (in the PUVA group). No patients had to discontinue treatment because of these side effects.

Discussion

This is a trial comparing the effectiveness and safety of narrowband UVB with psoralen UVA. Our main findings suggest NBUVB is comparable to PUVA regarding effectiveness but exposes patients to a lower UV. Dayal et al., (2010) also found similar results: both NBUVB and PUVA were effective, and PUVA had a lower number of sessions but a higher mean cumulative dose to achieve clearance [8]. Similar effectiveness between NBUVB and PUVA has also been shown in other studies [3], [9].

In our study, PASI75 was achieved after a mean number of sessions of 19.7, less than normally required (25 sessions). Dayal et al. used a lower starting dose (280 mJ/cm^2) compared with our study (500 mJ/cm^2) [8]. Also, we used the thrice-weekly regimen instead of a twice-weekly regimen. Kleinpenning et al., (2009) found that the high-dose regimen resulted in a shorter treatment course and a better outcome after 3-month follow-up but a similar cumulative dose [9].

In our study, the relapse rate was higher in the NBUVB group, but this difference was not statistically significant. The duration of remission in patients treated with PUVA has been reported to be longer than that in patients treated with NBUVB [10].

Despite superiority in effectiveness, NBUVB is considered the first-line option for some types of psoriasis [11] because it is more convenient and has fewer side effects. Although the two groups in our study had the same number of patients with erythema, patients treated with PUVA had higher severity (grade 2 and 3 erythema were seen in four patients in the PUVA group but none in the NBUVB). One-third of the patients treated with PUVA also reported gastrointestinal symptoms after taking psoralen. While NBUVB is associated with a better safety profile, PUVA is, however, still recommended for patients who failed to respond or is refractory to NBUVB [11], [12], [13].

In conclusion, thrice weekly NB UVB is as effective as thrice-weekly PUVA in treating psoriasis in Vietnamese patients.

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Serial Excision for the Treatment of Giant Congenital Melanocytic Nevus: The Vietnamese Way

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Keywords: Melanocytic nevus; Giant congenital melanocytic nevus; Plastic surgery

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Abstract

AIM: To investigate the efficacy of plastic surgery in the treatment of giant congenital melanocytic nevus (GCMN).

METHODS: We enrolled 20 patients with 44 lesions and performed one of the following procedures: serial excision, skin grafting, tissue expansion, primary skin closure, distant flap, and adjacent flap. We assessed the outcome at 10 days and 6 months after surgery.

RESULTS: Of 44 surgical sites, the most commonly used reconstruction surgeries were serial excision (16), skin grafting (16), and tissue expansion (6). Other types were rarely used. All patients with serial excision had good outcome. A total of 81% and 19% of the patients with skin grafting had good and fair outcome, respectively. Around 83% and 17% of the patients with tissue expansion had good and fair outcome. No cases had bad outcome.

CONCLUSION: In conclusion plastic surgery is effective in the treatment of GCMN. There are different techniques but serial excision, skin grafts, and tissue expansion are most commonly used.

Introduction

Giant congenital melanocytic nevus (GCMN) is a rare restricted dysplasia, with embryonic origin and associated with high risk of malignant melanoma (6.3%). In addition, they also cause aesthetic lacking, especially while appears in open areas, such as face and neck [1], [2]. Treatment of GCMN is mainly surgical and it depends on the position, size and malignant tendency of the nevus. Many surgical techniques are avaible and they could be very difficult, mostly with GCMN of excessive size, with very large injured area [3], [4].

We aimed to investigate the efficacy of plastic surgery in the treatment of giant congenital melanocytic nevus (GCMN)

Methods

We enrolled at National Hospital of Dermatology and Venereology and Saint Paul Hospital 20 patients who had been diagnosed with GCMN and operated through 44 surgeries, then monitored and evaluated from 2006 to 2010.

Results

We evaluated the results of each main type of reconstruction surgeries to propose the suitable method for every specific case: serial excision, skin grafting and tissue expansion. Other types of surgery are rarely used, so we cannot evaluate the results. There were no cases with bad result as shown in Table 1 and Table 2.

Table 1: Distribution of skin reconstructing methods after GCMN removal

Plastic surgery	n	%
Serial excision	16	36 %
Skin grafting	16	36 %
Tissue expansion	6	14 %
Primary skin closure	3	7 %
Adjacent flap	2	5 %
Distant flap	1	2 %
Total	44	100 %

Serial excision was used 16/44 sites, the result is 100% good. It is a method that takes advantage of natural skin dilation with many advantages: fast surgery, low cost, high aesthetic, no additional damage to the adjacent skin but it cannot be applied to the malignant de-generalized nevus.

Table 2: Surgical results

Surgery methods	Good	Fair	Bad	Total
Serial excision	16	0	0	16
	100%	0%	0%	100%
Skin grafting	13	3	0	16
	81%	19%	0%	100%
Tissue	5	1	0	6
expansion	83%	17%	0%	100%
Total	34	4	0	38

Arneja [3] recommended carrying out this method when the nevus can be completely removed after only 3 or 4 surgeries, otherwise the tissue expansion should be suggested. We found out that, the serial excision can be used simply to treat GCMN, especially the GCMN in the patient's back or abdomen.

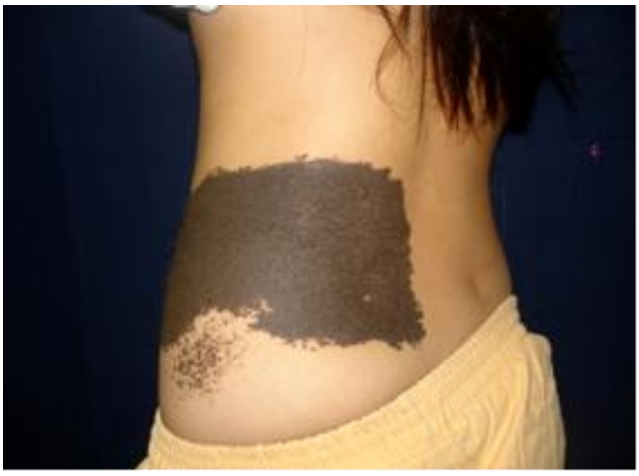

Figure 1: Clinical presentation of GCMN before surgery, baseline

Tissue expansion can create a sufficient volume of tissue to cover a large cell shortage. It is a complex technique with high cost, prolonged duration, capability of many complications. Tissue expansion was used 6/44 sites, the results were 83% good, 17% fair.

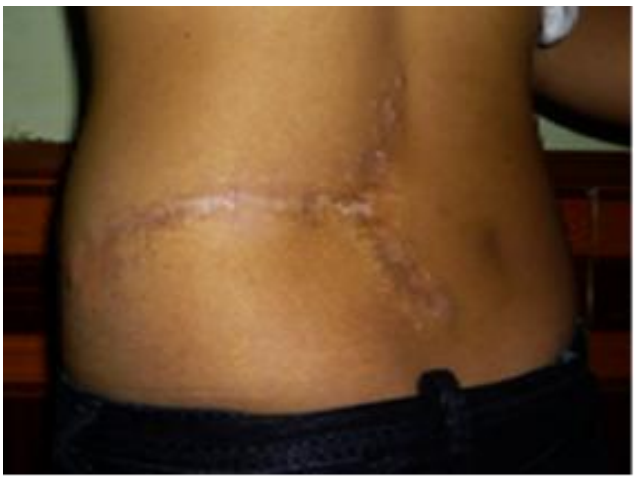

Figure 2: Clinical presentation of GCMN after three serial excision. The aesthetic outcome was satisfactory for the patient

None patients had infections and there was only one case of partial necrosis was not completely removed from the skin, however, it did not significantly affect the results of the surgery, so we assessed it fair, accounting for 17%. The remaining 5 cases, having no necrosis and scarring immediately and well, are rated as good, accounting for 83%. Arneja [3] recommends the use of tissue expansion for GCMN that cannot be operated by serial excision after the fourth surgery, available on children aged over 3 months [5].

Discussion

The flap is used as an indigenous or distant flap or as material for a skin graft. This is also the best indication for the scalp [5], [6].

Skin grafting can cover a very large area especially when it is associated with tissue expansion. It is an easy and low cost method. In our study skin grafting was used 16/44 sites, the results reached 81% good, 19% fair. There were 4 cases of thick skin grafts that were all slightly infected due to fluid gathered under grafts, get partial necrosis, which affected the outcome of the surgery. These 4 cases are evaluated as fair, accounting for 19%. The remaining cases were good, accounting for 81%. Skin graft should be used only if neither serial excision nor tissue expansion can be performed [7].

In conclusion, to reconstructing the skin after GCMN excision, the serial excision and tissue

expansion surgeries are preferentially selected; skin grafting is an alternative.

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The Efficacy and Safety of Hyaluronic Acid Microinjection for Skin Rejuvenation in Vietnam

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Keywords: Hyaluronic acid; Microinjection; Skin rejuvenation

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Abstract

BACKGROUND: Aging is an increasing concern of modern society, particularly facial ageing. In recent years, the microinjection technique has increasingly been emphasised as a skin rejuvenation strategy. Hyaluronic acid (HA) plays an important role in the hydration of the extracellular space and can thus improve skin hydration, firmness and viscoelastic properties.

AIM: To evaluate the efficacy and safety of HA microinjection in skin rejuvenation.

METHODS: We enrolled thirty participants underwent three sessions of HA microinjection involving multiple injections in the face or back of the hands at 2-week intervals. The aesthetic outcomes were assessed at baseline and after 2, 4 and 8 weeks. Clinical evaluation was based on the Global Aesthetic Improvement Scale (GAIS) and the Wrinkle Severity Rating Scale (WSRS).

RESULTS: Evaluation of photographs from 2, 4 and 8 weeks revealed significant clinical improvement in the brightness, texture and wrinkling of the skin. Analysis of the GAIS and WSRS scores revealed statistically significant results after 2 months.

CONCLUSION: Most of the participants felt satisfied with the treatment (93.3%).

Introduction

Ageing is an increasing concern of modern society, particularly facial ageing. This complex process involves two important factors: volume loss in the face and repetitive muscle movements resulting in wrinkles and folds. In recent years, the technique of intradermal microinjection with pharmacologic substances has been emphasised in skin rejuvenation.

This technique aims to restore or maintain youthful and healthy skin structures. The desired effect is firm, bright and moisturised skin via injection of appropriate, completely biocompatible and easily absorbable products into the superficial dermis. Among the skin rejuvenation microinjection products, hyaluronic acid (HA) plays an important role in hydration of the extracellular space due to its ability to attract water molecules, and HA is thought to give physiological conditions conducive to extracellular matrix production [1], [2].

Some clinical experiments have shown that HA microinjection can stimulate fibroblasts to express collagen type 1 (Col-1), matrix metalloprotease-1 (MMP-1), and tissue inhibitor of matrix metalloproteinase-1 (TIMP) [2], [3], [4]. This technique is safe when conducted by well-trained dermatologists. However, there have been few clinical studies on HA microinjection in Vietnam. We conducted this study to evaluate the safety and efficacy of HA microinjection in skin rejuvenation.

Subjects and Methods

This open clinical study was carried out at the HCMC Hospital of Dermato-Venereology. Thirty participants were enrolled in the study from October 2014 to October 2015. The inclusion criteria were as follows: healthy participants who presented with mild/moderate to severe photoaging and were not using any other treatments. Exclusion criteria included previous use of other medical-aesthetical treatments; any cutaneous pathology of infectious, inflammatory, viral and vascular type affecting the face; history of coagulation disorders; wound healing disorders; history of allergy to HA or any ingredient of the test product; and women who were pregnant or breastfeeding. All participants gave informed consent for enrollment in the clinical study.

All participants underwent three sessions of mesotherapy involving multiple microinjections with a 30 G/4 mm needle in the face or back of the hand at 2-week intervals. The study was conducted for 2 months. The photographic evaluation was performed at each treatment and 1 month later after the last session. The results were defined with a score derived from the Global Aesthetic Improvement Scale (GAIS), which was used as a reference parameter (Table 1).

Table 1: Global Aesthetic Improvement Scale (GAIS)

	Degree	Description
1	Exceptional improvement	The excellent corrective result after a session with the VISIA device
2	Very improved patient	Marked improvement in appearance, but not completely optimal. A touch-up would slightly improve the result
3	Improved patient	Improvement in appearance to better than the initial condition, but a touch-up is advised
4	Unaltered patient	The appearance remains substantially the same as the original condition
5	Worsened patient	The appearance has become worse than the original condition

Moreover, the Wrinkle Severity Rating Scale (WSRS) was used to evaluate the condition of the wrinkles and, therefore, the degree of ageing (Table 2). The participants were also asked for self-assessment of improvement.

Table 2: Wrinkle Severity Rating Scale (WSRS)

Score	Description
1	Absent
2	Slight
3	Moderate
4	Severe
5	Extreme

Results

A total of 30 women aged 30-65 years (mean age 46 years) were included in the study. Two participants were lost to follow-up after the first treatment. We had fourteen participants aged 41-50 years (46.7%), which was the most common age group seeking treatment. Most of the participants had significant improvement after the first treatment (50%), and the improvement continued to increase after the second (70%) and third treatments (83.3%), as indicated by the GAIS evaluation.

The difference between the GAIS scores at weeks 4 and 2 was not clinically significant. However, the improvement between week 8 and week 2 was clinically significant ($p < 0.05$). At all evaluation time points, the participants showed a significant improvement in their skin status compared with that at baseline ($p < 0.01$) as shown in Figure 1.

*Figure 1: Wrinkle Severity Rating Scale (WSRS) before (WSRS0), after 2 weeks (WSRS2), 4 weeks (WSRS4) and 8 weeks (WSRS8). * Comparisons of WSRS2, WSRS4 and WSRS8 to WSRS0 indicated statistically significant differences ($p < 0.01$)*

Adverse effects were generally of mild or moderate intensity and expected (pain, oedema, petechia, hematoma or dark eye circle). The most common expected adverse event was a pain (53.3%), followed by oedema (40%) and petechia (26.7%).

Among 30 participants, 23 (76.6%) felt satisfied with the result. Moreover, 5 (16.7%) felt very satisfied with the treatment.

Discussion

This clinical, open study with 30 participants demonstrated the efficacy of HA microinjection in skin rejuvenation. Most of the participants were aged 41-50 years, which is consistent with the studies conducted by Adele Sparavigna in 2015 (64 patients aged 37-60 years) [3], and Antonella in 2013 (50 patients) [4]. From 30 years of age, skin renewal decreases, so the very first signs of ageing become visible, such as uneven skin tone, wrinkles, unhealthy skin and elastin degeneration, resulting in decreased skin firmness. Therefore, this is the age when patients start to seek skin rejuvenation procedures.

Most of the participants had significant improvement after the first treatment and continued to improve after every subsequent session. In our study, this significant effect of HA mesotherapy on skin elastic properties and wrinkles was coupled to a sustained improvement after the last session. This finding is consistent with the study of Antonella conducted in Italy. To investigate the molecular effects on the skin caused by HA treatment, the authors analysed the expression levels of IL-6, IL-1b, MMP-1, and Col-1 at the beginning and end of the treatment using immunohistochemistry. The authors observed a decrease in IL-1β, IL-6 and MMP-1 levels and an increase in Col-1 levels. These results were statistically analysed and showed that treatment resulted in significant and long-lasting rejuvenation effects. These data were confirmed both subjectively and objectively by GAIS and WSRS score analysis (50 patients) [4].

Furthermore, HA microinjection can improve skin hydration, firmness and viscoelastic properties. These benefits were proven by Martine Baspeyras et al. when the authors conducted a study to evaluate the effect of microinjection of HA by histology and electron microscopy examination of skin biopsies. The results showed significant improvement after treatment with $p < 0.01$ [2].

Adele Sparavigna et al. reported a statistically significant improvement in profilometric parameters, skin brightness, pigmentation, and deep skin hydration when treating skin ageing and photoaging with HA microinjection in clinics ($p < 0.05$) [3].

Intradermal HA injection will stimulate fibroblasts, increase the collagen, elastin and HA synthesis in the treatment area, and promote extracellular matrix production and epithelial regeneration, resulting in skin rejuvenation [5].

WSRS2, WSRS4, and WSRS8 exhibited statistically significant differences compared with WSRS0. The improvement in wrinkles was observed after the first treatment and increased after every session. The efficacy of revitalization in skin rejuvenation was confirmed by the study of Adela Sparavigna et al. [3]. This study demonstrated the improvement in at least one grade of crow's feet, and the efficacy was found not only on the face but also on the décolletage and hand skin surface [3].

The new minimally invasive mesotherapy technique with HA can improve the clinical appearance of the skin in different age groups, as reported in a study conducted by Antonella et al. in Italy. This study demonstrated a significant and long-lasting effect on the brightness, texture, and firmness of the skin [4]. More interesting, HA microinjection also resulted in skin hydration, not only at the superficial level but also in the deep layers of the skin. This study showed that HA could have acted as a water content modulator in the skin layers, thus improving the epidermal barrier function, which is often affected by the ageing mechanism [3].

The most common side effects included pain, oedema, petechia, and hematoma. However, those side effects lasted for only three to four days and were completely tolerable by the participants. Martine Baspeyras et al. also showed some common adverse events, including hematoma, oedema, papule and erythema. All expected adverse events disappeared within a mean time of 5.9 days [2], [7].

Most of the participants felt satisfied or very satisfied with the treatment (93.3%). These data indicate that this technique is efficacious and safe and can be well tolerated by customers.

In conclusion, this study objectively demonstrated the efficacy and safety of HA microinjection for skin rejuvenation. In particular, we showed that intradermal HA mesotherapy might be of value to decrease the wrinkles and increase the suppleness of ageing skin when conducted by a trained physician. The improvement started from the first treatment and continued to increase after every session. Most of the participants felt satisfied or very satisfied with the treatment (93.3%). Adverse events included pain, oedema, petechia, and hematoma, but these effects lasted for three to four days only and were completely tolerable.

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Clinical Science

Efficacy of Adding Oral Simvastatin to Topical Therapy for Treatment of Psoriasis: The Vietnamese Experience

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Abstract

BACKGROUND: Psoriasis, the prevalence of which ranges from 2% to 3% of the general population, has been recently recognised as not only a chronic inflammatory skin disorder but also an immunometabolic systemic disease. Dyslipidemia is one of the most important comorbidities of psoriasis. Statins, frequently used as anti-hyperlipidemic agents, may be beneficial in the treatment of several autoimmune diseases, including psoriasis, due to their anti-inflammatory and immunomodulatory characteristics. Hence, we hypothesised that using this medication was not only beneficial for reducing hyperlipidemia but also improving psoriatic conditions.

AIM: We conducted a study to determine the prevalence of dyslipidemia in psoriatic patients as well as whether the addition of statins (simvastatin prescribed forms) to standard topical antipsoriatic treatment can improve skin lesions in psoriatic patients.

METHODS: A group of 128 psoriatic patients and 128 healthy controls who were matched with the patients regarding ethnicity, age, and sex were enrolled, and their lipid concentrations were determined. Furthermore, sixty patients were randomly selected from the former group and divided into two treatment subgroups to evaluate the effect of statins on the severity of psoriasis using the PASI score.

RESULTS: We found that the rate of dyslipidemia in the patient group was significantly higher than in the healthy group (53.9% versus 21.9%, $p < 0.001$), particularly the triglyceride concentration (1.86 ± 1.17 versus 1.43 ± 0.79 mg/dL, $p < 0.001$). Also, the PASI score reduction in the simvastatin-treated subgroup was significantly different from that in the placebo-treated one after eight weeks of therapy (8.63 ± 4.78 versus 5.34 ± 3.59, $p < 0.01$).

CONCLUSION: This study showed that simvastatin might play a role in controlling hyperlipidemia and in turn decrease the PASI score in psoriatic patients.

Introduction

Psoriasis is a chronic inflammatory skin disease the prevalence of which ranges from 2% to 3% of the general population, depending on region and ethnic origin [1]. Many recent studies support the hypothesis that psoriasis results from an interaction between an individual's genetic susceptibility and specific environmental factors. Nearly 20 psoriatic-susceptibility gene loci and genes with a fundamental role in psoriasis pathophysiology have been identified, including PSORS1 (a major susceptibility gene, mapped near the human leucocyte antigen HLACw6) [2]. Currently, the various treatment modalities are divided into local and systemic treatments, including topical steroids, vitamin D3, tar, anthralin, topical retinoids, phototherapy, retinoids, methotrexate, biologic agents and many other treatment modalities. Psoriatic prognosis is unpredictable, and its recurrence almost inevitably appears regardless of treatment [3].

Dyslipidemia is known as one of several comorbidities of psoriasis in addition to cardiovascular abnormalities, hypertension, atherosclerosis, diabetes mellitus type 2, and obesity [4]. Recently, there have been several clinical observations focusing on the risk of developing cardiovascular diseases, such as acute

coronary syndromes or arterial hypertension, in psoriatic patients. Additionally, other conditions, including hyperlipidemia, obesity and type 2 diabetes, were found to be more prevalent in the patient group than in the control group [5].

Statins, with the most common drugs being simvastatin and atorvastatin, form one type of compound that can reduce the amount of cholesterol in the blood. They were first discovered in 1971 by Akira Endo and constitute a rapidly growing class of medications that can modulate hypercholesterolemia. The beneficial effect of statins on lipids is directly linked to the inhibition of 3-hydroxy-3-methylglutaryl coenzyme-A reductase, which plays a central role in the synthesis of cholesterol in the liver and underlies the most beneficial effect of statins on lipids. Consequently, statin therapy has been used for the prevention of atherosclerosis and cardiovascular events [5], [6]. Many studies have shown that statins have anti-inflammatory and immunomodulatory properties which would be useful in the treatment of psoriasis and other cutaneous disorders [7], [8], [9].

We conducted a study to determine the prevalence of dyslipidemia in psoriatic patients as well as whether the addition of statins (simvastatin prescribed forms) to standard topical antipsoriatic treatment can improve skin lesions in psoriatic patients.

Patients and methods

Patient population

This study was conducted from January 2011 to December 2014 at the Outpatient Department, Hospital of Dermato-Venereology, Ho Chi Minh City, Vietnam.

Psoriatic patients, aged more than 18 years old, were recruited into the study. The exclusion criterion included hypersensitivity to simvastatin or calcipotriol/betamethasone dipropionate, renal and liver dysfunction, alcohol abuse, muscular disorders, use of topical or systemic psoriatic medication in the past 1 month, and pregnant and lactating women.

Two hundred fifty-six patients and healthy controls who gave informed consent provided blood samples for the evaluation of their lipid profiles. Also, sixty patients were randomly selected from the patient group and divided into two treatment subgroups. Subgroup 1 was treated with oral simvastatin (40 mg/d divided twice a day) plus topical calcipotriol/betamethasone dipropionate ointment for 8 weeks, and subgroup 2 received only the same topical regimen.

Efficacy assessment

A well-trained dermatologist evaluated the Psoriasis Area and Severity Index (PASI) score of the patients at the baseline, at the 4th week and the 8th week. Also, the lipid profile was assessed simultaneously. Safety was assessed by patients' reports of adverse events, clinical examination, and liver function tests.

Statistical analysis

Data were expressed as the means ± SDs and the ratio. Statistical analysis was performed using Epi Info™ (Epi Info™ version 3.5.1 for Windows; CDC). The data were analysed using Wilcoxon and Mann-Whitney tests, the Chi-square test, and two-tailed Student's tests. A P value < 0.05 was considered statistically significant.

Results

Baseline characteristics

The study included 128 patients and 128 healthy controls. The patients (30 patients in each subgroup) were treated for eight weeks. Their characteristics are shown in Table 1.

Table 1: Baseline patient characteristics

Characteristics	Group		P value	Subgroup		P value
	Control (n = 128)	Patient (n = 128)		Subgroup 1 (n = 30)	Subgroup 2 (n = 300)	
Gender:						
Men (%)	64 (50%)	64 (50%)	1[a]	17 (56.7%)	17 (56.7%)	1[a]
Women (%)	64 (50%)	64 (50%)	1[a]	13 (43.3%)	13 (43.3%)	1[a]
Mean ± SD. age (yr)	43.3 ± 12.6	41.9 ± 14.7	0.43[b]	36.0 ± 10.0	39.1 ± 14.5	0.34[b]
Mean ± SD. BMI	21.9 ± 3.2	21.9 ± 3.1	0.93[b]	-	-	-
Mean ± SD. Disease duration (yr)	-	7.7 ± 8.1	-	5.8 ± 5.4	5.6 ± 5.4	0.89[b]
Clinical features						
Psoriasis vugaris	-	100 (78.1%)	-	30 (100%)	30 (100%)	1[a]
Erythrodermic psoriasis		11 (8.6%)		0	0	
Pustular psoriasis		9 (7%)		0	0	
Arthritis psoriasis		8 (6.3%)		0	0	
PASI score: mean ± SD	-	10.9 ± 7.4	-	12.8 ± 5.8	11.8 ± 5.1	0.51[b]

[a] Chi-square test; [b] Two–tailed Student's test.

In total, 128 patients (64 male and 64 female) and 128 matched controls (64 male and 64 female) were included. Patients in subgroup 1 (oral simvastatin plus calcipotriol/betamethasone dipropionate ointment) consisted of 17 male and 13 female patients. Subgroup 2 (only calcipotriol/betamethasone dipropionate ointment) consisted of 17 male and 13 female patients. The

mean age of the healthy group was 43.3 ± 12.6 years, which was correlated with the patient group (41.9 ± 14.7 years). In subgroup 1, the average age was 36.0 ± 10.0 years, and in subgroup 2, the average age was 39.1 ± 14.5 years. There was no significant difference between sex ratios and mean ages in the two groups.

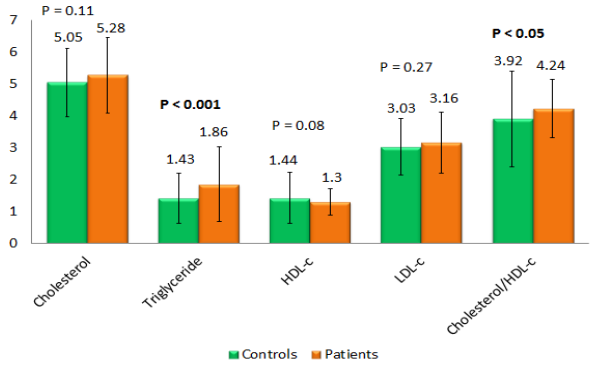

Figure 1: Comparison of lipid concentration profiles between study groups

The mean baseline PASI score in the patient group was 10.9 ± 7.4. Specifically, the mean baseline PASI score in subgroup 1 was 12.8 ± 5.87, and in subgroup 2 it was 11.8 ± 5.1. The difference in the mean baseline PASI scores of the two subgroups was not statistically significant (P = 0.51).

Dyslipidemia

The rate of dyslipidemia in the patient group was considerably higher than in the healthy control group (53.9% versus 21.9%, p < 0.001). The percentages of hypercholesterolemia in the psoriasis group and control group were 25.0% and 10.9%, respectively, (p < 0.01). When we compared the frequency of hypertriglyceridemia between the two groups, there was a significantly higher frequency in the patient group than in the control group (25.0% in psoriasis versus 8.6% in controls, p < 0.001). The frequency of hypo-HDL-c was significantly different in the patients and the controls (21.9% versus 3.9%, p < 0.001). Each element of the lipid profiles is shown in Table 2.

Table 2: Comparison of the lipid profiles between the study groups

	Group		P value
	Patient (n = 128)	Control (n = 128)	
Dyslipidemia	69 (53.9%)	28 (21.9%)	< 0.001
Hypercholesterolemia	32 (25.0%)	14 (10.9%)	< 0.01
Hypertriglyceridemia	32 (25.0%)	11 (8.6%)	< 0.001
Hyper-LDL cholesterolemia	19 (14.8%)	12 (9.4%)	0.18
Hypo-HDL cholesterolemia	28 (21.9%)	5 (3.9%)	< 0.001
Cholesterol/HDL-c > 5	26 (20.3%)	8 (6.3%)	< 0.01

[a] Chi-square test.

Analysing the mean concentration of each component in the lipid profiles, our study revealed a difference between the triglyceride levels of the patient group and the control group (1.86 ± 1.17 and 1.43 ± 0.79, respectively, p < 0.001). The ratio of cholesterol/HDL-c of patients was 4.24 ± 0.91. It was significantly higher in the patient group than in control (3.92 ± 1.50) (p < 0.05). However, the means of other components (cholesterol, HDL-c and LDL-c) were not significantly different between the two groups.

Assessment of statins in psoriasis treatment

Lipid profile

In subgroup 1, the mean baseline of cholesterolemia was 5.45 ± 1.21 mm/L, which diminished to 4.20 ± 0.82 and 4.18 ± 0.72 mm/L (p < 0.001) at the 4th week and 8th week, respectively. There was no difference between the triglyceride concentration at pretreatment and after 4 weeks of treatment, which was 2.07 ± 2.00 and 1.32 ± 0.84 mm/L (p = 0.07), respectively; however, after 8 weeks, the triglyceride concentration was 1.26 ± 0.65 mm/L (p < 0.005). While the mean baseline LDL-c level was 3.18 ± 0.7 mm/L, there was a significant difference in the 4th week (2.31 ± 0.80 mm/L, p < 0.001) and 8th week of treatment (2.26 ± 0.7 mm/L, p < 0.001). However, the increasing HDL levels were negligible after 8 weeks of treatment (1.33 ± 0.31, 1.29 ± 0.24 and 1.35 ± 0.24 at pretreatment, 4th week and 8th week, respectively). Meanwhile, in subgroup 2, without treatment, there were no changes in lipid levels over time.

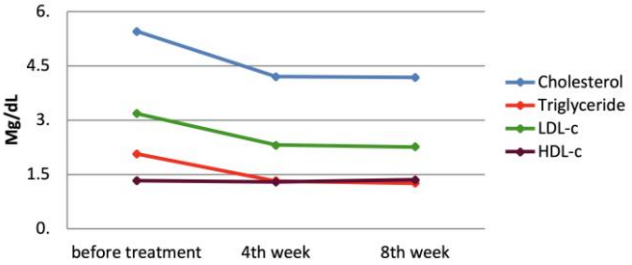

Figure 2: Changes in the lipid profile after 8 weeks of treatment with simvastatin

PASI score

In subgroup 1, in which the treatment was combination of topical therapy and simvastatin, the mean baseline PASI score was 12.8 ± 5.87, which considerably declined to 8.58 ± 5.62 after 4 weeks of treatment (p < 0.01) and ultimately to 4.17 ± 3.81 at the 8th week (p < 0.001) as shown in Table 3. Subgroup 2, treated only with topical therapy, did not have a significant difference in the mean PASI score between pretreatment and the 4th week (11.8 ± 5.13 vs 9.34 ± 5.01, p = 0.21); nevertheless, there was a considerable decrease to 6.52 ± 4.89 after 8 weeks of treatment (p < 0.001) as shown in Table 3.

Table 3. Change from baseline PASI score every 4 weeks according to treatment

Time	Baseline	4th week	8th week
Group 1	12.8 ± 5.87	8.58 ± 5.62 P < 0.01	4.17 ± 3.81 P < 0.001
Group 2	11.86 ± 5.13	9.34 ± 5.01 P = 0.21	6.52 ± 4.89 P < 0.001

The PASI score reduction was more significant in subgroup 1 than in subgroup 2 (Mann-Whitney test; $p < 0.0001$). After 4 weeks of treatment, the rates of patients who achieved PASI75 were 10% and 3.3% in subgroup 1 and subgroup 2, respectively. Patients who achieved PASI75 in subgroup 1 showed a significant increase compared with subgroup 2 after 8 weeks (70% versus 40%, $p < 0.05$).

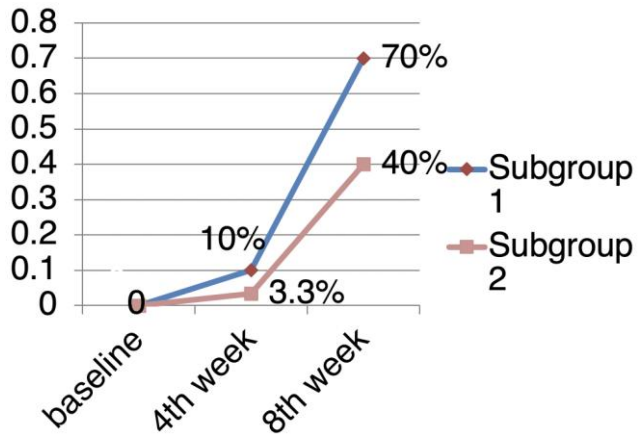

Figure 3: The rates of patient achievement of PASI75

Discussion

Studies on lipid metabolism in psoriasis patients, focusing on skin surface lipids, epidermal phospholipids, serum lipids, LDL-c of the dermis layer, oxidative stress, and the correlation between the inflammatory index of clinical lesions and lipid profiles, have been conducted since the 20th century10. Several studies confirmed that there was dyslipidemia and psoriasis coexist [10], [11].

Our study included 128 patients and 128 controls. There were no differences in age, gender, or BMI between the two study groups (Table 1). Our study used the Adult Treatment Panel III (ATP-III) guidelines from the National Cholesterol Education Program (NCEP) for the management of hypercholesterolemia, which was issued in 2001 and modified in 2004 as follows: cholesterol TP ≥ 6.20 mm/L, triglyceride ≥ 2.26 mm/L, LDL-C ≥ 4.13 mm/L, and HDL-C < 1.03 mm/L. We found that the frequency of dyslipidemia in psoriasis patients was 53.9% for hypercholesterolemia, 25% for hypertriglyceridemia, 21.9% for hypo-HDL-c, 20.3% for cholesterol/HDL-c > 5, and 14.8% for hyper-LDL-c.

The frequency of dyslipidemia in psoriasis patients varies among studies, ranging from 6.4 to 50.9% [12]. In a study on psoriasis, Salihbegovic EM postulated that the frequency of dyslipidemia was 62.8% (the frequencies of hypertriglyceridemia and hypo-HDL-c were 39% and 36%, respectively) [13]. A cross-sectional study of 120 Pakistani psoriasis patients found that the incidence of dyslipidemia was 55.8% [14], which was similar to the incidence found in our study (53.9%). However, the comparison of dyslipidemia frequency among patients with psoriasis was only relative because the standard definition of dyslipidemia was different among authors. Our study compared the rate of dyslipidemia between the two groups. The results showed that the rates of hypercholesterolemia, hypertriglyceridemia, hypo-HDL-c, and cholesterol/HDL-c > 5 in the psoriatic group increased significantly compared with those in the control group ($p < 0.05$).

There have been many studies with a variety of lipid levels in psoriatic patients. The studies by Sahu S, Taheri Sarvtin, El Asmi MA postulated a statistically significant difference in the concentration of lipids between patients with psoriasis and controls [15], [16], [17]. In our study, the triglyceride level of the patient group was 1.86 ± 1.17 mm/L, and that of the control group was 1.43 ± 0.79 mm/L ($p < 0.001$). The ratio of cholesterol/HDL-c of patients was 4.24 ± 0.91, which was higher than that of the control group ($p < 0.05$). Nevertheless, while comparing other elements of the lipid profile, we found no significant differences.

Our study also found that in patients receiving oral simvastatin plus calcipotriol/betamethasone dipropionate steroid ointment, there was a critical decrease in the levels of cholesterol, triglyceride, and LDL-C, while the level of HDL-C remained stable. This finding suggested that simvastatin had a beneficial effect on the modulation of dyslipidemia, as mentioned above. Interestingly, we also found that simvastatin improved the PASI score in psoriatic patients.

Treatment of plaque psoriasis after 8 weeks with calcipotriol/betamethasone dipropionate steroid ointment showed that there was a significant improvement in the PASI score. We also found a faster and more effective decrease in PASI score in patients with additional oral simvastatin than in patients without simvastatin. According to our study, after 4 weeks of treatment, in the subgroup that was treated with simvastatin, the efficacy of adding oral simvastatin was clear. The PASI score of subgroup 1 at the baseline was 12.8 ± 5.87, which significantly diminished after 4 weeks of treatment (8.58 ± 5.62) ($p < 0.01$). Meanwhile, in the subgroup that did not include simvastatin, the PASI score decreased between pretreatment and the 4th week from 11.86 ± 5.13 to 9.34 ± 5.01, respectively, which were not significantly different. This demonstrated that adding simvastatin (40 mg/d) to calcipotriol/betamethasone dipropionate ointment produced a significantly

beneficial effect in psoriatic treatment.

The anti-inflammatory and immune-modulatory effects of statins were identified as a potential experimental treatment for psoriasis in the 1990s. Meanwhile, some studies did not find any effect of statins on psoriasis [18], while others suggested that statins might be useful in the treatment of psoriasis and other dermatologic disorders [9]. We hypothesised that the inhibition of leukocyte function-associated-1 (LFA-1)-mediated adhesion of leukocytes to intercellular adhesion molecule-1 (ICAM-1) or the inhibition of pro-inflammatory mediators produced clinical effects [19], [20].

A variety of mechanisms of cholesterol level modulation produced beneficial effects on psoriasis lesions, including (1) the downregulation of LFA-1, (2) the inhibition of leukocyte-endothelial adhesion, (3) extravasation and natural killer cell activity, (4) the inhibition of pro-inflammatory cytokines such as tumour necrosis factor-alpha and interleukin-1 and -6, (5) lowering the level of C-reactive protein, (6) the promotion of Th1 to Th2 cells and (7) the inhibition of Th1 cytokine receptors on T cells. As mentioned above, the activation of lymphocytes was limited and consequently impaired infiltration into the cutaneous lesion [21]. This result improved plaque psoriasis, which was confirmed by a lower PASI score.

Few studies have reported that statins have been used specifically for the treatment of psoriasis. In 2007, Shirinsky et al. reported the efficacy of simvastatin in treating plaque psoriasis. Seven patients were prescribed simvastatin 40 mg/d and were assessed by the PASI and dermatology quality of life index (DLQI) at the 4th week and 8th week of treatment. After 8 weeks of treatment, they found a statistically significant improvement in the PASI score (47.34%) and DLQI score. Two patients achieved a 50 per cent PASI response, and two patients achieved a 75 per cent PASI response. Although there were many limitations of this study (small sample size, no control group), their results suggest that statins could have clinical benefits in plaque psoriasis treatment [22]. A double-blind study by Naseri M et al. recruited 30 patients with plaque psoriasis and divided them, two groups. One received oral simvastatin (40 mg/day) combined with a topical steroid (50% betamethasone in petrolatum) for 8 weeks, whereas the other group received oral placebo plus the same topical steroid. This study showed that the PASI score decreased significantly in both groups; however, the reduction in the PASI score was greater in patients who received simvastatin [23], which agrees with our results. Also, a study reported by Wolkenstein et al. disclosed that there was a decreased risk of psoriasis associated with the use of oral statins [24], [25], [26], [27].

In conclusion, the limitations of our study included small sample size, a lack of blinding to treatment, and a lack of assessment of recurrence. Nevertheless, our study found that oral simvastatin could enhance the effect of topical therapy in psoriatic treatment. Considering the safety and benefits of statins, we suggest that statins are worth researching for their dual effects in psoriatic treatment, including decreasing the atherosclerotic disease burden through their lipid-lowering effects and decreasing psoriatic disease activity through their anti-inflammatory, immunomodulatory properties.

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Superantigens of *Staphylococcus Aureus* Colonization in Atopic Dermatitis and Treatment Efficacy of Oral Cefuroxim in Vietnamese Patients

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Abstract

BACKGROUND: Atopic dermatitis (AD) is a common, chronic, relapsing, genetically determined inflammatory skin disorder. Staphylococcus aureus (S. aureus) plays an important role in the pathogenesis of AD. Atopic skin is susceptible to infection with *S. aureus*.

AIM: This study was aimed to compare the skin *S. aureus* colonisation status and its secretion of superantigens in adult AD and healthy subjects and to evaluate the efficacy of two treatment regimens (oral cefuroxime plus topical betamethasone dipropionate 0.05% versus topical betamethasone dipropionate 0.05%) in AD patients.

METHODS: A group of 128 AD and 40 healthy subjects were recruited in this study and treatment efficacy was assessed by the SCORAD score.

RESULTS: *S. aureus* was found in skin lesions in 83.8% of AD patients while only 37.5% of healthy subjects possessed this kind of bacteria in the external nares ($p < 0.001$). Superantigen production was more common in *S. aureus* strains isolated from AD than the control group (58.6% versus 6.6%, $p = 0.0006$) and staphylococcal enterotoxin B was predominant (88.89%). 68 AD patients who had positive cultures with *S. aureus* were included in a clinical therapeutic trial. The isolated bacteria were all sensitive to cefuroxime. Patients were randomised to receive either oral cefuroxime 500 mg b.i.d. Plus topical betamethasone dipropionate 0.05% twice daily for 2 weeks (so-called group 1, 36 patients) or only topical betamethasone dipropionate 0.05% twice daily for 2 weeks (so-called group 2, 32 patients). The mean SCORAD scores of group 1 at baseline and after 1 and 2 weeks of treatment were 44.61, 26.69 and 16.61, respectively. The corresponding values for group 2 were 43.03, 32.53 and 23.41, respectively.

CONCLUSION: The reduction in SCORAD scores was significantly higher in group 1 than group 2 in comparison to the baseline value of each study group ($p = 0.003$ after 1 week and $p < 0.001$ at the end of treatment).

Introduction

Atopic dermatitis is a common chronic inflammatory skin condition. The prevalence varies from 10% to 20% of children. The aetiology and pathogenesis of AD have not been completely understood, leading to many problems in its management. High recurrence rates contribute to increasing the prevalence of AD.

In the late 20th century, Cork [1], Abeck [2], and Shuichi [3] found that *S. aureus* plays a very important role in the pathogenesis of AD through the production of superantigens including staphylococcal enterotoxins A and B, and toxic shock syndrome toxin-1 [4], [5], [6]. These superantigens penetrate the skin barrier and contribute to the persistence and exacerbation of skin inflammation through the stimulation of massive T cells [7], [8].

Materials and Methods

Study populations: 128 AD patients were enrolled in our study during their visits to the Hospital of Dermato-Venereology in Ho Chi Minh City from August 2010 to August 2012. There was no selection of patients by gender, localisation and severity of lesions. Voluntarily informed consents in writing were obtained from all participants. AD was diagnosed according to Hanifin and Rajka's criteria, and AD severity was based on the SCORAD index. Clinical symptoms and SCORAD scores were regularly monitored at the end of week 1 and 2, and the culture of skin lesions was carried on at the end of week 2. The control group consisted of patients without personal or family history of skin or allergic diseases who visited the Dermatological Outpatient Clinic for other reasons during the same period.

AD patients were all over 12 years old and didn't have any infected skin lesions. Those who had positive cultures with *S. aureus* were recruited in a clinical therapeutic trial. All isolated bacteria were sensitive to cefuroxime on the antimicrobial susceptibility test. Patients were equally randomised to receive either oral cefuroxime 500 mg b.i.d. Plus topical betamethasone dipropionate 0.05% twice daily for 2 weeks (so-called group 1) or only topical betamethasone dipropionate 0.05% twice daily for 2 weeks (so-called group 2). A total of 74 AD patients were eligible for this clinical trial (37 patients in each group).

Exclusion criteria included treatment with topical antibiotics in the past two weeks; oral or intravenous antibiotic treatment in the previous 4 weeks; presence of severe heart, liver, lung diseases, or immunodeficient condition (AIDS, diabetes mellitus, utilization of immunosuppressive drugs...), pregnancy or breastfeeding status; history of side-effects related to the use of corticosteroids (skin atrophy, vasodilation, hirsutism); allergy to study drugs (either betamethasone dipropionate 0.05% or cefuroxime); not adherence to treatment protocol (one patient in group 1 and five patients in group 2). Therefore, 36 patients in group 1 and 32 patients in group 2 gave the final data for analysis.

Isolation of S. aureus and identification of staphylococcal superantigens: S. aureus was cultured and identified from new skin lesions in AD patients and skin area around the nostrils in healthy subjects. Staphylococcal superantigens were tested by multiplex PCR (Polymerase Chain Reaction). Antimicrobial susceptibility tests were performed using the broth microdilution method for antibiotics: cefuroxime, ampicillin, ciprofloxacin, doxycycline, erythromycin, linezolid, tetracycline and vancomycin.

Statistics: Data were analysed by the EpiInfo software (version 2002). Qualitative variables were presented as frequency and percentage while quantitative variables as mean and SD. Categorical variables were compared using chi-squared or Fisher's exact test, as appropriate. RR and 95%CI (confidence interval) were also used to measure differences in the relationship of results. One-way ANOVA test was used to compare average scores of clinical symptoms and SCORAD index in two groups at baseline, after 1, 2 weeks of treatment. A p-value < 0.05 was considered to be statistically significant.

Results

A group of 128 AD patients consisted of 58.6% of males and 41.5% of females, mean age: 37.65 ± 14.09. Clinical manifestations (in decreasing order of frequency) included itching (100%), dry skin (78.91%), insomnia (75%), non-specific hand dermatitis (57.81%), cheilitis (47.56%), anterior neck folds (42.18%), white dermographism (40.62%), orbital darkening (26.56%), Dennie Morgan infraorbital folds (21.09%), pityriasis alba (18.75%), keratosis pilaris (18.75%), ichthyosis vulgaris (7.81%), nipple eczema (3.9%).

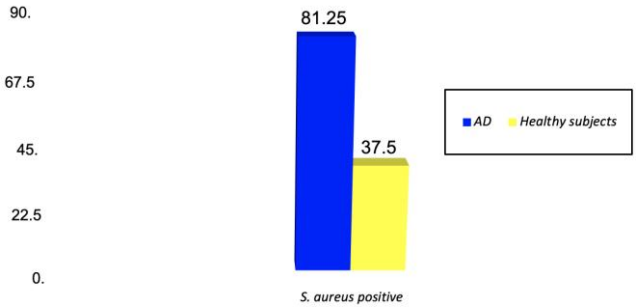

Figure 1: S. aureus was more commonly isolated from skin lesions in AD patients than on the perinotrils of healthy subjects (< 0.001, RR = 2.17, 95% CI 1.44-3.26)

The mean SCORAD score was 12.35 ± 40.55. AD severity was categorised as moderate in 44.53%, severe in 28.12%, and mild in 27.34% of patients. The rates of positive cultures with *S. aureus* in AD patients and healthy subjects were shown in figure 1 and the rates of *S. aureus* strains that secrete superantigens were shown in Figure 2.

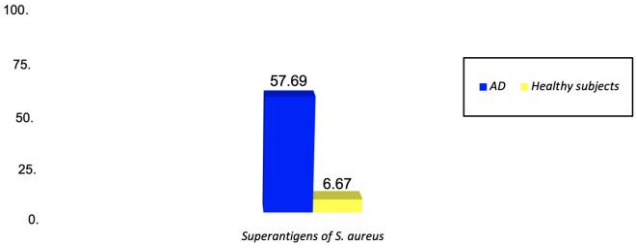

Figure 2: Superantigens were more commonly found from S. aureus strains isolated from AD patients than healthy subjects (p = 0.0006, RR = 8.65, 95% CI 1.29-57.9)

The efficacy of 2 treatment regimens was demonstrated in Table 1.

Table 1: Comparison of the therapeutic effect of the SCORAD index

SCORAD scores (Mean ± SD)	Group 1	Group 2	P values
At baseline	44.61 ± 8.34	43.03 ± 12.98	0.55
At the end of week 1	26.69 ± 6.05	32.53 ± 9.31	
At the end of week 2	16.61 ± 3.85	23.41 ± 7.49	
The difference in SCORAD scores			
Between baseline and end of week 1	-17.92	-10.5	0.003
Between baseline and end of week 2	-28	-19.62	< 0.001

After 2 weeks of treatment, 91.7% of group-1 patients achieved complete *S. aureus* elimination (negative culture) versus only 21.88% of group-2 patients (p < 0.001, RR = 5.1, 95% CI 2.57-10.12).

Discussion

Our study confirms that the proportion of *S. aureus* colonisation in AD patients was significantly higher than that in healthy subjects (p < 0.001, RR = 2.17, 95% CI 1.44 – 3.26), which is by other studies in the world [2], [3], [7]. In 1997, Goh [9] conducted a similar study on 33 AD patients in Singapore, showing that the rates of positive *S. aureus* detection were 89% in lesion areas, 42% in their healthy skin area, 55% in their outside nostril area, which were considerably higher than those in healthy group (5% in healthy skin area and 35% in outside nostril area).

There were 119 samples positive with *S. aureus*, including 104 samples taken from skin lesions of AD patients and 15 samples from the outside nostril of control subjects. All positive samples were tested by real-time PCR technique to find superantigen-encoding gene segments. Of 104 samples harvested from lesion areas, 60 samples were found to have superantigen-encoding genes, which was equivalent to 57.69%, whereas there was only 1 sample from healthy subjects having evidence of superantigen-encoding genes, which was equivalent to 6.67% (p = 0.0006, RR = 8.65; 95%CI 1.29 – 57.9). According to Breuer [9], the proportion of superantigen detection implemented by Latex methodology was 31%. In McFadden's study [10], 65% of *S. aureus* strains isolated from lesion areas of AD patients secrete superantigens.

The treatment efficacy between the two groups was assessed by the SCORAD index. Mean SCORAD scores at baseline were comparable between group 1 and 2 (p = 0.55). At the end of week 1, mean SCORAD scores decreased to 26.69 ± 6.05 (difference in-17.92 points) in group 1 and 32.53 ± 9.31 (difference in-10.05 points) in group 2. At the end of week 2, mean SCORAD scores continued to decrease to 16.61 ± 3.85 (difference in -28 points from baseline) in group 1, and 23.41 ± 7.49 (difference in -19.62 points from baseline) in group 2. The extent of SCORAD reduction within each group was statistically significant. SCORAD reduction was significantly greater in group 1 than group 2 either at the end of week 1 or week 2 (p = 0.003 and p < 0.001, respectively), which indicated that oral antibiotics in combination with topical corticosteroids lead to a higher decrease in SCORAD index compared to merely topical corticosteroids. This finding is in line with Boguniewicz's study [11].

The therapeutic regimen that associates oral antibiotics and topical corticosteroids also had a significantly higher rate of *S. aureus* elimination at the end of treatment (91.7% in group 1 versus 21.88% in group 2, p < 0.001, RR = 5.1, 95%CI 2.57 – 10.12). This finding is also in consistency with Weinberg's study [12].

In conclusion, *S. aureus* is the predominant pathogen among patients with AD, colonising much more frequently in AD patients than healthy people. *S.aureus* in AD patients also tends to produce superantigens much more frequently than healthy people. The oral cefuroxime combination with betamethasone dipropionate 0,05% is more efficacious than betamethasone dipropionate 0.05% alone in the treatment of AD patients in the first two weeks.

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Antifungal Susceptibility of Dermatophytes Isolated From Cutaneous Fungal Infections: The Vietnamese Experience

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Keywords: Cutaneous dermatophytosis; Dermatophytes; Antifungal resistance

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Abstract

AIM: Evaluate the resistance of dermatophytes to systemic antifungal drugs in the Vietnamese population.

METHODS: We enrolled 101 patients with cutaneous dermatophytosis at the Dermato-Venereology hospital in HCMC from August 2016 to March 2017. All the specimens were subjected to direct examination (10% KOH mount) and culture on Sabouraud dextrose agar. In vitro antifungal sensitivity testing was done on species isolated from a culture with broth microdilution method.

RESULTS: Direct microscopy was positive for dermatophytes in all patients. However this pathogen was found in fungal cultures in only 61.38% of patients. The main causative agent isolated was *Trichophyton spp.* (90.3%), followed by *Microsporum spp.* (8%) and *Epidermophyton spp.* (1.7%). *Trichophyton spp.* Has shown resistance to fluconazole, griseofulvin, ketoconazole, and itraconazole in 92.9%, 46.4%, 5.4% and 1.8% of strains, respectively. All Microsporum spp. Strains were found resistant to fluconazole and griseofulvin while resistance to ketoconazole was demonstrated in only 20% of strains and none of them was resistant to itraconazole. *Epidermophyton spp* strains were all resistant to fluconazole, griseofulvin, ketoconazole while none of them was resistant to itraconazole.

CONCLUSION: Based upon our results, Itraconazole shows the greatest probability of efficacy in the treatment of cutaneous dermatophytosis in Vietnamese patients.

Introduction

Dermatophytes are the most common cause of superficial cutaneous mycoses. *Dermatophytosis* are extremely frequent worldwide, affecting 20 – 25% of the global population [1], [2], [3]. *Dermatophytes* are divided into three genera: *Epidermophyton spp, Trichophyton spp, and Microsporum spp*. [2]. The treatment failure rate is increasingly encountered, leading to a prolonged or recurrent infectious status. Until now, studies on dermatophytes resistance to antifungal drugs have not been systemically performed in Vietnam.

Materials and Methods

Study population

This study was performed at the Dermato – Venereology hospital in HCMC where 101 patients with clinical signs and symptoms of dermatophytosis and positive direct wet method for dermatophytes by 10% KOH were enrolled, from August 2016 to March 2017.

Fungal identification and in-vitro antifungal sensitivity testing

Skin scrapings were collected from the edges of the lesions and transported immediately to the laboratory. All the specimens were subjected to direct examination by 10% KOH mount and culture on Sabouraud dextrose agar (SDA) for fungal determination, using MALDI – ToE technique. Antifungal sensitivity testing was done with Mueller – Hinton sterile agar plates separately containing itraconazole, fluconazole, griseofulvin and ketoconazole, at Mycological Department of Mycology of the Pham Ngoc Thach University of Medicine. Results of the antifungal susceptibility test were analysed according to the National Committee for Clinical Laboratory Standards (NCCLS).

Statistical analysis

Data were collected, tabulated, and analysed using SPSS version 16.0.

Results

Patients' mean age was 32.4 ± 16.7; males constituted 58.4% of participants.

Table 1: Fungal culture results from 101 patients with cutaneous dermatophytosis

	N	Percentage
Trichophyton spp.	56	90.3%
Microsporum spp.	5	8%
Epidermophyton spp.	1	1.7%

Clinical presentations consisted of itching (77.2%) usually in combination with scaly, well-defined, polygonal erythematous plaques. Culture results showed in Table 1 and Table 2.

Table 2: Identification of Trichophyton spp.

Trichophyton spp.	N	Percentage
Trichophyton rubrum	22	39.2%
Trichophyton tonsurans	18	32.1%
Trichophyton mentagrophytes	11	19.6%
Trichophyton equinum	1	1.8%
Trichophyton Sudanese	1	1.8%
Trichophyton violacecum	2	3.6%
Trichophyton schoenleinnii	1	1.8%
Total	56	100%

Antifungal susceptibility of *Trichophyton spp.* Showed in Table 3.

Table 3: In vitro antifungal susceptibility testing for Trichophyton spp.

Antifungal drugs	Sensitive (%)	Resistant (%)	Intermediate (%)
Itraconazole	98.2	1.8	0
Ketoconazole	91.1	5.4	3.6
Griseofulvin	50.6	46.4	0
Fluconazole	5.4	92.9	1.8

All *Microsporum spp.* Strains were found resistant to fluconazole and griseofulvin while resistance to ketoconazole was demonstrated in only 20% of strains and none of them was resistant to itraconazole. *Epidermophyton spp.* strains were all resistant to fluconazole, griseofulvin, ketoconazole while none of them was resistant to itraconazole.

Discussion

In our study, KOH mount was positive in all patients (100%) whereas culture was positive with *dermatophytes* in only 62 patients (61.38%). Ilkit's study found 94% of positive direct microscopy and 76% of positive culture [4]. The positive culture rate in Silva's study was lower (45.3%) [5]. In the species of *dermatophytes* in this study as results of Teklebirhan, Rezaei – Matehkolaei and Chadeganipour, *Trichophyton spp* and *T. rubrum* accounted for the highest proportion in dermatophytosis [6], [7], [8], [9], [10].

Our study showed that *Trichophyton spp.* resisted to fluconazole (92.9%), griseofulvin (46.4%), ketoconazole (5.4%), and itraconazole (1.8%), *Microsporum spp.* resisted to fluconazole and griseofulvin (100%), ketoconazole (20%). Non of them had resistance to itraconazole. All the *Epidermophyton spp.* resisted to fluconazole, griseofulvin and ketoconazole. None of them had resistance to itraconazole. No similar data exist in the medical literature for comparision with our study.

In conclusion, *Trichophyton spp.* are the most common cause of cutaneous dermatophytic infections (90.3%). Itraconazole is recommended in the treatment of skin dermatophytosis because of its excellent sensitivity to almost dermatophytic species.

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Clinical Science

Effectiveness, Safety and Tolerance of Methotrexate in Vietnamese Psoriatic Arthritis Patients

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Keywords: Psoriatic arthritis (PsA); Disease activity score (DAS)

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Abstract

AIM: To access the effectiveness, safety and tolerance of methotrexate (MTX) in psoriatic arthritis (PsA) treatment.

METHODS: We recruit 37 patients, admitted at HCMC Hospital of Dermato-Venereology from 1/2016 to 3/2017, with MTX dosage ranging from 10 mg to 15 mg per week.

RESULTS: Skin lesion response after 12 weeks improved PASI 50: 40.5%, PASI 75: 24.3%. Disease activity score decreased after 12 weeks with ΔDAS28 = -1.43 + 0.79, 37.8% PsA achieved complete remission. Nausea and vomiting were 8.1%. These symptoms were mild and transient. We did not stop MTX usage. The rate of elevating SGPT 2-3 times as much as the upper limit of the normal range was 2.7%.

CONCLUSION: We finally demonstrated that the rate of treatment response in Vietnam is the same as demonstrated by foreign authors in other countries.

Introduction

The incidence rate of psoriatic arthritis is 6-42%. Among drugs treating psoriatic arthritis, methotrexate (MTX) is approved by the Food and Drug Administration (FDA) in psoriatic arthritis treatment. Although the efficacy of MTX is variable among researches, it is the drug recommended by European League against Rheumatism-EULAR for moderate and severe psoriatic arthritis treatment [1].

Methods

Because of the absence of research or summary report on MTX in the treatment of psoriatic arthritis in Vietnam, we recruited 37 psoriasis arthritis patients, Between January 2016 to March 2017, admitted to HCMC Hospital of Dermato-Venereology.

Results

Female made up the majority (67.57%), more than male. 15.6% of patients had the family history of psoriasis as shown in Table 1.

Table 1: Characteristic of samples

Characteristic	Distribution
Sex: n (%)	
Male	12(32.43)
Female	25(67.57)
Age: mean (SD), year	48(13)
Family history: n (%)	7(18.2)
PA duration: median, year	1(1-8)
Habit:	
Smoking: n (%)	3(8.11)
Drinking: n (%)	7(18.9)
Swollen joints: median	2(1-18)
Painful joints: median	1(1-14)
ESR. mm/h: median	50(14-158)
Pain, 100 mm VAS: median	30(10-80)
First sign:	
Skin psoriasis: n (%)	26(70.27)
Arthritis: n (%)	10(27,03)
Skin psoriasis and arthritis at the same time: n (%)	1(2.7)
Nail dystrophy: n (%)	31(83.78)
Joint deformity: n (%)	15(37)
Peripheral arthritis: n (%)	30(81.08)
Sacroiliitis: n (%)	2(5.41)
Spinal arthritis: n (%)	6(16.22)
Distal interphalangeal joint arthritis: n (%)	13(35.14)
HLA B27(+): n (%)	12(32.4)
HLA Cw06(+): n (%)	1(2.7)
HLA DR7(+): n (%)	12(32.4)

Most cases (70.27%) had skin psoriasis before arthritis. Joint deformity rate was high (37.0%). Peripheral arthritis rate was also significant (81.08%), and the next was distal interphalangeal joint arthritis (31.3%). Nail dystrophy was also familiar (83.78%). Positive HLA-B27 and HLA-DR7 percentage was 32.5% and 32.4% respectively while the positivity for HLA Cw06 in our research was 2.7%.

Every patient stopped therapy with NSAIDs (non-steroidal anti-inflammatory drugs) and with DMARD (disease-modifying antirheumatic drug) at least 2 weeks and 1 month before, respectively.

After 12 weeks treatment by MTX, at dosage 10-15mg PO q12hr for 3 sequential doses per week. 5 mg Folic acid was used 24 hours after taking MTX; skin lesions were improved. 40.5%, 24.3% and 37.8% achieved PASI 50, PASI 75 and PASI 90, respectively as shown in Table 2, in comparison with Laura's study in which 27.2% patients reached PASI 75 [2].

Table 2: Efficacy of MTX in the treatment of psoriasis

Treatment monitoring indexes	Before treatment		After 4 weeks		After 8 weeks		After 12 weeks	
	n	%	n	%	n	%	n	%
PASI								
PASI 50			4	10.8	10	27.0	15	40.5
PASI 75			1	2.7	5	13.5	9	24.3
PASI 90			0	0.0	4	10.8	6	16.2
DAS 28								
> 5.1	11	29.7	6	16.2	0		0	
From 3.2 to 5.1	20	54.1	20	54.1	21	56.8	16	43.2
From 2.6 to <	6*	16.2	4	10.8	6	16.2	7	18.9
5.1	0	0	7	18.9	10	27.0	14	37.8
< 2.6								
ΔDAS28				-1,4 ± 0,8				

(*) *Psoriatic arthritis with bad prognosis: ≥ 5 joints are affected, damage on X-ray, severe inflammatory reaction, injury beside joints, especially dactylitis.*

At week 8, 27% psoriatic arthritis patients achieved remission (Table 2), no severe arthritis patients left. After 12 weeks, 37.8% of patients reached alleviation, which is compatible with the study of Laura et al. in which 22.4% patients accomplished complete remission.

The side effects at week 12 were mostly nausea and vomiting (8.1%). Fatigue and alopecia had the same rate (2.7%). These side effects were transient, and there was no need for treatment. Other side effects noted were elevated SGPT (2.7%), hemoglobin decreased (2.7%), neutropenia (2.7%) (Table 3).

Table 3: The abnormality on subclinical tests

Side effects	n	%
Fatigue	1	2.7
Nausea/Vomiting	2	5.4
Alopecia	1	2.7
Fever/Chill	0	0
Pneumocitis	0	0
SGPT elevation		
1.5 – 2 ULR* (60 – 80 U/L)	2	5.4
>2 – 3 ULR* (81 – 120 U/L)	1	2.7
Hemoglobin decrement above 2 g/dL	1	2.7
White blood cells below the normal range (< 5.0 x10^9/L)	1	2.7
Neutrophils below the normal range (< 1,8 x 10^9/L)	1	2.7
Platelets below the normal range (< 140 x 10^3/L)	0	0

(*) ULR: The upper limit of the normal range.

Discussion

Female was twice as likely as a man to get psoriatic arthritis, which was higher than the result of Reich's study suggesting the proportion of males was 58% [3]. This difference may be the characteristic of psoriatic arthritis in Vietnam because psoriasis relates to genetic and races.

Joint deformity rate was also significant (37%) which was higher than the rate suggested in Moll and Wright research, 5% [4]. Nail dystrophy rate was 83.78% which was compatible with those of Scarpa, 63% [4] So patient with psoriasis vulgaris having nail change should be monitored to discover arthritis. The psoriatic arthritis duration was about 0.8 (0.1-2.9) year on median which is lower than the study of Gabrielle et al., (1-5) year on median) [5]. So most of our patients had suffered from prolonged arthritis before we did our research.

Based upon our and published experiences, MTX is effective and affordable in psoriatic arthritis, affecting both skin lesions and joint damage. The price is more affordable than many biologic agents [6], [7], [8], [9], [10], [11], [12].

We finally demonstrated that the rate of treatment response in Vietnam is the same as demonstrated by foreign authors in other countries.

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Successful Psoriasis Treatment Using NB-UVB with Methotrexate: The Vietnamese Experience

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Keywords: Psoriasis vulgaris; Narrowband ultraviolet B; Methotrexate

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Abstract

AIM: To compare the effectiveness of narrowband ultraviolet B (NBUVB) and oral methotrexate (MTX) to oral MTX alone in Vietnamese psoriasis patients, from May 2016 to May 2018.

METHODS: We conducted a non-randomized trial on 70 patients with plaque-type psoriasis of moderate to severe. Thirty-five patients apply NBUVB once/day in 5 days/week for 4 weeks plus oral MTX 7.5 mg/week and 35 patients oral MTX 7.5 mg/week and both two groups treatment for 3 months. The extent of the lesion was assessed by the Psoriasis Area and Severity Index (PASI).

RESULTS: The proportion of decreasing PASI was comparable (68.49% in NBUVB and MTX versus 57.62% in MTX alone); $p < 0.05$. Inside, good 28.58%, moderate 68.57% and poor 2.85% in NBUVB and MTX better than good 2.85%, moderate 71.4% and poor 25.72% in MTX alone; $p < 0.05$. The recurrence rate after 24 months of the NBUVB and MTX group (42.9%) was lower than the MTX alone group (71.4%); $p < 0.05$.

CONCLUSION: NBUVB and oral MTX have affected treatment with chronic plaque psoriasis better than oral MTX alone.

Introduction

Psoriasis is a chronic skin disease. It happens to every gender, age and race develops in 1-3% world population [1]. The pathology of this disease is not fully understood. Until now, most authors consider it has a genetic base and autoimmune mechanism started with psychological distress, environment, infection, where Th17 and Th1 play a key role [2]. There are many methods and drugs used to treat psoriasis: topical ones, such as coal tar, salicylic, corticoid; systemic therapies like MTX, cyclosporine and biological drugs.

Narrowband ultraviolet B (NBUVB) have shown effectiveness in psoriasis treatment, few side effects, children tolerance and inexpensiveness. The result will be more promising if we combine the therapy with retinoid or MTX.

In Vietnam, the psoriasis treatment with NBUVB (UVB-311nm) in combination with low dose MTX has not been studied or reported. Because of this reason, our research evaluates the efficacy of this combination therapy.

Material and Methods

Study design

We conducted a non-randomized controlled trial on adults with chronic plaque-type psoriasis, from moderate to severe.

Including criteria: Patients with Fitzpatrick skin photo-types III and IV, age > 16 with no contraindication for UVB and MTX.

Excluding criteria: mild psoriasis and patients with contraindication for UVB and MTX.

Sample size: according to the formula of World Health Organization:

$n_1 = n_2 = \{[_{Z1\text{-}a/2}Ö[2P(1 - P) + Z_bÖP_1(1 - P_1) + P_2(1 - P_2)]\}^2 / (P_1 - P_2)^2$

n_1: Sample size of experimental group 1; n_2: Sample size of control group 2

$_{Z1\text{-}a/2:}$ reliability coefficient 95% (= 1,96); Z_b: validity (= 1,645)

$_{P1}$: percentage of good patients in NBUVB plus MTX group: estimation from previous studies was 85% (0.85); P_2: percentage of good patients in MTX alone: estimation from previous studies w as 55%. $P = P_1 + P_2/2$. Sample size of group 2 ($n_1 = n_2$) = 30 patients.

Treatment procedure

NBUVB and MTX group: Initial UVB dose was 500 mJ, increased after each treatment of 100 mJ until reaching minimal erythema dose or maximum dose, which was 2000 mJ. Lighted once a day, 5 consecutive days/week (from Monday to Friday) in association with methotrexate 7.5 mg/week on a fixed day, after dinner and phisiogel, twice a day, for four weeks. *MTX alone group:* Methotrexate 7.5 mg/week on a fixed day, after dinner and phisiogel twice a day for four weeks.

Both groups were treated for 4 weeks according to the study's guideline. After discharging both two groups continued oral MTX 7.5 mg/week until week 12. Monitoring for recurrence after 16 weeks and 24 weeks.

Applied techniques

To evaluate the disease activity according to PASI [3] $PASI = 0,1(E_H + I_H + D_H)A_H + 0,2(E_U + I_U + D_U)A_U + 0,3(E_T + I_T + D_T)A_T + 0,4(E_L + I_L + D_L)A_L$

Level :3 levels according to PASI: mild PASI: < 10, moderate: PASI: < 20, severe: PASI: ≥ 20. Evaluating the outcome: clinical improvement was evaluated through percentage decrease of PASI by using this formula:

% PASI = PASI before treatment-PASI after treatment/ PASI before treatment x 100

5 levels: very good: PASI decreases 100%; good: PASI decreases 75% - 99%; fair: PASI decreases 50 % ≤ 75%; moderate: PASI decreases 25% ≤ 50% and poor: PASI decreases < 25%.

Results

We recruited 35 patients from May 2016 to May 2018, to the NBUVB and MTX group and 35 to the oral MTX alone. Table 1 shows the baseline characteristics of the two groups, with no significant difference.

Table 1: Comparing the characteristics of the 2 groups. Note: the characteristics of 2 groups was similar, p > 0.05

Index	Experimental group	Control group	P
Mean age	51.46 ± 8.9	52.03 ± 9.3	> 0.05
Gender: male/female	30/5	30/5	> 0.05
Disease activity: moderate/severe	23/12	27/8	> 0.05

The treatment outcome of NBUVB and MTX group shows the proportion of decreasing PASI 68,49%, better than MTX alone (57.62%); p < 0.05 as shown in Table 2.

Table 2: Comparing the general outcome of 2 groups

Group	n	PASI before treatment	PASI after 4 weeks of treatment	PASI decrease	
				Number	%
NBUVB + MTX group	35	17.39 ± 6.3	5.48 ± 2.6	11.91	68.49
MTX alone group	35	16.66 ± 5.2	7.06 ± 2.8	9.6	57.62
p			< 0.05		

Note: The treatment outcome of NBUVB plus MTX group was better than MTX alone group, with p < 0.05.

The treatment outcome of experimental group and control group was 88.57% and 74.28% respectively, p < 0.05. Inside, good 28.58%, moderate 68.57% and poor 2.85% in NBUVB and MTX better than good 2.85%, moderate 71.4% and poor 25.72% in MTX alone; p < 0.05 as shown in Table 3.

Table 3: Comparing the treatment outcome according to the evaluation levels of 2 groups

Result	NBUVB + MTX group	MTX alone group	p
Very good	0	0	
Good	10/35 (28.58%)	1/35 (2.85%)	
Moderate	24/35 (68.57%)	25/35 (71.43%)	< 0.05
Poor	1/35 (2.85%)	9/35 (25.72%)	
Total	35 (100%)	35 (100%)	

Note: The treatment outcome which was evaluated as good and moderate of NBUVB plus MTX group and MTX alone group was 88.57% and 74.28% respectively, p < 0.05.

The recurrence rate after 24 months of the NBUVB and MTX group (42.9%) was lower than the MTX alone group (71.4%); p < 0.05. The side effects of 2 groups: Red blood cells, white blood cells, platelets, AST, ALT, urea, creatinine of 2 groups before treatment and after treatment 4 weeks were in

normal range. 5 patients in the experimental group referred a headache: 2 nausea, 2 erythema while in the MTX alone group: 3 nausea, 3 a headache. No patients had to discontinue treatment because of these side effects.

Discussion

According to Table 2, the experimental group showed PASI decreased 68.82% from 17.39 to 5.48 after 4 weeks treatment in hospital. Methotrexate alone group, PASI decreased 57.62% from 16.66 to 7.06 after 4 weeks. In conclusion, both groups had treatment efficacy, but NBUVB and MTX group were better than the control group, $p < 0.05$. Combined NBUVB and methotrexate were more promising than methotrexate alone in psoriasis treatment, but recurrence after 3 months, 6 months of 2 groups was not different [4]. Our study outcome was similar to Soliman et al. research, demonstrating that methotrexate and NBUVB are superior to methotrexate alone.

In Mahajan et al., study (2010) experimental group achieved PASI-75 faster than the control group, which used only UVB and placebo [5]. In conclusion, Mahajan's study result was not different from our research showing that the combination is more effective than NBUVB or methotrexate alone. According to Wolf et al., (2012), a combination of NBUVB and ustekinumab showed a better result than ustekinumab alone [6], and NBUVB with adalimumab demonstrated the same result [7]. According to Paul et al-1982, methotrexate plus UVB for 26 psoriasis vulgaris patients cleared lesions faster and decreased the dose of both methotrexate and UVB [8].

Evaluating the clearance of lesions or PASI decrease, table 3 showed that NBUVB and low dose methotrexate group and methotrexate alone group had good (28.58% and 2.85%), moderate (68.57% and 71.43%) and poor (2.85% and 25.72%) result, respectively. In conclusion, NBUVB plus MTX group had a better response than MTX alone group, $p < 0.05$. We think this result is suitable for the indication of these drugs. Moreover, in clinical practice, we used NBUVB for mild and moderate patients achieving good results. So moderate and severe patients used methotrexate even low dose can still acquire good response because both treatments inhibit interferon gamma and Th17 [9], [10], [11].

After four weeks treatment, the mean value of tests involving hematopoietic function (red blood cells, white blood cells, platelets), liver function (AST, ALT), kidney function (urea, creatinine) of both groups before and after treatment, were in normal range. Side effects included nausea, headache, erythema and pruritus happened in a few patients, and no one had to stop the treatment.

The recurrence rate after 24 weeks of the control group was 71.4% higher than the experimental group (42.9%). This difference had statistical significance with $p < 0.01$. These results showed that NBUVB plus methotrexate has not only better efficacy but also longer disease stability than methotrexate only. In literature, NBUVB is effective in psoriasis and had few side effects and can use for both children and pregnancy.

In conclusion, NBUVB and oral MTX have affected treatment better than oral MTX alone with chronic plaque psoriasis in Vietnam.

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The Decline of PUVA Therapy in Vietnam: Effective Treatment of Narrow Band UVB in Vietnamese Vitiligo Patients

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Keywords: Vitiligo; NB-UVB; PUVA; Phototherapy

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Abstract

AIM: To examine the efficacy and safety of Narrowband ultraviolet B (NB-UVB) in Vietnamese vitiligo patients.

METHODS: We recruited thirty-one patients (14 males, 17 females), aged from 7 to 67 years, with both segmental vitiligo (SV) and non-segmental vitiligo (NSV), treated three times weekly with NB-UVB. The starting dose for adults from 15 years old and children less than 15 years old was 200 mJ/cm^2 and 150 mJ/cm^2, respectively, with 50 mJ/cm^2 and 20 mJ/cm^2 dose increments at each subsequent visit, respectively, until mild erythema lasting less than 24 hrs reported by patient, given for a period of 6 months. Response to therapy was assessed based on VASI score changes.

RESULTS: Based upon our results, 38.7% (12/31) of patients achieved a very good response of more than 50% VASI changes, 41.9% (13/31) obtained a good response (VASI changed from 25 to 50%). Total good and very good response to therapy significantly increased with prolonged treatment, increasing from 19.4% to 64.5% and 80.6% after 2, 4 and 6 months, respectively. Localised NSV patients obtained good and very good response significantly more frequently than generalised NSV (55.6% versus 18.2%). Adverse effects were minimal, of which one case developed herpes simplex, and 4 cases reported mild photo burn reaction which completely disappeared after adjusting the dose.

CONCLUSION: NB-UVB therapy is an effective and safe tool in the management of Vietnamese vitiligo patients.

Introduction

Vitiligo is a common, chronic, acquired cutaneous de-pigmentation disorder with *serious emotional* and *psychological consequences* [1], [2]. There are many possible conventional or unconventional therapeutic choice for the treatment [3], [4]. Narrow-band ultraviolet B (NB-UVB) is one of the best treatment modality for vitiligo because of its safety, effectiveness and non-evasive nature, promoting stabilisation of the depigmenting process and stimulation of residual follicular melanocytes [5].

The present study aims to examine the efficacy and safety of NB-UVB therapy in Vietnamese vitiligo patients, attending the Vietnam National Hospital of Dermatology and Venereology from October 2016 to September 2017.

Methods

A total of 31 vitiligo patients (14 males, 17 females; 28 with Fitzpatrick skin's type IV and only 3 patients with Fitzpatrick skin's type III), mean age 30 years old. The majority of patients (29/31) had NSV, and only 2 patients had SV.

Local NB-UVB 311 nm irradiation was indicated for vitiligo patients with 2% and less than 2% body surface involved (12 patients). Whole body NB-

UVB 311 nm irradiation was indicated for those with more than 2% body surface involved (19 patients). Patients were treated with thrice-weekly exposures on non-consecutive days. The starting dose for adults from 15 years old and children less than 15 years old was 200 mJ/cm^2 and 150 mJ/cm^2, respectively, with 50 mJ/cm^2 and 20 mJ/cm^2 dose increments at each subsequent visit, respectively, until mild erythema lasting less than 24 hrs reported by patient, given for a period of 6 months. The response to NB-UVB therapy was examined based on changes of vitiligo area severity index (VASI) after treatment, which took into account of both percentage of re-pigmentation and the reduction of lesion's area [6].

Results

After 6-month treatment, 38.7% obtained a very good response, 41.9% patients achieved a good response, the proportion of poor, very poor and no response was equally and accounted for only 6.5% as shown in Figure 1.

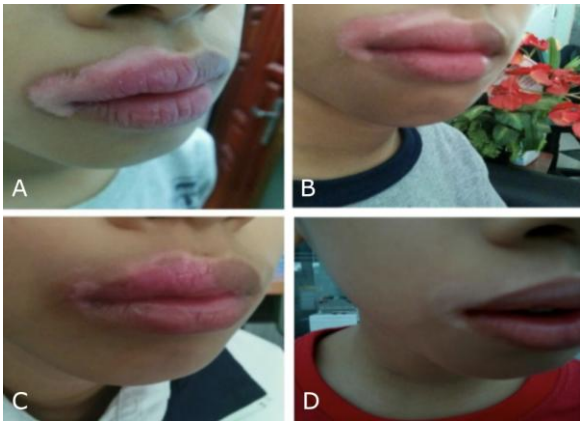

Figure 1: A case of 10 years old male with very good response to therapy: (a) before treatment, (b) after 2 months -VASI decreased 16.4%, (c) after 4 months - VASI decreased 58%, (c) after 6 months VASI decreased 95%

Association between response to therapy and the duration of the treatment was shown in Figure 2.

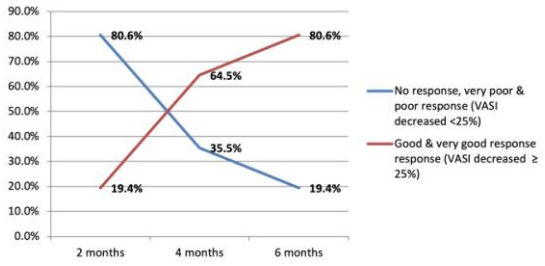

Figure 2: Association between response to therapy and the duration of the treatment

Among 31 patients, total good and very good response to therapy were significantly associated with prolonged treatment, increasing from 19.4% to 64.5% and 80.6% after 2, 4 and 6-month treatment, respectively. Association between response to therapy and localised or generalised NSV was shown in Figure 3.

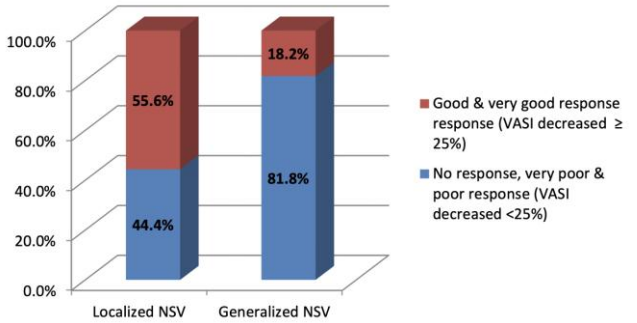

Figure 3: Association between response to therapy and localised or generalised NSV

Total good and very good response to therapy was observed in localised NSV significantly more frequently than in generalised NSV patients (55.6% versus 18.2%). This difference is statistically different.

In our study, good and very good response to therapy significantly increased with prolonged treatment and was observed in localised NSV significantly more frequently than in generalised NSV patients, which are consistent with previous studies [7], [8], [9], [10]. The actual good and very good response rate to therapy will properly be higher if the evaluation time is longer than 6 months. Adverse effects in our study were minimal which is similar to that reported in the literature.

In conclusion, our study proves that NB-UVB therapy is an effective and safe tool in the management of Vietnamese vitiligo patients. Further study is recommended to prolong the treatment duration and follow up the stability of re-pigmentation.

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The Efficacy of a Two-Fold Increase of H1-Antihistamine in the Treatment of Chronic Urticaria - the Vietnamese Experience

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Keywords: Chronic urticaria; Chronic idiopathic urticaria; Antihistamine; Fexofenadine; Levocetirizine

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Abstract

BACKGROUND: Chronic urticaria, a mast cell-driven condition, is common, debilitating and hard to treat. H1-antihistamines are the first line treatment of chronic urticaria, but often patients do not get satisfactory relief with the recommended dose. European guidelines recommend increased antihistamine doses up to four-fold.

AIM: We conducted this study to evaluate the efficacy of increased H1-antihistamine doses up to two-fold in Vietnamese chronic urticaria patients.

METHODS: One hundred and two patients with chronic urticaria were recruited for treatment with levocetirizine (n = 52) or fexofenadine (n = 50). Treatment started at the conventional daily dose of 5 mg levocetirizine or 180 mg fexofenadine for 2 weeks and then increased to 10 mg levocetirizine or 360 mg fexofenadine for 2 weeks if patients did not have an improvement in symptoms. At week 0, week 2 and week 4 wheal, pruritus, size of the wheal, total symptom scores, and associated side-effects were assessed.

RESULTS: With the conventional dose, the total symptom scores after week 2 decreased significantly in both groups compared to baseline figures, i.e. 7.4 vs 2.3 for levocetirizine group and 8.0 vs 2.6 for fexofenadine group ($p < 0.05$). However, there were still 26 patients in each group who did not have improvements. Of these 26 patients, after having a two-fold increase of the conventional dose, 11.5% and 38.5% became symptom-free at week 4 in levocetirizine group and fexofenadine group, respectively. At week 4 in both groups, the total symptom scores had significantly decreased when compared with those at week 2 (2.8 ± 1.5 versus 4.7 ± 1.6 in levocetirizine group; 2.1 ± 1.9 versus 5.1 ± 1.4 in fexofenadine group). In both groups, there was no difference in the rate of negative side effects between the conventional dose and the double dose.

CONCLUSION: This study showed that increasing the dosages of levocetirizine and fexofenadine by two-fold improved chronic urticaria symptoms without increasing the rate of negative side effects.

Introduction

Urticaria is an allergic reaction of the skin capillaries to many endogenous or exogenous allergens. This disease can be characterised by the formation of wheals, angioedema or both and can disappear within 24 hours [1]. Patients with urticaria often experience a sensation of itching or burning which can interfere with daily life. Based on chronology, urticaria is divided into acute and chronic. As opposed to acute urticaria, chronic urticaria is defined by recurrent episodes occurring at least twice a week for 6 weeks, possibly lasting for many months, or many years [2], [3], [4]. Urticaria is also classified as spontaneous and inducible with and without any specific eliciting factor involved. Chronic urticaria substantially impacts on a patient's quality of life with

an effect on both physical and mental health. Studies have shown that health status scores in chronic spontaneous urticaria patients are comparable to those with coronary artery disease [5].

The exact cause of urticaria is unknown, but there are some factors contributing to the development of the disease. In urticaria, mast cells are activated, release histamine and other mediators, which result in vasodilatation, inflammatory recruitment cells, as well as sensory nerve activation. The therapeutic approach to chronic urticaria involves the identification and elimination of its underlying causes, the avoidance of eliciting factors, tolerance induction, and/or the use of pharmacological treatment to prevent mast cell mediator release and/or the effects of mast cell mediators [1]. The main option in therapies aimed at symptomatic relief is to reduce the effect of mast cell mediators such as histamine and others on the target organs. Many symptoms of urticaria are mediated primarily by the actions of histamine on H_1-receptors located on endothelial cells (the wheal) and sensory nerves (neurogenic flare and pruritus). Thus, continuous treatment with H_1-antihistamines is of eminent importance in the treatment of urticaria. It is supported not only by the results of clinical trials but also by the mechanism of action of these medications [6], [7].

There have been some studies on the effectiveness of antihistamine and other drugs in the treatment of chronic urticaria with varying results. Mainstay therapeutics are antihistamines, which in chronic urticaria, shows poor response rates when used in standard dosage. The up-dosing of antihistamines to four-fold does improve the response rate [8], [1]. In Vietnam, conventional doses of H_1-antihistamine are widely used in the treatment of chronic urticaria, and in practice, the majority of patients have a good response to conventional doses. However, difficult-to-treat chronic urticaria patients remain a challenge and data on doses used for Vietnamese patients is scarce.

We conducted this study to evaluate the efficacy and safety of a two-fold increase of H_1-antihistamine (fexofenadine and levocetirizine) in the treatment of chronic urticaria.

Methods

From March to August 2013 we recruited 102 patients with chronic urticaria, aged 12 years and above at the National Hospital of Dermato-venereology. Exclusion criteria were: (1) urticaria with glottis oedema or accompanied by diarrhoea; (2) physical urticarial; (3) presence of other diseases such as liver, kidney, endocrine, psychiatric or systemic disease; (4) pregnant and lactating women; (5) women taking contraceptive drugs; (6) patients who had taken antihistamines or steroids in the past 2 weeks; (7) the use of any other drugs during the treatment period; (8) patients with biochemical abnormalities. Biochemistry was tested at week 0 and week 4 including urea, creatinine, glucose, liver enzymes, cholesterol, and triglycerides.

One hundred and two patients with chronic urticaria were randomly recruited into 2 groups: 1) levocetirizine group (52 patients) and 2) fexofenadine group (50 patients). Treatment started at the conventional dose in each group. 5 mg levocetirizine daily for the levocetirizine group and 180 mg fexofenadine daily for the fexofenadine group. After 2 weeks if the symptoms were persistent, the patients were given a double dose.

The patients underwent clinical examinations. Each of the following symptoms was scored according to the Urticaria Activity Score (UAS) 4 [9] at week 0, week 2 and week 4.

Pruritus score: none: 0 points; mild: 1 point (present but not annoying or troublesome); moderate: 2 points (troublesome but did not interfere with sleep); severe: 3 points (severe pruritus, which is troublesome enough to interfere with normal daily activities or sleep)

Wheal score: none: 0 points; 1-19 wheals/24 hours: 1 point; 20-50 wheals/24 hours: 2 points; more than 50 wheals/24 hours or large confluent areas of wheals: 3 points.

We also scored the size of the biggest wheal as following: none: 0 points; less than 1.25 cm in diameter: 1 point; 1.25-2.5 cm in diameter: 2 points; more than 2.5 cm in diameter: 3 points.

Total symptom score: 0 points: free of symptoms; 1-3 points: mild; 4-6 points: moderate; 7-9 points: severe.

This study used SPSS statistical software (version 16.0) with the use of a t-test for quantitative variables and a χ^2 test for qualitative variables.

This study was approved by the hospital ethics board of National Hospital of Dermatology and Venereology in 2013. The investigator ensured that the study was conducted by the Declaration of Helsinki.

Results

The background characteristics of patients in the two groups were not significantly different as shown in Table 1.

The mean age of our patients was 36.2 years (aged 14-65) for the levocetirizine group and 39 years

(aged 12-68) for the fexofenadine group. None of the patients was at a mild level at week 0. There were 69.2% female patients in the levocetirizine group and 64% in the fexofenadine group. The majority of patients (73.2% in levocetirizine group and 46% in fexofenadine group) had suffered from urticaria from 6 weeks to 1 year.

Table 1: The background characteristics of the patients

	Levocetirizine group (n = 52)	Fexofenadine group (n = 50)
Age		
Mean	36.2 ± 0.5	39 ± 0.7
Range	14-65	12-68
≤ 20	7 (13.5%)	10 (20%)
21-40	29 (55.8%)	25 (50%)
41-60	14 (26.9%)	14 (28%)
≥ 61	2 (3.8%)	1 (2%)
Sex		
Male	16 (30.8%)	18 (36%)
Female	36 (69.2%)	32 (64%)
The duration of disease		
6 week-1 year	32 (73.2%)	23 (46.0%)
1-5 years	16 (30.8%)	14 (28.0%)
> 5 year	4 (7.7%)	13 (26.0%)

At week 0, total symptom scores were 7.4 ± 1.3 in the levocetirizine group and 8.0 ± 1.0 in the fexofenadine group. At week 2 (2 weeks after treatment with a conventional dose) the total symptom scores 2.3 ± 2.6 and 2.6 ± 2.8 respectively as shown in Table 2 had decreased significantly when compared with those at week 0.

Table 2: The symptom scores of the two group treated with a conventional dose at week 0 and week 2

	Levocetirizine (n = 52)		p	Fexofenadine (n = 50)		p
	Week 0	Week 2		Week 0	Week 2	
Pruritus	2.7 ± 0.8	0.9 ± 0.9	< 0.05	2.9 ± 0.2	1.0 ± 1.1	< 0.05
Wheal	2.2 ± 0.6	0.8 ± 0.9	< 0.05	2.5 ± 0.7	0.9 ± 0.9	< 0.05
Size of wheal	2.7 ± 0.5	0.7 ± 0.9	< 0.05	2.5 ± 0.7	0.8 ± 0.9	< 0.05
Total symptom score	7.4 ± 1.3	2.3 ± 2.6	< 0.05	8.0 ± 1.0	2.6 ± 2.8	< 0.05

However, at this point, there were still 26 patients in each group who were still not symptom-free. Their total symptom scores were 4.7 ± 1.6 in the levocetirizine group and 5.1 ± 1.4 in the fexofenadine group (p > 0.05) as shown in Table 3. These patients were treated with a double dose for 2 weeks. The patients who had recovered maintained their conventional daily dose and left our trial.

At week 4, we evaluated the remaining 26 patients who were treated with a double dose in each group. The result showed that total symptom scores were significantly reduced (Table 3).

Table 3: The symptom scores of the two groups treated with a double dose at week 2 and week 4

	Levocetirizine (n = 26)		p	Fexofenadine (n = 26)		p
	Week 2	Week 4		Week 2	Week 4	
Pruritus	1.7 ± 0.6	0.9 ± 0.7	< 0.05	1.9 ± 0.7	0.7 ± 0.9	< 0.05
Wheal	1.5 ± 0.8	1.0 ± 0.7	< 0.05	1.7 ± 0.6	0.7 ± 0.6	< 0.05
Size of wheal	1.4 ± 0.7	0.9 ± 0.4	< 0.05	1.5 ± 0.7	0.7 ± 0.6	< 0.05
Total symptom score	4.7 ± 1.6	2.8 ± 1.5	< 0.05	5.1 ± 1.4	2.1 ± 1.9	< 0.05

With 2.8 ± 1.5 in the levocetirizine group and 2.1 ± 1.9 in the fexofenadine group. Between the two groups, there was no statistically significant difference (p > 0.05). In the levocetirizine group at week 4, 11.5% of the patients had a resolution of symptoms, 61.5% with a mild form of the disease, 26.9% moderate and no patient was severe. In the fexofenadine group at week 38.5% of patients had a resolution of symptoms, the proportion of patients with a mild level was 26.9% (versus 23.0% before treatment), and a moderate level was 34.6% (versus 57.8% before treatment). There was no patient with a severe form of the disease at week 4 (versus 19.2% before treatment) as shown in Figure 1.

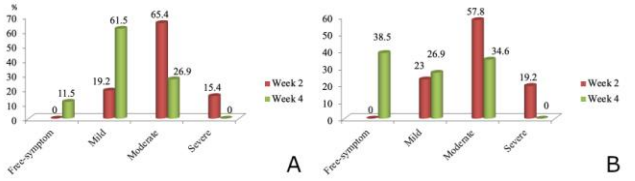

Figure 1: Severity of disease in the two groups at week 2 and week 4; A) Levocetirizine group; B) Fexofenadine group

The proportion of undesirable side effects at a conventional dose of the levocetirizine group was 9.6% and for the fexofenadine group 8.0%. When the dose was doubled the proportions of side effects were 11.5% and 10.2% respectively for the two groups. Overall the most common side effects were drowsiness and fatigue. Results concluded that no patients had any biochemical abnormalities after 4 weeks of treatment (at least with the level of urea, creatinine and liver enzymes).

Discussion

This study of H_1-antihistamines doses of 102 patients with chronic urticaria provided three important results. H_1-antihistamine at a conventional dose affected recovery in about half of the patients. In the remaining difficult-to-treat patients a two-fold dose of H_1- antihistamines improved symptoms of urticaria significantly. This study also found that levocetirizine seemed to be slightly more effective than fexofenadine, thought this didn't prove to be statistically significant.

H_1-antihistamine affected improving the symptoms of all chronic urticaria patients. More than half of the patients recovered from all symptoms on 5 mg levocetirizine or 180 mg fexofenadine per day. These patients continued to maintain this therapy for a long period after the trial. Though many patients still had symptoms after 2 weeks of treatment with a conventional dose. Pre-treatment, most had suffered from the disease for over 6 months, and the severity of urticaria was moderate to severe (results not shown).

Given that histamine mediates almost all

symptoms of urticaria through H_1-receptors located on nerves and endothelial cells, the European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA2LEN)/European Dermatology Forum (EDF) guidelines recommend that the first line of treatment should be with nonsedating H_1-antihistamine [10]. Trials support the use of this drugs in most forms of urticaria [10] howerver in a study of 390 patients, only about 44% responded well to this treatment: 29% were discharged asymptomatic with another 15% only showing a partial relief of symptoms [11]. This raises some questions as to the need for an increased dose of H_1-antihistamine also whether individual patients respond better to one antihistamine over another [12].

A two-fold increase in the dose of histamine H_1 reduced the symptoms in patients not responding to conventional doses. General concerns over increasing the dose are the negative side effects associated with the drug. However, this study found that side effects were not different between a conventional dose and an increased dose. Overall the most common side effects were drowsiness and fatigue. Second-generation H_1-antihistamines (such as levocetirizine and fexofenadine) represent a substantial therapeutic advance and often show a lack of cardiotoxicity, an absence of cholinergic side effects and display minimal sedation [12]. Increasing the dose of antihistamines is a good solution in difficult-to-treat urticaria, replacing the need to switch to other drugs such as systemic corticosteroids. With an increased dose of both levocetirizine and fexofenadine, there was a significant improvement in the quality of life of the patient.

European guidelines allow a four-fold increase to the normal dose of H_1-antihistamines [1] however as there are no published studies in Vietnam on an increased dose we increased the dose only 2 times as a precaution. After 2 weeks of double dose therapy, there were still many long-term and severe patients who were still not fully asymptomatic. From the fifth week, these patients were treated with alternative antihistamines before attempting other drugs such as montelukast, cyclosporin and systemic corticosteroid. The Staevska et al., (2010) study of 80 patients with difficult-to-treat urticaria showed that the 25 patients who failed to respond to 20 mg desloratadine, 7 became symptom-free on 20 mg levocetirizine [12]. As mentioned, in previous studies of urticaria other proinflammatory mediators such as interleukine-4 and leukotriene may contribute to clinical and histological images of the disease [13]. Mast and basophilic cells of volunteers without urticaria were incubated with serum from idiopathic chronic urticarial patients and produced interleukine-4 and leukotriene. These two mediators can cause perivascular infiltration of the inflammatory cells that affect skin cells. This infiltration creates the difference between a histological lesion of acute urticaria and that of physical urticaria. The use of antihistamines cannot cure all the symptoms of urticaria however several clinical trials using montelukast, in combination with antihistamines (cetirizine, fexofenadine, loratadine or desloratadine) revealed better results than those using antihistamines alone (improving symptoms and the quality of life). Interestingly, when used as a standalone treatment, monotherapy leukotriene antagonists have no effect on chronic urticaria [13].

Levocetirizine and fexofenadine have been known to have an equal effect in improving the symptoms of chronic urticaria. However, in this trial at week 4, the rate of symptomatic relief was higher in the levocetirizine group than in the fexofenadine group. Different H_1-antihistamines may have different effects in the treatment of urticaria. In a study of 886 patients, results revealed that levocetirizine 5 mg was significantly more efficacious than desloratadine 5 mg in the treatment of chronic urticaria [14]. Though it must be noted that fexofenadine is less dependent on liver function so it can be prescribed to patients with hepatic diseases.

Of course, there were some limitations to be noted in this study. Firstly, the effectiveness was evaluated based on clinical improvement, which can often be subjective between investigators and patients. Secondly, the study's duration was only 4 weeks; a long-term follow-up study is lacking thus far. Finally, UAS was used to evaluate the severity of chronic urticaria on the day in which the patients checked into the hospital, UAS7 was not used (which evaluates the last seven days). USA7 is clearly more precise than UAS but this information was not available at the time and therefore could not be used in this study.

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Efficacy of BAFF in Monitoring Treatment Response in Early Vietnamese Systemic Sclerosis Patients

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Abstract

BACKGROUND: B-cell activating factor (BAFF) is considered to have a role in the pathogenesis of systemic sclerosis (SSc).

AIM: We conducted a longitudinal study on early SSc patients to determine the change in BAFF serum level after treatment and its association with organ involvements.

METHODS: A total of 46 patients (32 diffuse, 14 limited) were recruited, among which 35 patients (24 diffuse, 11 limited) completed 12-month follow-up.

RESULTS: Higher pretreatment BAFF levels were observed in patients with positive anti-topoisomerase antibody (ATA) (2252.1 ± 899.7 pg/ml versus 1475.5 ± 697.6 pg/ml in ATA-negative patients; p = 0.01) and muscular involvement (2741.9 ± 1039.9 pg/ml versus 1897.2 ± 762.9 pg/ml in patients without muscular involvement; p = 0.005). Lower levels were observed in patients with interstitial lung disease (ILD) (1926.7 ± 757.9 pg/ml versus 2721.6 ± 1131.4 pg/ml in non-ILD patients; p = 0.01). After treatment, BAFF level reduced significantly in diffuse SSc patients (1652.2 ± 892.7 pg/ml versus 2147.6 ± 945.5 pg/ml before treatment; p = 0.03).

CONCLUSION: Patients with worsening outcome had the highest pretreatment BAFF level and was associated with increased BAFF level after treatment. BAFF can be used to predict and monitor patients' response to therapy.

Introduction

BAFF (B lymphocyte stimulator, BlyS) plays the most important role in the survival and maturation of B lymphocytes (B cells) [1]. Recent studies have shown that B cells may play an important role in mediating immune responses in systemic sclerosis (SSc). In SSc patients, although the amount of B cells does not increase in skin lesions, activating markers are found to increase. Functional abnormalities of B cells can cause systemic diseases independent with antibody-producing function [2]. The BAFF/BAFFR family are present in almost all the stages of B cell differentiation and maintain the survival of B cells in bone marrow. BAFF also has strong *in vitro* B cell stimulating function [3]. Therefore, excessive BAFF increase causes self-activation of B cells, playing an important role in the development of autoimmune diseases. Previous studies on SSc Japanese patients with systemic lupus erythematosus (SLE), rheumatoid arthritis, and Sjogren's syndrome have demonstrated high serum levels of BAFF. Belimumab (a soluble monoclonal anti-BAFF antibody) has been approved by the Food and Drug Administration (FDA) for the treatment of SLE patients [4]. Other studies have also

shown that in SSc patients, increased BAFF levels are associated with sclerotic skin lesions, lung's vital capacity, and musculoskeletal involvements. This suggests that BAFF is a signal of abnormal B cell activation and the development of SSc [5]. A multi-centre clinical randomised controlled trial on rituximab, a monoclonal anti-CD20 antibody that inhibits B cells, has shown improvement on ILD and decreased mRSS [6]. Therefore, BAFF is one of the targets that should be considered in the treatment of SSc.

To evaluate B cells' activity in early SSc patients, we conducted a study with two aims:

1. To determine the change in serum BAFF level in SSC patients before and after treatment at the National Hospital of Dermatology and Venerology;

2. To explore the association of changes in BAFF level with skin and organ involvement in SSC patients.

Methods

We recruited 46 patients diagnosed with SSc based on the 2013 EULAR/ACR classification criteria [7] who were treated at the National Hospital of Dermatology and Venereology (NHDV) from December 2014 to December 2017. Selection criteria included patients who had an onset of ≤ 36 months, were naïve to treatment or had stopped immunosuppressive and antifibrotic therapy for ≥ 2 months, had no concomitant skin diseases such as skin infection or overlap syndrome. The patients were treated with methylprednisolone, methotrexate, vasodilators, and other symptomatic treatments according to the European guidelines on SSc management [8] and were followed up in at least 12 months.

Data collection included demographics (sex, age, onset, disease duration) and clinical and laboratory parameters at baseline and 12-month follow-up. Patients were assessed for skin lesions (using the modified Rodnan Skin Score-mRSS), digital tip ulcer, telangiectasia, interstitial lung disease (ILD, using high-resolution computed tomography-HRCT), pulmonary arterial hypertension (PAH, using the cutoff ≥ 35 mmHg of the systolic pulmonary artery pressure-PAPs on transthoracic echocardiography-TTE), urinalysis abnormality (observed on ≥ 2 tests), difficulty swallowing, joint pain, and muscle injury (at least 2 out of 3 findings: muscle pain/weakness, creatinine kinase-CK level higher than normal limit at the time of presentation, and needle electromyography-EMG demonstrating muscle diseases). Severity was classified as mild, moderate, and severe if patients had zero, one, and two or more organ involvements, respectively. Improvement and worsening were determined by changes in constitutional symptoms and at least two systems (healing or new lessons of digital tip ulcer, improved or worsened difficulty swallowing, joint pain, or muscular involvement, a difference of ≥ 2 points in the ILD score, and a difference of ≥ 5 mmHg in PAPs between recruitment and follow-up).

Serum specimens were obtained and stored at baseline and 12 months after treatment, following the standard operating procedures at the NHDV-3 mL of venous blood was drawn into a collecting tube without anticoagulant, left in the room temperature in 30 minutes, and centrifuged at 2000 rpm in 15 minutes. The serum was then extracted to a 1.5 mL Eppendorf tube and stored in a minus 80°C freezer.

Some autoimmune antibodies were tested in Vietnam. Antinuclear antibody (ANA) and anti-centromere antibody (ACA) were tested using indirect immunofluorescence on Hep-2 cells (Fluoro Hepana, MBL, Japan). Anti-topoisomerase antibody (ATA) was tested by enzyme-linked immunosorbent assay (ELISA; Medical & Biological Laboratories, Nakaku, Nagoya, Japan).

Anti-RNA polymerase antibody (RNAP) was tested by ELISA in Japan (Mesacup anti-RNA, Japan). The level of BAFF was measured by ELISA, using Quantikines ELISA Human BAFF/BLyS/ TNFSF13B Immunoassay (R&D Systems China Company).

Data analysis was performed using SPSS 20.0 (IBM Corporation). Continuous variables were tested for the difference by the independent *t*-test (for normally distributed variables) or the Mann-Whitney U test or the Kruskal-Wallis test (for not normally distributed variables). Paired continuous variables were tested for the difference by the paired *t*-test (for normally distributed variables) or the Wilcoxon Signed Ranks test (for not normally distributed variables). Categorical variables were tested for the difference by the chi-squared test.

The study has been approved by the Hanoi Medical University and the NHDV.

Results

A total of 46 patients were recruited in our study, among which 32 (65.9%) patients had diffuse SSc and 14 (30.4%) limited SSc. The mean age of onset was 50.1 ± 14.1 years, and the mean duration from the onset was 11.5 ± 8.4 months; no difference was observed between diffuse and limited SSc patients. Before treatment, 36 out of 45 patients had positive ATA. The mean level of ATA in diffuse SSc patients was higher than in limited SSc patients (p = 0.008). Only two patients had positive ACA and one positive RNAP. The mean pretreatment mRSS was

15.0 ± 8.9 (18.7 ± 7.9 and 6.6 ± 3.8 in diffuse SSc and limited SSc patients, respectively; $p < 0.001$). The proportions of other involvements were presented in Table 1.

Table 1: Patient baseline characteristics

	Total (n = 46)	Diffuse SSc (n = 32)	Limited SSc (n = 14)	p^*
Female:male (n)	32:14	2:1	11:3	NS
Age of onset (year; mean ± SD)	50.1 ± 14.1	49.0 ± 14.7	52.5 ± 12.9	NS
Duration from onset (month; mean ± SD)	11.5 ± 8.4	11.5 ± 7.7	11.4 ± 9.9	NS
ATA (mmol/ml; mean ± SD)	123.1 ± 82.6	143.3 ± 75.7	73.3 ± 80.4	0.008
ATA (n; %)	36; 80%	28; 87.5%	8; 61.5%	NS
ACA (n; %)	2; 4.3%			
RNAP (n; %)	1; 2.2%			
mRSS (mean ± SD)	15.0 ± 8.9	18.7 ± 7.9	6.6 ± 3.8	0.0001
Digital tip ulcer (n; %)	10; 21.7%	7; 21.9%	3; 21.4%	NS
Telangiectasia (n; %)	14; 30.4%	10; 31.2%	4; 28.6%	NS
ILD (n; %)	36; 78.3%	25; 78.1%	11; 78.6%	NS
PAH (n; %)	16; 34.8%	9; 28.1%	7; 50.0%	NS
Urinalysis abnormality (n; %)	10; 21.7%	6; 18.8%	4; 28.6%	NS
Difficulty swallowing (n; %)	9; 19.6%	7; 21.9%	2; 14.3%	NS
Joint pain (n; %)	25; 54.3%	19; 59.4%	6; 42.9%	NS
Muscular involvement (n; %)	11; 23.9%	8; 25.0%	3; 21.4%	NS

*: *t*-test for continuous variables; chi-squared test for categorical variables. NS: not significant; SD: standard deviation.

Pretreatment BAFF level

There was no difference in the pretreatment BAFF level in diffuse and limited SSc patients (2010.4 ± 907.6 pg/ml versus 2177.2 ± 1009.3 pg/ml; $p = 0.58$). BAFF level was higher in patients with positive ATA, and this difference was more prominent in diffuse SSc patients. BAFF level was lower in patients with ILD, but the difference was not statistically significant in limited SSc patients. BAFF level was higher in patients with muscular involvement, and this difference was more prominent in limited SSc patients. The number (proportion) of patients with mild, moderate, and severe SSc was 10 (21.7%), 13 (28.3%), and 23 (50%), respectively as shown in Table 2.

Table 2: BAFF level by SSc types and clinical and laboratory findings

BAFF (pg/ml)	SSc		Diffuse SSc		Limited SSc	
	Concentration	P^*	Concentration	P^*	Concentration	p^*
ATA		0.02		0.01		NS
Present	2252.1 ± 899.7		2202.2 ± 822.7		2426.7 ± 1180.0	
Absent	1475.5 ± 697.6		1104.5 ± 491.7		1772.3 ± 737.6	
Digital tip ulcer		NS		NS		NS
Present	2440.3 ± 1033.0		2191.2 ± 736.4		3021.6 ± 1565.7	
Absent	2004.4 ± 853.4		2029.7 ± 908.7		1946.9 ± 749.5	
Telangiectasia		NS		NS		NS
Present	2142.1 ± 762.8		2117.6 ± 822.7		2203.4 ± 695.7	
Absent	2080.4 ± 966.8		2041.1 ± 901.9		2166.8 ± 1144.4	
ILD		0.01		0.03		NS
Present	1926.7 ± 757.9		1895.2 ± 783.2		1996.9 ± 728.6	
Absent	2721.6 ± 1131.4		2671.4 ± 930.9		2838.7 ± 1769.6	
PAH		NS		NS		NS
Present	2220.2 ± 849.1		2431.0 ± 860,6		1949.1 ± 813.9	
Absent	2034.6 ± 936.0		1921.8 ± 842.4		2405.4 ± 1192.9	
Urinalysis abnormality		NS		NS		NS
Present	1806.2 ± 661.2		1855.8 ± 857.6		1731.8 ± 271.2	
Absent	2180.6 ± 949.4		2113.3 ± 876.7		2355.4 ± 1150.4	
Difficulty swallowing		NS		NS		NS
Present	1982.9 ± 1062.1		1838.9 ± 1170.0		2486.9 ± 396.8	
Absent	2127.4 ± 872.5		2128.3 ± 778.5		2125.6 ± 1081.3	
Joint pain		NS		NS		NS
Present	2158.0 ± 901.7		2225.5 ± 953.8		1944.3 ± 745.0	
Absent	2029.1 ± 918.6		1830.4 ± 685.2		2351.9 ± 1189.1	
Muscular involvement		0.005		NS		0.04
Present	2741.9 ± 1039.9		2570.3 ± 924.8		3199.6 ± 1407.9	
Absent	1897.2 ± 762.9		1896.6 ± 794.1		1898.4 ± 727.1	
Severity [median (min-max)]**		NS		NS		NS
Mild	1532.0 (649-3012)		1536.7 (1178-3012)		1532.0 (650-2499)	
Moderate	1897.1 (430-3564)		1764.7 (430-3564)		2665.1 92563-2767)	
Severe	2279.1 (1201-4820)		2279.5 (1201-3735)		2242.7 (1204-4820)	

*: *t*-test; **: Mann-Whitney U test; ***: Kruskal-Wallis test. NS: not significant.

Changes of BAFF level after treatment

In 35 (76.1%) patients (24 diffuse SSc, 11 limited SSc) who completed 12-month follow-up, the mean BAFF level significantly reduced compared to before treatment (1652.2 ± 892.7 pg/ml versus 2147.6 ± 945.5 pg/ml; $p = 0.03$). However, when stratified by types of SSc, only diffuse SSc patients demonstrated significant reduction in BAFF level (1440.8 ± 637.0 pg/ml versus 2094.7 ± 875.9 pg/ml; $p = 0.002$) while this reduction in limited SSc patients was not significant [median (min-max) 1641.5 (1333.2-5523.2) versus 2279.1 (648.9-4820.4) pg/ml; $p = 0.52$] as presented in Figure 1a.

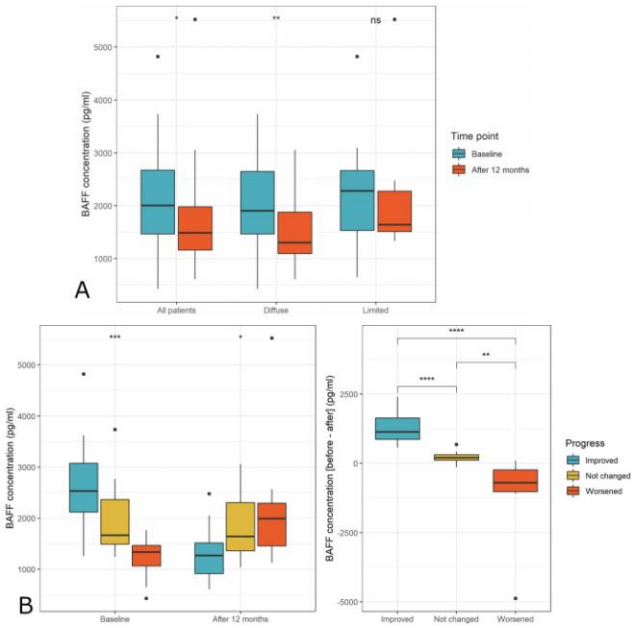

*Figure 1: BAFF level before and after treatment; a) BAFF level before and after treatment in all patients and stratified by types of SSc; b) BAFF level before and after treatment among patients with clinically improved, not changed, and worsened outcome. Comparisons between before and after treatment were made by the paired t-test (for all patients and diffuse SSc patients) and the Wilcoxon signed rank test (for limited SSc patients). Comparisons among outcome groups were made by the Kruskal-Wallis test. NS: not significant; *: p < 0.05; **: p < 0.01; ***: p < 0.001; ****: p < 0.0001*

When stratified by outcomes at follow-up (18 improved, 9 not changed, and 8 worsened), there were differences in the BAFF level among outcome groups both at baseline and follow-up, and the differences in the reduction of BAFF level after 12 months were significantly different as presented in Figure 1b. In particular, patients with clinical improvement had the highest baseline BAFF level (median 2531.1, min-max 1257.5-4820.4) and was associated with the greatest reduction in BAFF level (median difference 1137.5, min-max 572.0-2405.5) while patients with clinical worsening had the lowest baseline BAFF level (median 1333.8, min-max 429.5-1764.7) and was associated with an increase in BAFF level (median difference 1993.15, min-max 1123.4-5523.2).

Discussions

In our study, higher BAFF levels were observed in patients with positive anti-topoisomerase antibody (ATA), ILD, and muscular involvement. ATA is more prevalent in diffuse SSc patients, and its presence has been associated with lung involvement [9]. BAFF's relationship with ATA in SSc has not been established, but a previous study has shown no correlation between ATA and BAFF in systemic lupus erythematosus (SLE) and rheumatoid arthritis [10].

Although decreased lung vital capacity has been observed in patients with elevated BAFF, pulmonary fibrosis, the hallmark of ILD, seems to be associated with high APRIL (a proliferation-inducing ligand) levels but not high BAFF levels [11]. While BAFF is related to the survival and proliferation of B cells, increased levels of BAFF were not shown to correlate with the number of B cells in peripheral blood—in fact, studies have shown that the number of B cells was decreased in SSc [12], [13]. Findings from studies on experimental animals suggested interleukin-6 (IL-6) and IL-10 play a more prominent role in the development and attenuation of lung fibrosis, and BAFF might suppress regulatory B cells (which produces IL-10 and decreases immune response) [14]. Based on a study in 15 years, Yoshizaki and Sato have proposed a model of abnormal B cells' activity [15]. In this model, augmentation of B-cell antigen receptor (BCR) signalling, along with overproduction of BAFF and TLR stimulation, induces activation of memory B cells and increases apoptosis. This, in turn, decreases the number of peripheral B cells. To maintain the number of inactivated B cells, bone marrow will increase the production of naïve B cells into peripheral blood. Therefore, there is an increase in the number of naïve B cells but a decrease in the number of memory B cells in early SSc patients [16]. B cells are mainly active in peripheral blood but not in organ tissues, and the number of peripheral B cells increases after treatment [17] in this study and another study [18]. BAFF antagonist or genetic ablation of BAFF attenuated lung fibrosis. However, these findings are limited to animal experiments and might not reflect the whole picture of a more complex cytokine network in human.

Studies on cytokines in muscular diseases started in 1986 with the identification of IL-2 and interferon (IFN) in polymyositis. Since then, researchers have described multiple cytokines relating to a spectrum of muscular diseases. However, there was no association of muscular involvement with levels of cytokines in SSc [19]. Our study is the first study to show a higher level of BAFF in patients who had muscular involvement.

Although both diffuse and limited SSc patients in our study demonstrated a reduction in the level of BAFF after 12 months of treatment, only diffuse disease patients had a significant reduction. Matsushita et al. found that the reduction of BAFF levels in SSc was more modest than in SLE but still more significant than in dermatomyositis [5]. Patients in both Matsushita's and our study had an onset within 2–3 years, suggesting BAFF can be elevated at a very early stage of SSc.

The most surprising finding in our study was that higher pretreatment BAFF levels were observed in patients with clinical improvement but not in patients with clinical worsening. Patients with improvement also had more significant reduction of BAFF levels after treatment. In a previous study, increased levels of BAFF have been considered to herald the development or worsening of major events in SSc whereas decreased levels of BAFF was associated with regression of skin involvement [5]. The evidence suggests the level of BAFF before treatment could be used for prognosis and changes in BAFF level can help monitor patients' treatment progress.

In conclusion, the level of BAFF was significantly higher in early SSc patients and related to ATA production of B lymphocytes. Pretreatment BAFF level was lower in the presence of ILD on HRCT and higher in the presence of muscular involvement. Clinical worsening after 12 months of treatment was associated with higher pretreatment BAFF level and increase in follow-up BAFF level compared to baseline. This suggests that baseline BAFF level as well as it changes after treatment can be used to predict and monitor patients' response to therapy.

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Efficacy of 10% Potassium Hydroxide Solution Versus 10% Salicylic Acid Ointment in Treatment of Molluscum Contagiosum - the Low - Cost Dermatologic Therapy in Vietnam

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Keywords: Molluscum contagiosum; Potassium Hydroxide; Salicylic pomade

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Abstract

BACKGROUND: Molluscum contagiosum is a common viral disease primarily affecting children.

AIM: The objective is to compare the efficacy of 10% potassium hydroxide (KOH) solution versus 10% salicylic pomade in the treatment of molluscum contagiosum.

METHODS: Clinical trials on 70 patients were randomised into 2 groups: 39 patients treated with 10% KOH solution and 31 patients treated with 10% salicylic pomade. The evaluation was based on the complete clearance of lesions, side effects and complications of the drug.

RESULTS: The clearance of all lesions after 2, 4, 6, 8 weeks of treatment in both groups were 7.7%; 23.1%; 53.8%; 79.5% and 0%; 3.2%, 9.7% 22.6%, respectively ($p < 0.05$). Side effects were seen in both groups include burning (76.9% versus 19.4%; $p < 0.05$); redness (59% versus 14%; $p < 0.01$); desquamation (12.8% versus 19.3%; $p < 0.05$).

CONCLUSION: The efficacy of KOH solution in the treatment of MC was better than that of salicylic pomade and both products are safe, effective, and easy to apply at home.

Introduction

Molluscum Contagiosum is caused by a Pox virus family, affecting mainly children with prevalence in immunocompetent children of approximately 7% and human immunodeficiency virus (HIV) positive adult patients up to 18% [1].

Previous studies have shown the efficacy of KOH solution in various concentrations to treat molluscum contagiosum [2], [3].

This study aims to compare the efficacy of 10% KOH solution and 10% salicylic acid pomade for treating molluscum contagiosum in Vietnamese children.

Methods

Seventy patients were randomly divided into 2 groups: 39 patients were treated with 10% KOH, 31 patients were treated with 10% salicylic. The 2 groups had no differences in age, gender, or location and severity of their condition.

All procedures performed in studies involving human participants were by the ethical standards of institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the institutional review board of the National Hospital of Dermatology and Venereology, Hanoi, Vietnam.

The products were applied directly on the lesions by a small cotton swab one time/day before going to bed until the lesions disappeared.

Results

After 8 weeks of treatment, the rates of complete resolution in 39 patients treated with KOH 10% solution and 31 patients treated with salicylic 10% were 79.5% and 22.6% ($p < 0.01$), respectively. The rates of partial resolution in the group treated with KOH solution and in patients treated with salicylic 10% were 20.5% and 77.5% ($p < 0.01$), respectively. Patients in group 1 took less time to be cured. After 2 weeks, 7.7% (3/39) of patients in group 1 and 0 patients in group 2 were cured. After 4 weeks and 6 weeks, the complete clearance of lesions in group 1 and group 2 were 23.1% and 3.2%, 53.8% and 9.7%, respectively.

It was also noted that, in both groups, the rate of resolution in the patients having no other skin diseases was higher than that in patients with other skin disorders such as dermatitis or dry skin (28.2% of the patients suffering from atopy dermatitis or dry skin in group 1 were cured versus 9.7% in group 2 ($p < 0.05$) as shown in Table 1 and Figure 1.

Table 1: The resolution of skin lesions after 8 weeks treatment in both groups

Result		KOH 10% (n = 39)		Salycilic 10% (n = 31)		p
		n	%	n	%	
Complete resolution	Atopy dermatitis + dry skin	11	28.2	3	9.7	< 0.05
	No combination skin diseases	20	51.3	4	12.8	
Partial resolution	Atopy dermatitis + Dry skin	5	12.8	10	32.3	< 0.05
	No combination skin diseases	3	7.7	14	45.2	

Treatments were also found to influence other skin diseases. We found that a 10% KOH solution was more effective than 10 % salicylic acid. 28.2% (11/16) of patients suffering from atopy dermatitis or dry skin in group 1 were cured, compared to only 9.7% (3/10) (Table 1; $p < 0.05$) in group 2. In patients with atopy dermatitis or dry skin, molluscum contagious lesions tend to diffuse and recur.

Investigating the side effects of both products revealed that 76.9% of patients in group 1 had burning sensations immediately after application.

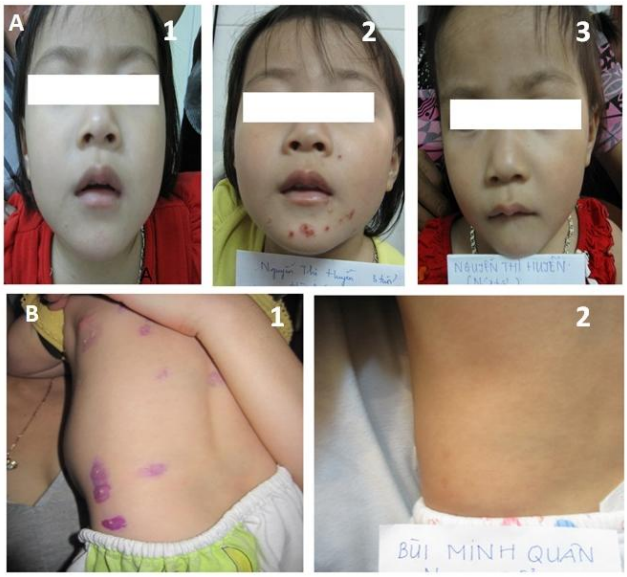

Figure 1: A) 8-year-old girl after 2 days of treatment; B) Another child had excellent improvement after treatment by KOH solution

The rates of erythema, itching, and desquamation were 59%, 17.9% and 12.8% respectively. In group 2, the data is 19.4%, 14%, 16.1% and 19.3%, respectively (Table 2; $p < 0.05$). These results are similar to a study by Melkar [2].

Table 2: Side effects immediately after applying for medicines

Symptoms	KOH 10%		Salicylic 10%		p
	n	%	n	%	
Burning	30	76.9	6	19.4	< 0.05
Erythema	23	59	4	14	< 0.01
Itching	7	17.9	5	16.1	> 0.05
Desquamation	5	12.8	6	19.3	< 0.05

Discussion

Sang-Hee Seo et al. showed that 77% (10/13) of the patients treated with KOH 10% were cured after 8 weeks [3]. The Mahajan BB et al., a study on 27 children with molluscum contagiosum treated by topical 20% KOH solution once daily, demonstrated that 88.9% of patients who completed the trial experienced complete clearance [4]. A study by Leslie et al. showed that salicylic acid was effective for treating molluscum contagiosum, with 87.5% (21/24) of patients being cured. They used 12% salicylic acid gel, and the results were assessed after 24 weeks [5].

Evaluating and comparing the 10% KOH solution versus the 10% salicylic pomade in the treatment of molluscum contagiosum at the National Hospital of Dermatology and Venereology, we noted that both products are safe and easy to apply at home.

Use of 10% KOH shows the best

effectiveness, useful for the domestic therapy in children with many lesions, especially those with atopy dermatitis.

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Efficacy of Azole Antifungal in Treatment of Pityriasis Versicolor

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Keywords: Pityriasis versicolor; Malassezia; Yeast

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Abstract

AIM: Compare itraconazole alone, fluconazole combined with ketoconazole and ketoconazole in the treatment of patients with pityriasis versicolor.

MATERIAL AND METHODS: A group of 240 pityriasis versicolor patients (confirmed with KOH and culture) were classified into 3 groups: Fluconazole 300 mg a week and 2% ketoconazole foam twice a week for 2 weeks (Category I), Itraconazole 200 mg daily for one week (category II); Ketoconazole 2% foam daily for 2 weeks (Category 3). Clinical (colour of macule, scale, pruritus) and mycological assessment were done after 4 weeks of therapy.

RESULTS: After 4 weeks of treatment, clinical cure was observed in 62.4% (Category I), 36.3% (Category II) and 37.5% (Category III).

CONCLUSION: It was reported in our study that the most effective regimen for PV patients is fluconazole 300 mg per week combined with ketoconazole 2% twice a week for 2 weeks.

Introduction

Pityriasis versicolor is a common, chronic, superficial fungal infection caused by *Malassezia spp* [1]. It is characterised by hyperpigmented, hypopigmented macules and patches on the face, upper trunk, back, chest paralleling the density of sebaceous gland. Several topical and systemic antifungal agents are effective against pityriasis versicolor. However, recurrence is common. Therefore, approaching an effective, safe and affordable treatment regimen should be taken in consideration.

Our study aimed to assess and compare the efficacy and the safety of oral fluconazole combined with foam ketoconazole, oral itraconazole and foam ketoconazole alone.

Material and Methods

A group of 240 patients with pityriasis versicolor over 16 years old attending our out-patient dermatology clinic from January 2016 to December 2016 were included in the study. Patients with other superficial and systemic fungal infections, history of treatment with oral antifungal drugs during the previous month or with topical anti-fungal drugs within 1-week, pregnant females, and patients with the serious concurrent disease were excluded from the study

Eligible patients were randomised to receive one of the following categories of treatment regimen: Category I: Fluconazole 300 mg a week for 2 weeks and foam ketoconazole 2% biweekly in 2 weeks; Category II: Itraconazole 200 mg daily for 1 week,

Category III: foam ketoconazole 2% daily in 2 weeks.

Clinical signs and symptoms such as pruritus, hypo or hyperpigmentation, and desquamation were classified (0 = none, 1 = mild, 2 = moderate, 3 = severe), lesion measurement (0: none, 1: < 10% BSA, 2:10 - 30% BSA, 3: > 30% BSA).

A group of 240 pityriasis versicolor patients were randomly classified into 3 groups: Fluconazole 300 mg a week and 2% ketoconazole foam twice a week for 2 weeks (Group I), Itraconazole 200 mg daily for 1 week (Group II); Ketoconazole 2% foam daily for 2 weeks (Group 3).

Results

During the study period, 240 patients were enrolled in our study: the itraconazole group, the fluconazole associated with ketoconazole shampoo group and the ketoconazole foam group. There were no statistically significant differences regarding age, sex, disease severity for patients in the two groups as shown in Table 1 (p > 0,05).

Table 1: Characteristics of patients

	Group 1	Group 2	Group 3	P
Gender (Male/Female)	50/30	54/26	52/28	> 0,05
		Age		
16-19	6/80	6/80	5/80	> 0,05
20-29	39/50	40/80	43/80	
30-39	23/80	22/80	23/80	
40-49	8/80	9/80	6/80	
> 50	4/80	3/80	3/80	
Disease severity				
Mild	19/80	20/80	15/80	> 0,05
Moderate	49/80	49/80	59/80	
Severe	12/80	11/80	6/80	

The mycological examination is considered the most important factor in determining the efficacy of treatment. The negative result showed that the patient had recovered from the microorganism despite still having skin lesions. It was reported in our study as shown in Table 2 that negative mycological examination was highest in group 1 (81.3%); lowest in group 3 (60%).

Table 2: Clinical and mycological assessment after 4 weeks of therapy

		Group 1 (n = 80)		Group 2 (n = 80)		Group 3 (n = 80)	
		Baseline	28 days	Baseline	28 days	baseline	28 days
Scale	Present	80	17	79	25	80	26
	Absent	0	63	1	55	0	54
Pruritus	Present	67	26	64	37	63	28
	Absent	13	54	16	43	17	52
Disease activity score		4.7 ± 1.5	2.2 ± 1.2	4.5 ± 1.6	2.5 ± 1.4	4.6 ± 1.4	2.5 ± 1.2
Decrease in DAS		2.5 ± 1.1		2.0 ± 1.0		2.1 ± 0.8	
Mycological culture	Positive	80	15	80	27	80	32
	Negative	0	65	0	53	0	48

It was also reported in Table 2 that 53/80 patients (66.3%) treated with itraconazole 200 mg daily for 7 days have negative KOH examination.

As reported in our research, the highest cure rate was observed in group 1 (81.2%), followed by Group 2 (66.3%) and Group 3 (60.0%).There were statistical significant difference meaning between Group 1 and Group 2 (p < 0,01), Group 1 and 3 (p < 0,05).

In our study, a new regimen-oral fluconazole 300 mg a week combined with ketoconazole 2% foam 3 times a week for 2 weeks was first applied. The overall cure rate after 4 weeks was 81.2%. It was lower than Badri T's study (90%), relapse rate was not assessed in both study. Compared with fluconazole treatment alone in Montero-Gei's research, ninety patients with tineaversicolor were randomly assigned to treatment with either a single 450 mg dose of fluconazole, two 300mg doses of fluconazole given for one week, or itraconazole 200 mg daily for 7 days. At the end of treatment, the cure rate for itraconazole (20%) was significantly higher (*P* = 0.024) than that for fluconazole 450 mg (0%).

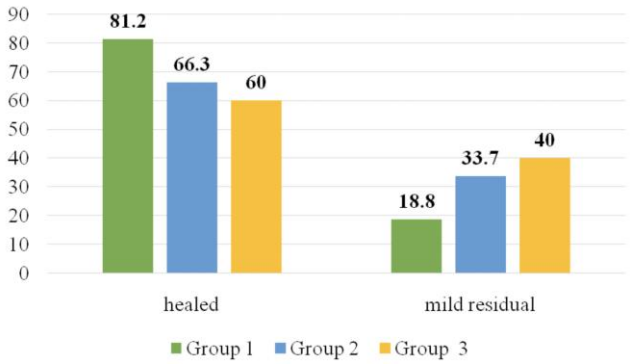

Figure 1: Treatment efficacy after 4 weeks

Discussion

It was 91% in Talel Badri's research on patients treated with oral fluconazole and 2% for ketoconazole [2]. 100% of patients had negative KOH result after 5weeks of ketoconazole cream 2% in Fonzo's study [3]. It was demonstrated by Mehme Karakas's study that 77% and 77.5% of patients treated with fluconazole 300 mg for 2 weeks have negative mycological result after 4 weeks, respectively [4], [5]. There were several studies in which fluconazole was applied in various durations and dosages in the treatment of tinea versicolor (450 mg/single dose, 400 mg/single dose, 300 mg with a 1-week interval, 300 mg a week for 2 weeks, 150mg a week for 4 weeks). In these studies, the mycological cure varied between 44%-100% [3]. Accordingly, the clinician may opt to use regimen 300 mg a week for 2 weeks for treating tinea versicolor.

There were several studies in which ketoconazole shampoo and foam was applied in treatment tinea versicolor. According to Di Fonzo [3], the cure rate was observed in 100% of patients after 2

weeks of ketoconazole shampoo 1% and 2%. It was 81%, 55% and 72% in Rigoponlos (2007), Cantrell (2014) and Shi (2014)'s study [6], [7], [8].

In our research, we have assessed one of the most common regimen antifungal drugs in Vietnam – itraconazole 200mg daily for 7 days. Kose et al. reported equivalent efficacy between a daily 200 mg dose of itraconazole for 7 days and a single 400 mg dose [9]. Kokturk et al., reported greater efficacy of 400 mg of itraconazole a day over 3 days and 200 mg a day over 5 days than 400 mg in 1 day [5]. It was demonstrated in our study that the cure rate was seen in 66.3% of patients when they were treated by itraconazole 200mg daily for 7 days. When cure plus improvement was considered, response rates among the three treatment groups were comparable (97, 100, and 97% for fluconazole 450 mg, fluconazole 300 mg, and itraconazole, respectively) [10].

The unsimilar result between authors can be explained by the difference in criteria for efficacy assessment. The mycological cure rate was always higher than the clinical cure rate in all study groups. As a mycological cure is the only reliable criterion in assessing treatment efficacy, this implies that a proportion of patients rated as clinically improved were cured with residual colour changes (mostly hypopigmentation) [11], [12].

In conclusion, topical combined with systemic therapy is effective against tinea versicolor, especially extensive disease, frequent relapses, or history of failed topical treatment. In the current study, we found the highest mycological cure rate, 62.4%, with a single oral dose of fluconazole 300mg along with ketoconazole foam 2% twice a week, higher than with itraconazole 200 mg daily for one week (35.3%) and ketoconazole foam (37.5%).

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Clinical Science

Successful Treatment of Intralesional Triamcilonon Acetonide Injection in Keloid Patients

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Keywords: Keloid; Triamcinolone acetonide

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Abstract

AIM: Evaluation the effect of intralesional corticosteroid injection on keloid, at the National Hospital of Dermatology and Venereology from 1/2009 to 12/2009.

METHODS: A group of 65 patients with keloid were randomly assigned into three groups. In the studied group, 33 patients were intralesionally injected 7.5 mg/1 cm^2 of TCA. In the control group, TAC 32 patients were intralesionally injected 15 mg/1 cm^2 of TCA. The result was evaluated basing on the criteria of Henderson (1998) and El-Tonsy (1996).

RESULTS: In comparison between 2 groups, good to excellent improvement in the studied group was statistically higher than the control group (90.7% versus 68.7%; $p < 0.05$). After each injection, the thickness of the scar was reduced 1.24 ± 0.53 mm in the studied group and 0.81 ± 0.39 mm in the control group. The disappearance of pain and itching after treatment were 86.6% and 95.5% in the studied group and 78.1% and 80% in the control group ($p > 0.05$). Ulceration, acne and troublesome with menstrual cycles were sometimes were noted more frequently in the control group than in the studied group.

CONCLUSION: Intralesional triamcinolone acetonide injection had a good result, and 7.5 mg/1 cm^2 scar is the best dose for treatment of keloid.

Introduction

Keloid is a benign condition of the skin caused by excessive deposition of fibrous cells and collagen fibres in the body. It occurs at all ages, both sexes and all races. Blacks have the highest rates of keloid, followed by yellow and white.

In recent years, thanks to advances in molecular biology, the pathogenesis of keloids and hypertrophic scars has been clarified. Particularly, fibroblast growth factor (FGF) and transforming growth factor-beta (TGF-β) play a pivotal role in the development of scars [1], [2].

Although there are many different treatments of keloids nowadays, such as surgical excision, laser, cryotherapy, radiotherapy, silicone gel, corticosteroid injection. PDT, however, each method has its advantages and disadvantages, and the results also vary depending on each study [3]. Injections of corticosteroids have also been introduced in Vietnam. However, up to now, there have been no studies about the doses, effects and the unwanted effects of keloids treatment with Triamcinolone injections.

We aimed evaluation the effect of intralesional corticosteroid injection on keloid, at the National Hospital of Dermatology and Venereology from 1/2009 to 12/2009.

Methods

An open clinical trial (self-comparison before and after treatment) on 65 patients with keloids was conducted at the Department of Laser and Surgical of Dermatology Central Hospital of Vietnam from January 2009 to December 2009.

Included 65 patients were randomised into 2 equal groups: a studied group of 33 patients received TAC injection with a dose of 7.5 mg/1 cm^2 scars acreage and control group of 32 patients received TAC injection with a dose of 15 mg/1 cm^2 scars acreage.

Patients are given repeated doses every 4 weeks, and totally does not exceed 60 mg/each time. Average treatment times 4-6 times.

Evaluation of treatment outcome: Based on clinical evaluation criteria of Henderson (1998) and El-Tonsy (1996) [4].

- Flat scars: 1 point.
- Soft scars (equivalent to surrounding normal skin): 1 point.
- Bright colour scars (equivalent to surrounding normal skin colour): 1 point.
- No functional symptoms (itching, pain): 1 point.
- No recurrence: 3 points.
- Recurrence on a small acreage of scar: 1 point.
- Recurrence on a large scale: 0 points.
- No side effects: 3 points.
- Side effects do not stop treatment: 1 point.
- Side effects stop treatment: 0 points.
- The maximum score is 10 points; minimum is 0 points.

Evaluate treatment results in three levels: Good at 9-10 points, Quite good at 7-8 points and Poor when below 7 points.

- Evaluation of side effects and complications:

+ Local:

An ulcer caused by treatment, ulcer healing time.

I am surrounding area vasodilation.

Atrophic skin in the surrounding area.

+ Whole body:

Acne.

Menstrual disorders in women.

Hypertension.

Chronic gastritis.

+ Other undesirable effects (if any).

- Treatment stop:

+ When results are good: scars are stable, flat, soft and free of local functional symptoms, and the thickness of scars after the ultrasound is equivalent to the surrounding normal skin. The injection can be stopped at any time ≤ 6 times when clinical show success.

+ When the patient does not respond to treatment: the patient follows the right course of treatment from 4 to 6 times, but scars continue to develop, local functional symptoms do not decrease.

+ When the patient has some side effects or newly infected diseases such as gastrointestinal ulcer, gastrointestinal bleeding, systemic tuberculosis infection, severe menstrual disorders, Cushing's syndrome.

Results

General characteristics of the included objects

At the initiation time of treatment, there was no difference in age, gender, number, area, thickness and progression of scar between the two groups.

Treatment results

The good and quite good results in the studied group (66.7%, 24.2%) are higher than in control group (53.1%, 16.5%) with $p < 0.05$ as shown in see Table 1.

Table 1: Evaluation of treatment results

After scars treatment evaluation score	Studied group		Control group	
	n	%	n	%
Good (9 – 10 pts)	8	24.2	5	15.6
Quite good (7 – 8 pts)	22	66.7	17	53.1
Poor (< 7 pts)	3	9.1	10	31.3
p	< 0.05			

Unwanted effects

Side effects may include ulcers, acne, menstrual disorders and frequency of occurrence in the control group is higher than the studied group as shown in Table 2.

Table 2: Side effects in two study groups (n = 65)

Side effects		*Studied group*		*Control group*		Summary	
		n	%	n	%	n	%
Local	Ulcers	1	3.0	6	18.6	7	10.8
	Vasodilatation and atrophic skin	0	0	0	0	0	0
Whole body	Acnes	0	0	2	6.4	2	3.1
	Menstrual disorders	1/18	5.6	4/16	25	5/34	14.7
	Hypertension	1	3.0	1	3.1	2	3.1
	Gastritis	0	0	0	0	0	0
Other		0	0	0	0	0	0

Discussion

Keloids are benign, but severely affect the quality of life. Especially with continuous development feature, keloids can cause distortion, limiting joint mobility. Until now, there are no measures to cure keloids completely. Study shows that corticosteroid intralesional injections in both groups yield good results. In studied group, the number of patients receiving TAC injections at doses of 7.5 mg/square cm achieved quite good and good results (90.7%) is higher than control group who received TAC injection at doses of 15 mg/square cm (68.7%), this difference was statistically significant at $p < 0.05$. Triamcinolone inhibits the growth of fibrous cells and reduces collagen deposition in lesions [6], [7].

Tingling and pain at the lesions sites are very common functional symptoms and also cause the patient to come to the clinic. These symptoms heavily affect the quality of life of patients [8]. Our results show that 82.3% of the cases had no itch on the lesions after treatment in both groups; over 75.9% had no pain on the lesions in both groups.

The case of itching and pain can be due to the nerve extremities are no longer confined due to the decrease in density of fibrous cells and collagen fibres after corticoid injection. Corticosteroids also have an anti-inflammatory effect that reduces vascular permeability, inhibits the production of chemical intermediates that reduce inflammation, itch and pain.

Accurately measurement of the thickness of the scars is a very difficult matter. In the past, most studies assessed the thickness by measuring the elevation of the scar compared to the surrounding normal skin [2], [4]. This method is simple but inaccurate because most of the thickness of the scar is in the dermis. To determine the thickness of the scar we use Philip HD II ultrasound machine with high-frequency probes. This is a highly reliable measure, first used to accurately measure the thickness of the scar with a deviation of 0.01 mm. We are determining the thickness of scars before treatment and the average level of slack after each injection helps us to plan treatment.

In both groups, the mean scar thickness before treated was 5.50 mm. The mean scar thickness reduction after each injection in the studied group was 0.81 ± 0.39 mm, in the control group was 1.24 ± 0.53 mm. After treatment, the scar thickness was 2-3 times lower than before treatment ($p < 0.05$), the thickness of the scar corresponded to normal skin (1.9 mm).

Evaluation of skin flatness after treatment showed that in the studied group, 78.8% of patients had flattened scars, while in the control group, this rate was 65.6%. To achieve flatness compared to the surrounding skin, the studied group had to inject 3.5 times on average, while the control group had to inject 3 times on average. The results of Manuskiatti's research are similar to our results. After 2 injections of TAC (8 weeks), the thickness of the scar returned to normal compared with the surrounding skin [5]. None of the 65 patients in our study had flattened scars after one injection.

The softness of the skin is also an important criterion for evaluating treatment success. After treatment, the softness of scar in both groups improved significantly. However, there was no significant difference in comparison between the two groups.

There were 7 patients with scars ulcer after injected, one in studied group (3.0%) and 6 in the control group (18.6%). The cause of ulcer may be due to high dosage. This explains our results in the control group, patients treated with high doses (30 mg/1 ml) twice as often as studied group (15 mg/1 ml) should have more ulcer patients. The study of A. Darougheh in 20 keloids patients treated with triamcinolone of 20 mg/1ml injections showed no cases of the ulcer. However, our results in the studied group, one patient treated with lower doses (15 mg/1 ml) also have an ulcer after injection. This may be due to too-shallow injection techniques, which are also responsible for ulcers. Most cases of scar ulcers occur after 3 to 4 treatment times. Therefore, after the second injection the thickness of the scar should be noted, and especially injections should not be too shallow to avoid ulceration in this injection.

In the control group, there were 2 cases (6.25%) of acne reappearing in a total of 6 patients with a history of stable, treated acne. No cases of acne appear in patients with no history of acne before treatment. In the studied group, we did not find any cases of post-treatment acne (9 patients had a history of acne before treatment). Thus, when using high-dose topical corticosteroid therapy for keloids in patients with a history of acne, there is a risk of recurrence of acne. Therefore, for patients with post-acne keloid, it is best not to use corticosteroids therapy. These patients should take other therapies such as cold surgery or colour laser.

There were 5/34 female patients in both groups with menstrual disorders, with only 1/18 patient in the studied group and 4/16 patients in the control group. These patients had bleeding days increased 2-3 days, in contrast to the cycle is shortened by 5-7 days. This menstrual disorder usually occurs after 2 to 4 treatments but not severe, and after a short rest period from treatment, the menstrual period returns to normal.

There are two cases of hypertension during treatment, in which one patient in the control group suffered hypertension and ulceration at the lesion after treatment 4 times, so we stopped this patient treatment. A study by Daruogheh A. found that 37% of patients exhibited atrophy skin and vasodilatation [2]. However, we do not see any cases of skin atrophy around scars, vasodilatation or drug-induced gastritis.

This may be due to the fact that most of our patients have a low number of lesions, scar acreage is small, so the amount of drug used is not much. Therefore, in our experience, to minimise the side effects of the drug, patients should not be injected more than 60 mg each injection.

In conclusion, triamcinolone injections were effective in treating keloids: Studied group had a higher proportion of patients with quite good and good treatment results (90.7%) than in control group quite good and good results (68.7%) with $p < 0.05$. The rate of patients ceased itching, and pain post-treatment in the studied group was 86.6%, and 95.5%; Similar in control group is 78.1% and 80%. Although the average reduction in scars thickness after each injection in the control group (1.24 ± 0.53 mm) was significantly higher than in the studied group (10.81 ± 0.39 mm) ($p < 0.05$), however, some side effects such as ulceration at the lesions, acne, menstrual disorder, are less common in the studied group (7.5 mg/1 cm^2). Therefore, the treatment of keloids with Triamcinolone injection dose of 7.5 mg/1cm^2 showed best results.

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Efficacy of Oral Low-Dose Isotretinoin in the Treatment of Acne Vulgaris in Vietnam

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Keywords: Acne vulgaris; Plasma homocysteine level; Serum folic acid level; Low dose isotretinoin

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Abstract

BACKGROUND: Oral isotretinoin is an effective therapy for acne. However, isotretinoin can induce hyperhomocysteinemia and decreased serum folic acid level, which may be a risk for cardiovascular disease and thrombosis, as well as psychoses. Besides, many recent types of research emphasise the safety and effects of the low dose isotretinoin therapy.

AIM: The aim of our study was to evaluate the effect of the low-dose isotretinoin on the plasma homocysteine and serum folic acid level in the Vietnamese population.

METHODS: We conducted a longitudinal study to evaluate the effectiveness of the low-dose therapy on the plasma homocysteine and serum folic acid level of 52 acne patients after 6-8-week treatment at University Medical Center Ho Chi Minh City, Viet Nam. Patients had moderate-severe acne with the prolonged course, and most of them had a scar.

RESULTS: With a low dose of oral isotretinoin (0.37 ± 0.11 mg/kg/day), after 6-8-week treatment, patients dropped the severity of disease, increased the plasma homocysteine level and decreased the serum folic acid level with significant differences in comparison to those before treatment. However, these changes do not exceed the normal range.

CONCLUSION: In overall, low dose isotretinoin treatment had effectiveness in decrease the severity of disease and no increasing the plasma homocysteine level as well as the serum folic acid level.

Introduction

Acne is a popular skin disease with the incidence in adolescence of up to 85-100%, including 30% moderate and 10% severe acne [1], [2], [3], [4]. Isotretinoin has been used to treat moderate-severe acne where standard treatment was not effective. Compared to other treatments, isotretinoin has been shown to be more responsive in decreasing the size and secretion of sebaceous gland [5]. However, isotretinoin may result in elevated plasma homocysteine and decreased serum folic acid which in turn contribute to cardiovascular diseases, thrombosis, cognitive function disorders and dementia [6], [7], [8].

Many researchers have evaluated which isotretinoin dose would have the most efficacy and less adverse events. Recent studies indicated the safety of the oral isotretinoin therapy where the low dose of isotretinoin (< 0.5 mg/kg/day) had no significant effects in metabolic disorders [9], [10]. Effective treatment and less severe side effects were found in a study among 638 patients, both male and female, with moderate acne that were treated with isotretinoin at 20 mg/d (approximately 0.3-0.4 mg/kg per day) for 6 months [9]. Another study among 150 Malaysian patients treated with isotretinoin at 10mg on the daily basis until a cumulative dose of 90-110 mg/kg showed that after 24 weeks of treatment, all patients cleared of acne lesions with a low rate of elevated liver enzymes and serum lipid at 3.3% and 2.7% respectively. There was no case of discontinuation in treatment [11]. The hyperhomocysteinemia with low serum folic acid level

cause many severe side effects, but there was no study in the literature about this disorder in low-dose isotretinoin therapy.

Therefore, in this study, we evaluated the changes of the homocysteine and folic acid level during oral isotretinoin treatment in Vietnamese acne patients. Findings from this study might contribute to the literature whether we should monitor the plasma homocysteine and serum folic acid in patients treated with oral low-dose isotretinoin to prevent hyperhomocysteinemia, decrease folic acid level and possibly related disorders.

Methods

Setting and Participants

In September 2014, a longitudinal study was conducted at the Skin Care Department, University medical centre HCMC. We recruited 52 acne patients above 18 years old. All patients received the explanation of objects and procedures and signed the consent form. Patients were then treated with oral Isotretinoin once a day for 6 – 8 weeks. Those who had hepatic/kidney failure or under treatment with drugs such as phenytoin, L-dopa, methotrexate, theophylline, penicillamine, vitamin B12, vitamin B6, acid folic were excluded. All procedures in this study were approved by the Ethics Committee at HCMC University of Medicine and Pharmacy, Vietnam.

Procedures

All patients were asked about their medical history and examined to assess the skin type and acne status by a dermatologist from the Department of Dermatology, HCMC University of Medicine and Pharmacy. They have then measured the concentration of plasma homocysteine and serum folic acid level. After 6 – 8 weeks of treatment, patients were re-measured the concentration of the plasma homocysteine and serum folic acid level as well as re-assessed the clinical characteristics and the severity of acne.

Measurements

The plasma homocysteine level was measured by a quantitative method, direct chemiluminescent immunoassay with the ADVIA Centaur machine of Simen. The serum folic acid level was quantified by the Architect C16000 machine of Abbott using chemiluminescent microparticle immunoassay technology. Patient's history was assessed by onset age (< 25 years old and ≥ 25 years old) and disease duration (≥ 24 months and < 24 months). Clinical symptoms of acne are assessed by skin types (oily, normal, combined variants), acne lesions (papule, pustule, nodule, cyst, opened and closed comedones), affected areas (face, chest, back, arm) and scar (atrophic + keloid scar, no scar).

The severity of acne is evaluated using GAGS (Global Acne Grading System) of Doshi, Zaheer and Stiller. The GAGS considers six locations on the face (forehead, cheeks, nose, chin, chest and back). Each is derived by multiplying the factors-2 for forehead, 2 for each cheek, 1 for nose, 1 for chin, 3 for both chests and back by the most heavily weighted lesion within each region (1 for ≥ one comedone, 2 for ≥ one papule, 3 for ≥ one pustule, and 4 for ≥ one nodule).

The score for each area (local score) is calculated using the formula: Local score = Factor × Grade (0-4). The global score is the sum of local scores, and acne severity is graded using the global score. A score of 1-18 is considered mild; 19-30 as moderate; 31-38 as severe; and ≥ 39 as very severe.

The 25th percentile of the mean cumulative isotretinoin dose in our research was 18.5 mg/kg. We use this cut-off value to compare pre- and posttreatment plasma homocysteine levels and serum folate levels based on the accumulative dose of isotretinoin.

Data analysis

We described data using frequency and percentage for qualitative variables, the mean and standard deviation for quantitative variables. Association between patients' characteristics and plasma homocysteine and serum folate levels was evaluated using t-test. Comparison of mean plasma concentrations of plasma homocysteine and folic acid before and after treatment was conducted using a paired t-test. Type I error was set at 5%. All data analysis was done using SPSS 20.0.

Results

In 52 acne patients treated with oral isotretinoin therapy at University Medical Center, the majority was female (80.8%) with the mean age of 22 years old and the mean weight of 52.77 kg (SD = 8.97 kg). Almost all patients had oily skin (90.4%), onset age under 5 years old (94.2%) and had acne on the face (98.1%). Most patients suffered from moderate and severe acne and had scars.

The mean severity of disease evaluated by GAGs score was 25.98 ± 6.5 score as shown in Table 1.

Table 1: Characteristics of acne patients treated with oral isotretinoin

		N (%)	Homocysteine (µg/l)		Folate (ng/ml)	
			M (SD)	p	M (SD)	p
Sex	Male	10 (19.2)	10.59 (9.94-11.55)	0.001	6.72 (1,85)	0.112
	Female	42 (80.8)	7.69 (6.63-9.20)		8.27 (2,88)	
Onset age	≥ 25 years old	3 (5.8)				
	< 25 years old	49 (94.2)				
Duration of disease	≥ 24 months	40 (76.9)	8.79 (2.37)	0.30	7.94 (2.84)	0.860
	< 24 months	12 (23.1)	8.01 (1.97)	0	8.10 (2.59)	
Skin type	Oily	47 (90.4)	8.6 (2.37)	0.98	8.01 (2.74)	0.790
	Other	5 (9.6)	8.64 (1.41)	0	7.65 (3.32)	
Acne lesion	Close comedone	51 (98.1)				
	Open comedones	47 (90.4)				
	Papule	50 (96.2)				
	Pustule	47 (90.4)				
	Nodule	39 (75.0)				
	Cyst	18 (34.6)				
Affected area	Face	51 (98.1)				
	Chest	19 (36.5)				
	Back	21 (40.4)				
	Arm	2 (3.8)				
Scar	Atrophic scar	38 (73.1)				
	Keloid	0 (0)				
	Atrophic scar + keloid	2 (3.8)				
	No scar	12 (23.1)				
Severity of acne	Mild	6 (11.5)	8.4 (2.13)	0.114	9.65 (3.84)	0.086
	Moderate	32 (61.5)	8.17 (2.09)		8.17 (2.49)	
	Severe- very severe	14 (27.0)	9.68 (2.57)		6.81 (2.55)	

The oral Isotretinoin dose during 6-8-week treatment was 0.37 ± 0.11 mg/kg/day; the accumulative dose was 14.67 (18.5-21.95) mg/kg. After 6-8-week treatment with oral Isotretinoin, the severity of acne followed GAGs and serum folate level was statistically significantly decreased; plasma Homocysteine levels were significantly statistically elevated ($P < 0.05$) as shown in Table 2.

Table 2: The severity of acne, the plasma homocysteine and serum folate levels in patients before and after 6-8 weeks on isotretinoin treatment

	Before treatment	After treatment	P
The severity followed GAGs	25.98 ± 6.50	15.56 ± 6.87	< 0.001
Homocysteine (µg/l)	8.61 ± 2.29	9.23 ± 2.37	0.016
Male	10.58 ± 1.12	11.42 ± 1.96	0.252
Female	7.69 (6.63 – 9.20)	8.27 (7.20 – 10.05)	0.018
Folate (ng/ml)	7.98 ± 2.76	7.16 ± 2.42	0.005

Post-treatment plasma homocysteine and serum folic acid were significantly changed compared with the initial values in a group of patients with the higher mean accumulative dose of isotretinoin (> 18.5 mg/kg), as shown in Table 3. There were no statistical differences in others.

Table 3: Comparison of pre- and post-treatment plasma homocysteine levels and serum folate levels based on accumulative dose of isotretinoin

Accumulative dose		≤ 18.5 mg/kg *(N = 26)*	> 18.5 mg/kg *(N = 26)*
Homocysteine	Before treatment	8.43 ± 2.54	8.78 ± 2.04
	After treatment	8.79 ± 2.38	9.67 ± 2.31
	p	0.300	0.019
Folate	Before treatment	8.29 ± 2.98	7.66 ± 2.54
	After treatment	7.55 ± 2.50	6.77 ± 2.31
	p	0.110	0.012

Discussion

This was the first Vietnamese study that evaluates the effects of low dose isotretinoin on the plasma homocysteine and serum folic acid level in acne patients. The results showed that the severity of disease of patients treated with a mean dose of isotretinoin 0.37 ± 0.11 mg/kg/day after 6-8 weeks decreased statistically. This demonstrated that the low dose oral Isotretinoin therapy is an effective treatment in acne. Besides, the plasma homocysteine level increased and the serum folic acid level decreased with significant differences in comparison to those before treatment. However, these changes do not exceed the normal range. Our findings were consistent with previous studies where low dose isotretinoin has been showed to be beneficial in the treatment and a decrease in relapse [9], [10], [11]. Hence, to minimise the side effects of drugs, the low dose isotretinoin should be considered in the treatment of acne disease.

The hyperhomocysteinemia is a risk factor for cardiovascular diseases and venous thrombosis and also affects negatively on endothelial cells, smooth muscle cells in recent reports [6], [7], [8], [12]. The hyperhomocysteinemia was also reported in some researches in acne patients treated with isotretinoin. In these studies, the plasma Homocysteine level significantly increased after treated with oral isotretinoin (≥ 0.5 mg/kg/day) during 45 days or more [13], [14], [15], possibly because the inhibitions of cystathionine β synthase, leading to disrupt the metabolism of homocysteine [16]. Another possible reason could be that the drug decreased the level of folic acid and vitamin B12, resulting in rising homocysteine level [14]. Our results also indicated that the plasma homocysteine level after 6-8 week treatment increased significantly in comparison with the initial level (8.61 ± 2.29 µg/l with 9.23 ± 2.37 µg/l). However, this plasma homocysteine level after treatment did not exceed the normal biologically range of the plasma homocysteine level (15 µg/l).

Regarding the level of folic acid, our results confirmed the conclusions of previous national studies, in which the serum folic acid dropped markedly after oral isotretinoin therapy [17], [18], [14]. Karadag et al. observed a decrease of serum acid folic level during treatment isotretinoin 0.5 mg/kg/day for 4 months [14]. In our study, the serum folic acid level after 6-8-week treatment was significantly lower in comparison with the initial level (7.98 ± 2.76 ng/ml with 7.16 ± 2.42 ng/ml). Nevertheless, similarly to the changes in homocysteine level, although this difference was statistically significant but not clinically meaningful because this decreased level was in normal range. The deficiency of folic acid may induce some disorders such as neuropathy, psychoses and dementia. This deficiency also contributes to advance homocysteine level, leading to adverse events of hyperhomocysteinemia. According to the results, there is no risk for folic acid deficiency-induced disorders when the low dose isotretinoin is used.

Generally, the adverse effects of isotretinoin depend on dose. In our study, patients treated with

the higher mean accumulative dose of isotretinoin had more markedly changes of the serum homocysteine and folic acid. Consequently, when using of high dose or long term of isotretinoin therapy which may increase the cumulative dose, it is essential to prevent the risk of rising homocysteine or falling folic acid. Vitamin intake such as vitamin B12 or folic acid might be proved an effective preventive measure against some complication due to hyperhomocysteinemia [13], [14], [16].

This study was subject to several limitations. First, the effects of the long-term low dose isotretinoin could not be assessed due to the limited followed-up period. Second, we could not clarify the changes in homocysteine and folic acid due to the hepatic dysfunction or effect on a certain enzyme involved by the drug in the synthetic process of 2 substances. Third, because there was no control group, the different effects of high dose and low dose isotretinoin on homocysteine and folic acid level were not able to describe. Finally, we were only able to sample clients from one hospital in HCMC. Thus, it is possible that climatic, socio-economic and/or other differences existed among clients across different areas and settings. In this regard, further studies were needed.

In conclusion, we found that moderate and severe acne patients treated with low dose isotretinoin (< 0.5 mg/kg/day) had no change in the homocysteine and folic acid level of the blood, which can induce adverse events biologically. Therefore, during treatment with the low dose isotretinoin, it is unessential to monitor the level of homocysteine and folic acid. However, when treated with the higher dose or for a long-term period, the risk of increasing of the plasma homocysteine and decreasing serum folic acid level should be considered.

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Successful Treatment of Vitiligo Vietnamese Patients with Vitilinex® Herbal Bio-Actives in Combination with Phototherapy

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Keywords: Vitiligo; Bio-actives; UVB narrow band (311 nm); Phototherapy; Re-pigmentation

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Abstract

BACKGROUND: Vitiligo is an acquired pigmentary disease, that causes progressive loss of melanocytes, resulting in hypopigmented skin patches. Current treatments aim at stopping the disease progression and achieving repigmentation of the amelanotic areas. Corticosteroids, surgery, topical immunomodulators, total depigmentation of normal pigmented skin and phototherapy are current treatment options for vitiligo although phototherapy remains the treatment of choice. There is no documented evidence that herbal bio-active products may also be effective treatment options for vitiligo.

AIM: This study aimed to investigate the efficacy and safety of Vitilinex® (herbal bio- actives) alone and in combination with UVB narrowband (311 nm) phototherapy, in the treatment of localised stable or active forms of vitiligo.

MATERIAL AND METHODS: Sixty two subjects with mean age 34.5 years (range: 18-58 years) with mild to moderate vitiligo, consisting of 36 females and 26 males were randomly divided into three treatment groups – Group A (13 females, 10 males) treated with Vitilinex® alone; Group B (12 females, 11 males) were treated with Vitilinex® in combination with narrowband UVB (311 nm) phototherapy for 15 seconds, using a handheld lamp and Group C (8 females, 8 males) were treated with nbUVB (311 nm) phototherapy alone, for 15 seconds over a 12-week period.

RESULTS: In Group A, 9 patients (39%) achieved outstanding improvement with a re-pigmentation rate higher than 75%, with 2 patients experiencing total repigmentation. 6 patients (26%) had marked improvement with a repigmentation rate between 50-75% while 5 patients (22%) showed a moderate response between 25-50% re-pigmentation rate. 3 patients (13%) had minimal or no improvement. In Group B, 16 patients (69.5%) achieved outstanding improvement with a re-pigmentation rate higher than 75%, with 12 patients experiencing total re-pigmentation. 4 patients (17.5 %) achieved a marked improvement with a re-pigmentation rate between 50-75%; 2 patients (8.7%) showed a moderate response with a re-pigmentation rate between 25-50%. 1 (4.3%) patient had minimal or no improvement. In Group C, 6 patients (37.5%) achieved a re-pigmentation rate higher than 75%, with 2 patients experiencing total re-pigmentation. 4 patients (25%) achieved marked improvement with a re-pigmentation rate between 50-75% while 3 patients (18.75%) had a re-pigmentation rate between 25-50%. 3 patients (18.75%) had minimal or no improvement.

CONCLUSION: Vitilinex® herbal bio-actives in combination with nbUVB is a more effective treatment option for vitiligo with 87% of the patients achieving a re-pigmentation rate higher than 50%, compared to Vitilinex® alone (65%) or nbUVB alone (62.5%).

Introduction

Vitiligo is an acquired idiopathic of unknown origin and is a common de-pigmentation disorder, that causes progressive loss of melanocytes, resulting in hypopigmented skin patches, hair and mucosa.

Vitiligo is the most common disorder of pigmentation, affecting between 0.5-2% of the world's population, and the prevalence appears to be equal between men and women. Although neither life-threatening nor symptomatic, the effect of vitiligo can be cosmetically and psychologically devastating, resulting in low self-esteem, poor body image and

other negative quality of effects [1].

The exact pathogenesis of vitiligo is still to be elucidated [2]. Multiple mechanisms, including metabolic abnormalities, oxidative stress, generation of inflammatory mediators, cell detachment and autoimmune responses, are contributing factors in the pathogenesis [3], [4]. Vitiligo may appear at any age and affect both sexes equally [1], [5].

The clinical diagnostic features of the vitiligo are discolouration of the skin, characterised by well-circumscribed, ivory or chalky white macules [6]. These hypopigmented macules or patches occur on the skin in different parts of the body including the face, genitalia, areolae and areas subjected to repeated trauma like elbows and knees. Involvement of mucous membranes and hair shaft is also possible [7]

The current vitiligo treatments aim at stopping the disease progression and achieving repigmentation of the amelanotic areas, thus restoring the loss of melanocytes in the lesions. Corticosteroids, surgery, topical immunomodulators, total depigmentation of normally pigmented skin, lasers and phototherapy are current treatment options for vitiligo although phototherapy remains the treatment of choice [8], [9], [10]. However, many patients are now investigating other treatment options including herbal bio-active products [11].

This study aimed to investigate the efficacy and safety of Vitilinex – herbal bio-active products alone; Vitilinex in combination with UVB narrowband (311 nm) phototherapy; phototherapy alone, in the treatment of localised stable or active forms of vitiligo.

Material and Methods

This multi-centred observational retrospective study was conducted in Italy, India, Vietnam, Germany and Australia. Sixty-three (63) patients (30 males, 33 females), aged from 18 to 58 years with a mean 34.5 years, suffering from stable or active vitiligo were evaluated over 12 weeks. They had not received any treatment for the cutaneous disease for at least two years. The results were subjected to statistical analysis.

The patients were randomly assigned to the following groups:

1) Group A- (18 females, 17 males)- Vitilinex® herbal bio-actives alone

2) Group B- (15 females, 9 males) – Vitilinex® in combination with nb-UVB 311 nm phototherapy

3) Group C- (8 males, 8 females) – nb-UVB 311nm phototherapy alone.

Vitilinex® consists of two products: Skin Prep lotion (containing-Centipeda cunninghamii, aloe vera, terpinol-4-ol and dihydro avenanthramide – D) and Emmolient (containing- black cumin seed oil, black pepper coleus forskohlii, Psoralea coryfolia, thyme oil, myrrh and neroli extracts. These oil extracts have shown to have very strong anti-oxidant properties.

The Skin Prep lotion was applied to the affected areas and allowed to dry, followed by the application of the emollient. The area was then irradiated weekly week over 12 weeks at 311 nm, with a starting dose of 20% less than the minimal erythema dose (MED) for each patient, evaluated on a vitiliginous lesion 7 days before the start of treatment. The irradiation dose was progressively increased by 20%. In cases where erythema was noted, we reduced the dose by 20% in the following treatment.

The assessment was based on assigning a 0% score for each lesion before therapy and improvement based on a percentage value to represent the level of repigmentation. Digital photos were taken at week 0 and each follow-up session.

Results

In Group A, with Vitilinex® treatment alone, 9 patients (39%) achieved outstanding improvement with a re-pigmentation rate higher than 75%, with 2 patients experiencing total repigmentation. 6 patients (26%) had a marked improvement with a repigmentation rate between 50-75% while 5 patients (22%) showed a moderate response between 25-50% re-pigmentation rate. 3 patients (13%) had minimal or no improvement. In Group B, with Vitilinex® in combination with nb-UVB 311 nm, 16 patients (69.5%) achieved outstanding improvement with a re-pigmentation rate higher than 75%, with 12 patients experiencing total re-pigmentation. Four patients (17.5 %) achieved a marked improvement with a re-pigmentation rate between 50-75%; 2 patients (8.7%) showed a moderate response with a re-pigmentation rate between 25-50%. 1 (4.3%) patient had minimal or no improvement. We noted that when we increased the irradiation dose by 20%, erythema developed. We, therefore, kept the treatment does the same as the starting dose throughout the treatment, hence minimising the UVB exposure. As the emollient contains a mixture of oils, the development of erythema may be attributed to a burning effect with increased oil temperature during irradiation.

While in Group C, phototherapy alone, 6 patients (37.5%) achieved a re-pigmentation rate higher than 75%, with 2 patients experiencing total re-pigmentation. 4 patients (25%) achieved marked

improvement with a re-pigmentation rate between 50-75% while 3 patients (18.75%) had a re-pigmentation rate between 25-50%. 3 patients (18.75%) had minimal or no improvement.

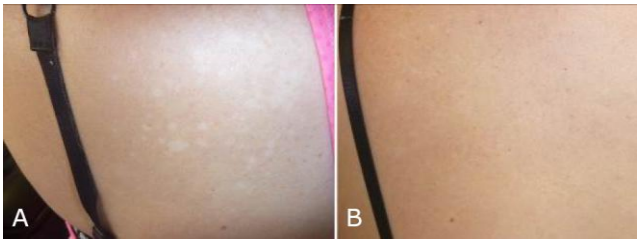

Figure 1: A) Before Treatment – Week 0; B) - After Combination Treatment– Week 12

There were no adverse effects reported or observed following adjustment of the treatment dose in the combination therapy before and after treatment photographs are shown in Figures 1, 2, 3, and 4.

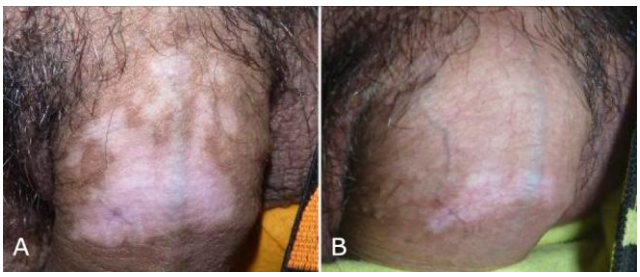

Figure 2: A) Before Treatment – Week 0; B) After Combination Treatment–Week 12

Discussion

We evaluated the efficacy of Vitilinex® alone and in combination with nb-UVB 311 nm phototherapy, in the treatment of 63 patients with stable or active forms of vitiligo. The results clearly show that Vitilinex® in combination with phototherapy is significantly more effective than Vitilinex or phototherapy alone. In the combination therapy, 87% of the patients had repigmentation rate higher than 50%, compared to Vitilinex® (65%) and phototherapy alone (62.5%). The irradiation dose for the combination therapy was kept at the minimal starting dose. This is also of great benefit, as it minimises the UV radiation exposure, which has been linked to intracellular mutations, which may, in turn, induce malignant transformation.

Centipeda cunninghamii in the Prep Lotion, contains caffeic acid and sesquiterpene lactones, having strong anti-inflammatory and antioxidant activity [12]. Terpinol-4-on, a potent constituent of tea tree oil, possesses antioxidant and anti-inflammatory properties by suppressing superoxide production and pro-inflammatory cytokines – TNF-alpha, IL-1beta, IL-8, IL-10 and PGE2 [13].

The antioxidant benefit of aloe vera is well documented and believed to impart its benefit in vitiligo treatment by inhibiting COX2 and PGE2 [14] whilst dihydro avenanthramide – D, has been shown to prevent UV-irradiated generation of reactive oxygen species and expression of matrix metalloproteinase-1 and -3 in human dermal fibroblasts at 5 ppm [15].

Black cumin seed oil (Nigella sativa), used in the embodiment, contains thymoquinone which has been shown to induce melanin production and dispersion [16]. Piperine, from Piper nigrum, and its synthetic analogues, have been shown to stimulate mouse and human melanocyte proliferation [17], [18], [19]. Thyme oil, myrrh and neroli extracts have shown to have very strong anti-oxidant properties in cell culture studies [20].

The repigmentation in vitiligo is believed to be linked to a synergistic effect of all the antioxidant action of these herbal bio-actives. The availability of any new treatment that can reduce the use of UVB from high to low, and still be efficacious, is of immense benefit to both patients and treating physicians [21], [22], [23], [24], [25], [26], [27], [28], [29].

In this study, we confirmed the efficacy of nb-UVB in the treatment of vitiligo. However, the combination therapy with Vitilinex® herbal bio-actives proved more effective, using a lower than normal irradiation dose, thus reducing the potential for serious DNA intracellular mutations. The results also confirm that Vitilinex® bio-actives are effective alone.

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Successful Treatment of Freckles by Alex Trivantage Laser Wavelight 755 nm in Vietnamese Patients

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Abstract

OBJECTIVES: This study aims to evaluate the effectiveness of Alex Trivantage laser wavelength 755 nm (ATL) in the treatment of freckles at Hanoi Hospital of Dermatology and Venereology, Vietnam.

PATIENTS AND METHODS: A group of 30 patients with freckles were treated by ATL (Alex Trivantage-Candela Co America) with spots size 3 mm, wavelength 755 mm, and energy 5-6 j/cm^2. All the patients were treated 2 times with 4-weeks interval. The results were evaluated at 4, 8, and 12 weeks after treatment. The colour of the lesions was evaluated by using Von-Luchan's chromatic scale and Visia® complex analysis system. Brown spot index (BSI) was calculated by the VISA complexion analysis system devices. The data was analysed by SPSS 16.0.

RESULTS: After 2 times of treatment, the lesion colour of all of the patients had been improved. The good and very good levels of improvement were noted in 63.3% of patients; there was 26.7% of them had partial improvement. Brown spots index was significantly improved (39.13 ± 20.66 before and 54.23 ± 16.78 after treatment; $p < 0.001$). Hyperpigmentation was noted in 6.7% of patients.

CONCLUSION: freckles have been improved by treatment with Alex trivantage laser wavelength 755 nm with safety.

Introduction

Vietnamese, as well as the Asian people, belongs to skin types III-V (Fitzpatrick skin type). However, melasma, freckles, and lentigines are the epidermal disorders commonly seen [1].

Freckles are typical pigmentation disorders presenting by hyperpigmentation dark – brown or light – circular brown spots on face, especially on the cheeks. Freckles should be distinguished from lentigines [2]. Lentigines are well-circumscribed, small, brown spots which appear both on sun-exposed and no exposed areas [3], [4]. Freckles can appear on all types of skin tones [2], [5].

Several treatments effectively diminish the appearance of freckles. Some of the treatments include skin-lightening creams such as hydroquinone, prescription medications containing retinoid, chemical peels that are shown to improve pigmentation irregularities, IPL therapy [6] and others pigment lasers [7], [8], [9]. Alex TriVantage is a q-switched laser which is built upon the proven performance of

755 nm, Q-switched Alexandrite laser with the addition of 1064 nm and 532 nm, Q-switched Nd: YAG wavelengths. With the 755 nm Long-Pulse mode, it is used for treating a wide variety of epidermal and subdermal pigmented lesions safely. The acquirement of freckles treatment is recently increased in Vietnam and many medical facilities in our country in the past few years applied the different pigment lasers in treating pigmentary disorders.

Our study aimed to assess the effectiveness of Alex TriVantage laser on freckles treatment at Hanoi Hospital of Dermatology and Venereology (HHDV).

Patients and Methods

The prospective controlled clinical trial on 30 patients with freckles treated by QS Alexandrite laser at HHDV. Informed consent was obtained from the patients before the laser treatment. Photographs were taken before treatment. The treated areas were numbed with topical anaesthesia using EMLA 5% cream. Eyes of patients were protected with specific protective glasses. In all cases, test spots were done, and the results were checked after 1 month to determine the parameters before performing the laser treatment on the entire area.

The used laser machine was an AlexTriVantage of Candela company – the USA, wavelength 755 nm. The patients have treated 2 sections with power 5.0-6.0 j/cm^2; spot size 3 mm, at week 0 and week 4. Ice packs were applied to the treated areas to reduce erythema and oedema.

After these procedures, all patients were asked to avoid unnecessary sun exposure. None combination treatment was indicated after the laser treatment once the scabs had fallen off along with daytime use of sunscreen. The final results were analysed after 4, 8 and 12 weeks after treatment. The colour of the lesion was assessed by using colour to Von Luschan's chromatic scale:

Grade 1: same skin colour with normal skin;

Grade 2: light pigmentation (scale 19-24) ;

Grade 3: medium pigmentation (scale 25-27) ;

Grade 4: hyperpigmentation (scale 28-32) ;

Grade 5: very high pigmentation (scale 33-36).

The results were evaluated based on the improvement of the lesion colour before and at 4, 8 and 12 weeks after treatment with very good improvement, if colour of lesion improved ≥ 3 scales or the lesion, becomes normal skin; good improvement if colour of lesion improved ≥ 2 scales and no improvement if the colour of lesion improved less than 1 scale.

Table 1: Characteristics of study subjects

	n	%
Sex		
Female	29	96.7
Male	1	3.3
Age		
11-≤20	3	10
21-≤30	6	20
31-≤40	15	50
41-≤50	4	13.3
>50	2	6.7
Skin type		
III	11	36.7
IV	19	63.3
Severity (Basing on the number of lesions)		
<100	4	13.3
>100	26	86.7

We also analysed the improvement of the lesion colour by Visia® complex analysis system. The Canfield Imaging Systems was used for capturing multi-spectral photos of the face. Brown spot index was calculated and analysed at pre- and post-treatment by digital images technologies (BS-320 facial skin analysis)

The side-effects including hyperpigmentation, hypopigmentation, scars, were reported. The data was collected and analysed by SPSS 16.0.

Results

Thirty female patients were recruited for the study. Almost all of them were female (96.7%). Nine of patients (30%) were less than 30 years old, and 11 (70%) of them were older than 30 years old as shown in Tablet. All of them were finished at 2 sections of treatment, and no patients were needed in the third section. In overalls, the good and very good levels were noted in 63.3% of patients; there was 26.7 % of them had partial improvement. Brown spots index before and after treatment were 39.13 ± 20.66 and 54.23 ± 16.78 ($p < 0.001$; respectively); and after 12-weeks, there were no recurrences as shown in Table 2 and Figure 1.

Table 2: The effectiveness of QS Alexandrite laser on freckles treatment *(n = 30)*

		Improvement	
		good and very good	Partial
		n (%)	n (%)
Age	< 30	7 (23.3)	2 (6.7)
(years old)	> 30	12 (40.0)	9 (30.0)
Skin Type	III	10 (33.3)	1 (3.3)
(Fitzpatrick classification)	IV	9 (30.1)	10 (33.3)
	Chin	6 (20.0)	1 (3.3)
Location	forehead	2 (6.7)	2 (6.7)
	Check, nose	11 (36.7)	8 (26.6)
Total		19 (63.3)	11 (26.7)

The improvement of lesions on patients with skin type III was higher than that on patients with type

IV skin; however, the statistic was not significant. The result was not also different between the location of the lesions as well as of the age of the patients as shown in Table 2.

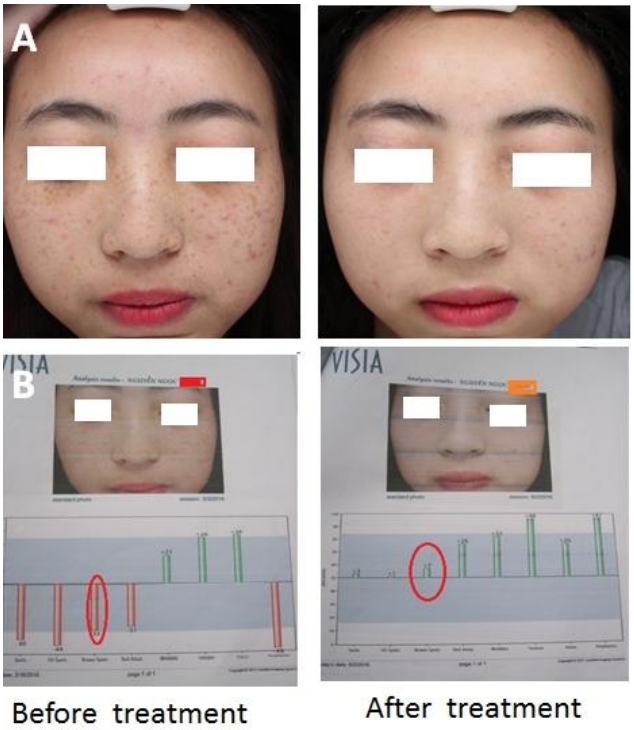

Figure 1: A 19 years old woman before and after 2 sections of treatment by QS Alexandrite A); Brown spots index before was -35.5 and +7 after treatment B)

The Brown index before and after treatment are 39.13 ± 2066 and 54.23 ± 16, 78 ($p < 0,005$; test T student).

Investigating side effects, we noted that 2 patients had hyperpigmentation post laser treatment, accounting for 6.7%. No patients suffered from hypopigmentation and scars as shown in Table 3.

Table 3: The unwanted effects after QS Alexandrite treatment

Unwanted effects	n	%
Hyperpigmentation	2	6.7
Hypopigmentation	0	0
Scars	0	0
No side effects	28	93.3
Total	30	100

Discussion

The associated factors are affecting the efficiency of the QS Alexandrite laser treatment.

Alex TriVantage laser is a Q-switched Alexandrite laser with the addition of 1064, 532 and 755 nm. Composing of 755 nm Long-Pulse mode, Alex TriVantage laser is used for treating a wide variety of epidermal and subdermal pigmented lesions safely**.** The Alexandrite allows deep penetrating rays in the skin to destroy melanocytes selectively while limiting post hyperpigmentation.

Freckles are commonly found in skin types I-IV as small, poorly marginated, pale brown macules on sun-exposed skin areas. They are not dangerous for the health, but they cause mainly cosmetic troublesome. Nowadays, many pigmentation lasers have been used for treating freckles such as the 755 nm alexandrite, 694 nm ruby, 532 nm, and 1064 nm neodymium: YAG nanosecond lasers appear to be safe and effective modalities.

In our study, 30 patients with freckles treated 2 sections with power 5.0-6.0 j/cm^2; spot size 3 mm, at week 0 and week 4. Three patients needed only 1 session of treatment for clearing the lesions, and 2/30 patients needed 2 sessions. No patients needed 3 sessions. After 12-weeks, 100% of patients had improvement. After 2 sessions of treatment, the very good and good degree was found with 63.3% as shown in Table 2.

The study of Jang KA *et al.* carried out a study with 197 patients, using the Q-switched alexandrite laser at 8-week intervals with 7.0 J/cm2, and they also demonstrated 100% patients had improvement with only 1.5 sections [8]. It elicits that using the lower power with shorter time interval as in our study giving the similar results of Jang group [8].

An alexandrite laser is one that uses an alexandrite crystal as the laser source for producing a specific wavelength of red light (755 nm). Q-switched Alexandrite lasers refer to the technique of making the laser produce a high-intensity beam in very short pulses. Thus alexandrite lasers work by process of photothermolysis for melanin destruction.

Comparing between section 1 and 2, we noted that there was a statistically significant difference in colour's improvement ($p < 0.05$). Although freckles do not have an increased number of the melanin-producing cells or melanocytes, freckles may instead of having melanocytes that overproduce melanin granules (melanosomes) changing the colouration of the outer skin cells (keratinocytes). Some other studies also demonstrated the improving after 1 to 3 lasers sessions in the treatment of pigmentation disorders [10], [11].

We used the VISIA machine to evaluate the efficacy of treatment. Brown Spots index supported us to assess the excessive concentration of melanin in freckle lesions. Brown spots index before and after treatment were 39.13 ± 20.66 and 53.23 ± 16.78 respectively; the difference is statistically significant with $p < 0.05$.

Regarding factors such as age, skin type, our study showed that people less than 30 years old, and early onset before the age of 30 had good improvement with 77.8% and 66.7% respectively. The

improvement is better for young people. Then there was a noticeable reduction in sebum secretion, skin dehydration and pigmentation.

The improvement of lesions located in the chin, nose and forehead area was 87.5%; 50% and 57.9% respectively. In the present study, there were only 2 patients, accounting for 6.7%, with post-inflammatory hyperpigmentation, as a side effect. This is similar to other studies in Asia [8], [9], [12]. Our findings, as well as the results of other investigations, noted that post-inflammatory hyperpigmentation was temporary, resolving within one month, and no long-term complications were noted.

Also, we also founded no patients presented hypopigmentation, keloids, atrophic scars, keloids, atrophic scars and ochronosis. It was noted that there were no recurrences after 12 weeks.

In conclusion, laser QS – Alexandrite had a good device for freckles treatment. All of the patients had improvement in lesion's colour, about 63.3% of patients with a very good and good level of improvement. Only 6.7% of patients had temporally post-inflammatory hyperpigmentation. The Q-switched alexandrite laser is a safe and highly effective modality for removing freckles without scarring or permanent pigmentary changes in Vietnamese skin.

Author contributions

NHS, TCV and LVC designed, performed experiments, collected and analysed data, and collected informed consents. NHS, TCV and LVC interpreted the results. All authors wrote the manuscript. DTC and DHB edited the manuscript. All authors approved the final manuscript.

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Clinical Science

The Effectiveness of Oral Mini-Pulse Methylprednisolonein - the Treatment of Alopecia Areata in Vietnam

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Keywords: Prednisolone; alopecia areata

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Abstract

BACKGROUND: Systemic corticosteroid is used to treat alopecia areata, but it is associated with side effects. Mini-pulse therapy is thought to be effective but able to reduce side effects.

AIM: The study aimed to evaluate the effectiveness of oral mini-pulse methylprednisolone in the treatment of alopecia areata.

METHODS: Patients received methylprednisolone 16 mg orally for 2 consecutive days every week.

RESULTS: After 3 months, among patients, 40% recovered well, and 55.6% recovered fairly. After 6 months, 82.2% recovered well, 17.8% recovered fairly. No adverse events were detected, and the recurrence rate was low (2.2%).

CONCLUSION: Oral mini-pulse methylprednisolone therapy is an effective and safe therapeutic option for alopecia areata without side effects, and the time of the treatment is short.

Introduction

Alopecia areata is an autoimmune disease, affecting 0.2% of the world population, in both genders and all age groups but primarily in young people (aged 15-45), with an unclear aetiology [1]. The most characteristic symptom is hair loss in one or several small rounds or elliptic patches, without pain or itchy. Also, alopecia areata could also cause loss of pubic hair, beard, eyebrows and eyelashes [2].

Systemic corticosteroid therapy has been used to therapy. Though it has beneficial effects, long-term use leads to multiple and note side effects. Pulse and mini-pulse therapy have been introduced to treat several conditions, including alopecia areata, which have been shown to minimise the side effects of corticosteroids. The effectiveness of oral mini-pulse corticosteroids in treating alopecia areata has not been studied in Vietnam.

The study aimed to evaluate the effectiveness of oral mini-pulse methylprednisolone in the treatment of alopecia areata.

Methods

We recruited a total of 45 patients with diagnosed alopecia areata by clinical symptoms,

including hair loss in round or elliptic patches with no pain, itching, or scaling, age ≥ 15 years and with an indication to oral corticosteroids. The mini-pulse regimen was methylprednisolone 16 mg/day for two consecutive days every week for 6 months. All patients adhered to the study procedure and none dropped out.

Results

After 1 month, there were 5 patients (11.1%) recovered fairly. After 3 months, 40% recovered well (18 cases), and 55.6% recovered fairly (25 cases). After 6 months, 82.2% recovered well (35 cases), 17.8% (8 cases) recovered fairly, and all these patients got better hair regrowth days every week as shown in Figure 1.

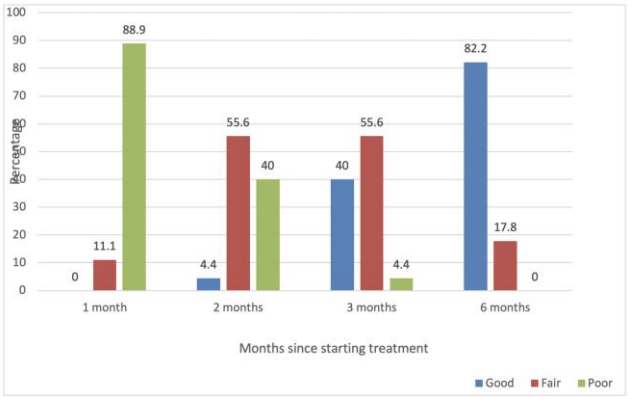

Figure 1: Overall treatment outcome

Severity and gender groups as shown in Table 1 and Table 2.

Table 1: Outcome by severity

Severity	Outcome				p
	Good		Fair		
	n	%	n	%	
Mild	35	85.4	6	14.6	P > 0.05
Moderate	2	50	2	50	

After six months, no side effects were recorded. We had two patients developing new hair loss patches during study participation (one during the therapeutic stage and one during the follow-up stage). This rate was much lower than in patients treated with injected triamcinolone (9.9%).

Table 2: Outcome by gender

Gender	Outcome				p
	Good		Fair		
	n	(%)	n	(%)	
Male	21	77.8	6	22.2	P > 0.05
Female	16	88.9	2	11.1	

Discussion

In comparison with Doulat Rai Bajai's [3] pulse prednisolone therapy concluding 30 mg per day within 3 days every week, and this treatment lasted for 6 months. After Bajai's treatment, among patients, 85.6% recovered well, which is approximately equivalent with our result. Jea Won Jang and partners' [4] pulse betamethasone therapy consisted in treatment in which patients took 5mg per day within two consecutive days every week. After a one-month treatment, 67.4% of patients got better. Pankaj [5] used pulse betamethasone (5 mg/day within two conservative days every week). After 6 months, 73.3% of the patients recovered well. In another group, patients took 40 mg betamethasone once per month in 6 consecutive months, and 42.9% of the patients recovered well [6].

In conclusion**,** oral mini-pulse methylprednisolone was effective, simple, with short-term use of medication, and had no side effects.

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Microneedling Therapy for Atrophic Acne Scar: Effectiveness and Safety in Vietnamese Patients

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Keywords: Atrophic acne scarring; Skin needling; Derma roller

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Abstract

AIM: To evaluate the effectiveness and safety of micro-needling therapy in atrophic acne scar treatment.

METHOD: A prospective, single centred study was implemented in a total of 31 patients suffering from atrophic acne scar grade 2 to 4 of Goodman and Baron scaring grading system was recruited. They were treated by microneedle derma roller every week in 3 months. The scars were evaluated by a magic system camera and by dermatologists clinically using Goodman and Baron scaring grading system, and Lipper and Perez score at baseline, at final treatment, 1 month and 2 months after the final treatment.

RESULTS: The results showed improvement in all patients. The mean of Goodman and Barron's grade was decreased from 3.29 ± 0.59 at baseline, 2.23 ± 0.56 at final treatment, 1.93 ± 0.58 one month after the completion of therapy and to 1.77 ± 0.57 two months after the completion of therapy (with the p-value < 0.05). Similarly, Lipper and Perez score also dropped significantly from 36.48 ± 12.07 at baseline to 23.16 ± 15.01 at final treatment, to 17.83 ± 7.00 one month after the final treatment and to 16.37 ± 7.29 at two months after the final treatment (p-value < 0.05). Skin roughness and hyperpigmented spots got improved significantly. History of having nodular-cystic or vulgaris acne did not affect the effectiveness of the therapy. Side effects of the therapy were burning sensation, erythema but they were very mild and recovered in 1-2 days. No severe complication and post-inflammatory hyperpigmentation were noted. 83.3% of the patients satisfied after the completion of the therapy.

CONCLUSION: Skin needling is an effective and safe method for the treatment of atrophic acne scars.

Introduction

Acne is a very common skin disease with the prevalence among adolescent is up to 80% [1]. The atrophic scar is a common acne complication, accounted for 11% of the acne vulgaris cases [2], [3] and affects patients' quality of life very much. Effective atrophic acne scar treatment is desired and has been challenging dermatologists. Many techniques have been used to improve acne atrophic scars such as subcision, punch technique, chemical peeling, dermabrasion, laser, trichloroacetic acid application etc. Skin needling, one of the collagen induction therapy, is considered safe and effective. The technique uses sterilised microneedles to puncture skin superficially, resulting in stimulating new collagen synthesis and collagen deposition through activating an inflammatory response. Skin micro-needling induces normal wound healing, in which, collagen is formed in the dermis over 12 to 18 months in the remodelling stage [3], [4], [5], [6].

In 1994, Orentreich described the use of a skin needling to release fibrous strands responsible for depressed cutaneous scars and wrinkles [7]. The process involved the insertion and manoeuvring of a tri-bevelled hypodermic needle into the skin to disrupt the underlying connective tissue that tethered down

the skin**.** In 1997, Dr Andre Camirand et al. reported that needle dermabrasion procedure using a tattoo gun devoid of ink could improve surgical scars both in their appearance and texture as well [1]. He experimented a needling procedure using high-speed tattoo gun to treat non-pigmented facelift scars once every 2 to 8 weeks. The expected end-point of the procedure was pinpoint bleeding at scars' base. He found that the scars were improved in both texture and colour and no side effects or complication was documented. However, Dr Desmond Fernandes said that the procedure penetrated the skin too shallow and needles which penetrate deeper could stimulate the production of elastin fibres better. Based on these principles, Dr Fernandes designed a needle roller, consisting of a circular cylinder mounted on tiny needles. In 1999, he presented his invention of the needle at a conference in San Francisco [9]. In 2005, Dr Fernandes and colleagues conducted a study on concave scars, wrinkles, skin ageing of 480 patients in Germany and South Africa. The results were good in most patients [6].

Some studies showed that there was a substantial improvement from 400% up to 1000% in elastin and collagen fibre volume 6 months after derma roller therapy. One year after the therapy, epidermal thickness increased by 40% [10].

This study was implemented in Vietnam to evaluate the effectiveness and safety of micro-needling therapy in atrophic acne scar treatment.

Methods

A prospective, single centred study with convenient sampling with a sample size of 31 was implemented in Vietnam National Hospital of Dermatology and Venereology from March 2013 to Dec 2013. Subject recruitment criteria were acne patients suffering atrophic acne scar of grade 2 to 4 of Goodman and Baron scaring grading system, having a good health condition, do not have any disease that affects wound healing such as diabetes, collagen diseases etc. Exclusion criteria included history of keloids or hypertrophic scars, skin infection (herpes simplex, wart, impetigo, tinea…), skin cancer or active skin disease other than mild acne, active systemic or local skin disease likely to alter wound healing, treatment within the last 6 months or pending treatment within the subsequent 6 months with injecting fillers or ablative or non-ablative laser resurfacing, medication with isotretinoin or other oral retinoids within the past 6 months, current treatment with anticoagulants or antithrombotics, or do not agree to participate in research. Patient participation was voluntary, and the subjects could stop their attendance at any time. Inform consent form was obtained before the subject entered the study.

The materials of the study included microneedle derma roller (MTS Roller, 192 needles in 8 rows, 0.25 mm diameter and 1.5 mm long needles), local anaesthetic (Emla 5%, lidocaine 10%), topical antibiotic cream (Fucidin cream), and facial skin analysis machine.

Each subject was treated by derma roller every week in 3 months. The patients' faces were prepared by cleaning, applying local anaesthetic for 40 minutes, then washed off by saline and sterilised by 70% isopropyl alcohol. Derma roller then was rolled on the scar area in 4 directions (horizontal, vertical, both oblique directions) and repeated 4-10 times on a treatment area. Pinpoint bleeding at the base of the scar was expected end-point, and then saline pads were kept over the treated area, following by application of topical antibiotic cream. After treatment, all patients were recommended to avoid sun exposure, makeup and to swim.

The result was evaluated by facial skin analysis machine and clinically by dermatologists using Goodman and Baron's global acne scar grading [11] and Lipper-Perez score [12] at baseline, at final treatment and 1, 2 months after the final treatment. According to Goodman and Baron grading, an improvement by ≥ 2 grades was labelled excellent, by 1 grade – labelled good, no change – labelled poor) [13]. Besides, acne scar severity score was assessed by Lipper and Perez score: M = number of rolling scars x 1 + number of boxcar x 2 + some icepick x 3 [12].

The study was approved by the Hospital reviewing Board. The subjects were explained about the study, and their participation was completely voluntary. The informed consent form was signed before the subject enters the study.

Data were analysed by SPSS 16.0 software. Descriptive analysis was used for continuous variables, the frequency for categorical variables. Chi-square test/ Fisher's exact test and paired T-test was used to compare the differences between variables. The results were statistically significant if $p \leq 0.05$.

Results

General information

A total of 31 patients (10 males, aged 26.80 ± 7.87; 21 females, aged 23.95 ± 5.59) were recruited. 15 of them (accounted for 48.4%) had a history of nodular-cystic acne, and 14 patients (45.2%) had a history of acne vulgaris before attending the study. Percentage of nodular-cystic acne in male and female patients was not significantly different (60.0% vs. 47.4%, Fisher's exact test, p = 0.4). The mean time of suffering acne of the subjects was 3.62 ± 2.09 years

and of suffering scar was 4.00 ± 3.23 years. 19.4% of them had not got acne treatment; only 3.2% took isotretinoin orally. The most common location of acne was cheek (n = 31, 100%), followed by forehead (n = 19, 61.3%), chin (n = 7, 22.6%) and lastly nose (n = 1, 3.2%). Rolling scar and icepick were very common, accounted for 90.3% (n = 28), box scar was seen in 65.5% of the patients (n = 20).

Clinical assessment

Goodman and Baron's global acne scar grading system has 4 grades ranging from 1 to 4 in which grade 1 meaning least severe and grade 4 meaning most severe. At baseline, scar grade of 2, 3 and 4 accounted for 6.5%, 58.1% and 35.5% consecutively, meaning most of the scars were severe. The therapy improved the scar grading significantly, with the decrease of the mean of Goodman and Baron's grade from 3.29 ± 0.59 at baseline, to 2.23 ± 0.56 at final treatment, to 1.93 ± 0.58 one month after the completion of therapy and to 1.77 ± 0.57 two months after the completion of therapy (with the p-value of paired T-test comparing the mean of baseline to the final treatment, the final treatment to one month after final treatment, the one month to two months after the final treatment was 0.0001, 0.002 and 0.023 consecutively). About 43.3% (n = 13) of the patients had good improvement and 53.3 % (n = 16) had excellent improvement. History of having nodular-cystic or vulgaris acne did not affect the effectiveness of the therapy (percentage of good improvement in nodular-cystic acne group was 66.7%, and in acne, vulgaris group was 46.2%, Chi-square test, p = 0.239).

Lipper and Perez's scoring system also was used to evaluate the efficacy of the modality. The score dropped dramatically from 36.48 ± 12.07 at baseline to 23.16 ± 15.01 at final treatment, to 17.83 ± 7.00 one month after the final treatment and to 16.37 ± 7.29 at two months after the final treatment, as shown in Figure 1. The differences were statically significant.

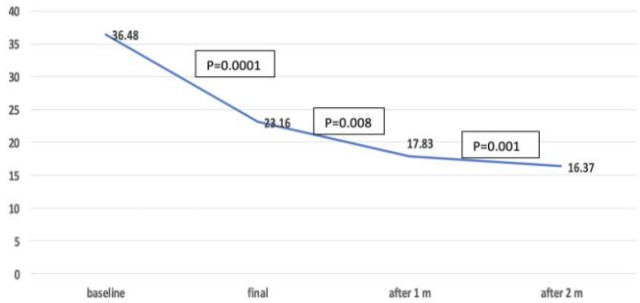

Figure 1: Changing in Lipper and Perez score

Assessment by magic machine

The measurement by facial skin analysis showed that the skin roughness got improved significantly from baseline to final treatment (p = 0.0001), from final treatment to 1 month after that (p = 0.045) but not significantly from 1 month after the final treatment to 2 months after final treatment (p = 0.063), as shown in Table 1.

Table 1: Changes in roughness and hyperpigmented spot by Magic camera

Time of assessment	Roughness score (m ± SD)	p-value	Spot score (m ± SD)	p-value
Baseline	37.66 ± 11.27		33.58 ± 20.09	
		P = 0.0001		P = 0.009
Final treatment	31.46 ± 7.29		26.76 ±15.44	
		P = 0.045		P = 0.024
1m after final treatment	29.04 ±6.98		22.41 ±13.58	
		P = 0.063		P = 0.006
2m after final treatment	27.26 ±6.67		16.71 ± 9.56	

Hyperpigmented spot score also got decreased by the time significantly from baseline to final treatment, 1 month after that and 2 months after that (p = 0.009, p = 0.024 and p = 0.006 consecutively).

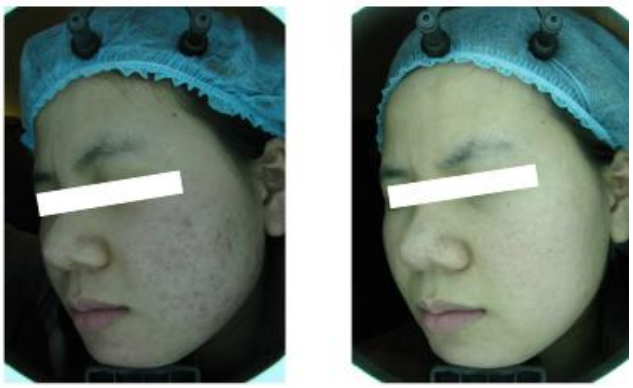

Figure 2: a 20-year-old female showing improvement following three sessions of micro needling

Two months after the final treatment, most of the patient was satisfied with the result (n = 25, accounting for 83.3%). Regarding the side effects, all patients felt burning and had erythema after the therapy, 16.7% (n = 5) had to scale. However, the burning feeling disappeared right after the rolling process, erythema reduced after 1-2 days; scaly skin only lasted for 2-3 days. No severe side effect including itchy, blister, pustules, and hyperpigmentation was noted.

Discussion

Skin needling is a modality for skin rejuvenation, tightening and scar remodelling. This method enhances dermal extracellular matrix proteins [3], [13] without ablation of the epidermis, so limiting side effects and minimising downtime. Many studies have been implemented to evaluate the efficacy of skin needling method. Authors found that skin

needling was simple, effective and safe technique to treat atrophic scars. It did not damage the skin, had a short recovery time and created more dermal papillae [14].

Our results showed that this modality was safe and good effects in atrophic acne scars, fairly similar to the results of other studies such as of Imran Majid [13], Fabbrocini et al., [15]. In Imran Majid's study, 37 patients suffering atrophic acne scars of Goodman grade 2 to 4 were treated by derma roller up to 4 months. The assessment was carried out at baseline, last treatment, one month and two months after the last treatment. The results showed that 26 patient (accounted for 72.2%) reached good response, 6 patients (accounted for 16.7%) reached moderate response — about 80% of the subjects satisfied with the therapy. No significant side effect and short recovery time were noted [13]. The higher good response compared with our results may be due to the differences in duration and type of the acne scars.

Another study implemented by Fabbocini and his team in Italy [15] recruited 32 patients (aged 17-45, 20 females, 12 males) having rolling scars. The good and classification were used to evaluate the results. The patients were treated by derma roller for 4 months. Similarly to our study, after 4 months, the scars got marked improvement ($p < 0.05$) and the skin became thicker and smoother. No side effect and no post-inflammatory hyperpigmentation was reported [15].

Acne atrophic scars are very common and affect patients' quality of life. Therefore, there are many therapies used to deal with this problem such as chemical peeling, dermabrasion, laser, TCA.

CO2 laser and Erbium YAG laser could lead to 50% to 80% scar improvement but had a risk of infection, long-lasting erythema, hyper/hypopigmentation. According to Elizabeth LT et al., (2002), after YAG laser treatment, all of 25 acne atrophic scar patients got erythema lasting 3 weeks, 11 patients (accounted for 44%) developed post inflammatory hyperpigmentation. Other side effects such as dermatitis and infections were noted [8].

A study of Woraphong Manuskiatti et al., [17] treating 13 patients showed that after 3 treatments (7-week interval) by fractional CO2 laser, 50% of the patient had good response, erythema lasted 7-10 days, some other complications included light hyperpigmentation seen in 92%, acne in 31%, herpes in 7.7%, allergic contact dermatitis in 15% of the patients [17].

Tran Thi Thai Ha et al. implemented a study in which 100% TCA was applied to atrophic acne scars of 30 patients [18]. Only 14.3% of them reached good response. Side effects including itchiness, erythema, scaling, lasted longer, about 2 weeks [18].

In conclusion, micro needling therapy is effective and safe for atrophic acne scar treatment. It does not damage the skin, causes a little side effect, short recovery time. Also, it does not require expensive equipment leading to less expenditure in comparison to laser or dermabrasion modality. It could be done in all skin type patients as post-inflammatory hyperpigmentation is rarely seen after the therapy.

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Clinical Science

Successful Treatment of Intralesional Bleomycin in Keloids of Vietnamese Population

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Abstract

BACKGROUND: Keloid is an overactive condition of the skin tissue to early lesions characterised by proliferation of fibroblasts, excessive collagen production in the lesion. Treatment of keloids is a big challenge because of the poor response rate and high risk of recurrence after treatment. We found that bleomycin offers promise in the treatment of keloids.

AIM: To evaluate the efficacy of bleomycin injected in the injury for keloids treatment.

METHODS: The treatment was carried out in 55 patients having 120 keloids of different sizes and locations. Average treatments were 4 times.

RESULTS: Complete flattening was 70.8%, highly significant flattening was 8.3%, no patient of minimal flattening. Systemic side-effects of bleomycin were not evaluated, but local side-effects were mainly pains (100%), blisters (78.3%), ulceration (5.8%), and hyperpigmentation (56.7%).

CONCLUSION: The percentage of patients recurring 6, 12, 15, 18 months after the last treatment were 3.8, 15.4, 45.5, 50%, respectively.

Introduction

Keloid is an overactive condition of the skin tissue to early lesions characterised by proliferation of fibroblasts and excessive production of collagen in the lesion, with mechanisms not yet fully understood [1]. Areas most frequently affected are chest, shoulder, ear lobe. Keloid is usually itchy and painful [2]. Nowadays, therapy is a challenge although many treatments are recommended, without agreement on the effectiveness of different choice. Bleomycin-induced apoptosis with sclerosing action on endothelial cells inhibited collagen synthesis by inhibiting the lysyl-oxidase enzyme and TGF-β, and it was used in keloid treatment for the first time by Bodokh and Brun in 1996 [3].

We aimed to evaluate the efficacy of bleomycin injected in the injury for keloids treatment.

Methods

A group of 55 patients with 120 studied scars were selected (aged from 15 to 70 years)**.** Scar duration varies from several months to years, not been treated before, not ulcerated or infected.

An injectable solution of bleomycin was prepared by diluting 15 units of bleomycin in 10 ml of sterile saline. The medication was injected into the mid-lesion in depth, 0.2-0.4 ml/cm^2 (maximum volume per session 3.5 ml). The interval between injections

was 4 weeks, and the total number of treatment sessions depended on the cosmetic outcome of each lesion. Patients received chest X-ray before treatment every 3 months and 6 months after the last treatment.

Evaluation of the treatment response is conducted by VSS (Vancouver Scar Scale).

Results

The average number of injections was 3.9 ± 1.1. After treatment, 80.8% of patients got itchiness relief, and 73.3% of patients got pain relief. Blood vessel status, scar stiffness, and scar thickness improved at 70.6%, 89.3% and 87%, respectively, by the VSS scale. In particular: 70.8% of scars became completely flat, 8.3% fairly flat, 17.5% comparatively flat, 3.3% averagely flat and no poorly flat scars.

Regarding undesirable effects, this study showed that 100% scar tissue lasted on average of 3.6 ± 1.4, 94/120 scars accounted for 78.3% have blisters, with an average length of 4.5 ± 1.3; 5.8% of ulcer scars with an average length of 10.6 ± 1.3; Hyperpigmentation was frequently noted after therapy (56.7%) and much thicker and harder the scar was, more treatment times was needed, with stiffness improvement poorer than in the treatment of soft and thin ones. The condition of vascular, pigmentation, and scar location had no relationship to some treatment as well as the level of scar thickness improvement as presented in Table 1.

Table 1: Efficacy of the treatment

Variable	Value		
VSS scores	Before treatment	After treatment	p
Vascularity	1.7 ± 1	0.5 ± 0.6	
Pigmentation	0.2 ± 0.6	1.1 ± 1	< 0.05
Pliability	2.8 ± 0.9	0.3 ± 0.5	
Height	2.3 ± 0.6	0.3 ± 0.5	
Functional Symptoms			
Pruritus		80.8%	
Pain		73.3%	
Scar thickness improvement			
The complete flattening		70.8%	
Highly significant flattening		8.3%	
Significant flattening		17.5%	
Moderate flattening		3.3%	
Minimal flattening		0%	
Local side-effect			Lasting days
Pain	120 (100%)		3.6 ± 1.4
Swollen	26 (21.7%)		3.3 ± 1.2
Blisters	94 (78.3%)		4.5 ± 1.3
Ulceration	7 (5.8%)		10.6 ± 1.3
Scaled	101 (84.1%)		13.6 ± 1.7
Hyperpigmentation	68 (56.7%)		
Recurrence			
After 3 months (n = 32)		0	
After 6 months (n = 26)		1 (3.8%)	
After 12 months (n = 13)		2 (15.4%	
After 15 months (n = 11)		5 (45.5%)	
After 18 months (n = 6)		3 (50%)	

Due to many technical and financial constraints, our study did not measure bleomycin concentrations in the blood. However, in surveying complete blood count, liver and kidney function and chest X-ray, we did not record any systemic side effect. Local side effects were noted significantly, with 100% scars with pain during treatment.

Discussion

We found that bleomycin improved vascular condition by 70.6% after treatment (mean VSS score from 1.7 ± 1 to 0.5 ± 0.6) and mean VSS of stiffness decreased by 89.3%. Some injections needed, itch and pain relief was similar to Saray et al., and S. Srivastava et al., studies [4], [5], [6].

The recurrence rate in our study was higher than in Saray (2005), with 14% of patients recurring after 18 months [4]. We found that the rate of recurrent scars in the thorax, the front of the breastbone was higher than in other surgical areas. The difference is statistically significant. In contrast, there was no relation between pre-treatment thickness and recurrence risk.

In conclusion, bleomycin is a safe and effective method for treating keloids. However, the high rate of recurrence after treatment confirms the difficulty in the correct management of keloid scars.

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Letter to the Editor

The Relationship between HLA-B27, HLA-Cw06, HLA-DR7 and Psoriatic Arthritis in Vietnamese Patients: Disease Progression and Therapeutic Burden

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Abstract

We conducted a prospective, cross-sectional study at Ho Chi Minh City Hospital of Dermato Venereology from January 2016 to March 2017 in 40 psoriatic arthritis (PsA) patients to evaluate the disease progression and therapeutic burden about the HLA patterns. Based upon our results, PsA with HLA-B27 (+) had a threat of severe arthritis. PsA with HLA-Cw06 (+) had a higher risk of earlier onset and shorter duration for plaque psoriasis to transform into PsA. HLA-DR7 (+) in PsA delayed the time for conversion from plaque psoriasis into PsA. These findings are quite similar to other studies in the literature.

Dear Editor,

We conducted a prospective, cross-sectional study at Ho Chi Minh City Hospital of Dermato Venereology from January 2016 to March 2017 in 40 PsA patients, 37 plaque psoriasis patients, and 33 healthy people. They were tested HLA-B27, HLA-Cw06, HLA-DR7 by Sequence Specific Primer-Polymerase Chain Reaction (SSP-PCR) technique.

The rate of HLA-B27 in PsA was 32.5%, in plaque psoriasis was 1.92%, in the healthy group was 9.09%. The rate of HLA-Cw06 in PsA was 7.5%, in plaque psoriasis was 18.92%, in healthy group was 3.03%. The rate of HLA-DR7 in PsA was 32.5%, in plaque psoriasis was 27.30%, in healthy group was 24.24%. HLA-B27 (+) patients had a high risk of PsA with RR = 1.6. PsA with HLA-B27 (+) had a threat of severe arthritis. PsA with HLA-Cw06 (+) had a higher risk of earlier onset and shorter duration for plaque psoriasis to transform into PsA. HLA-DR7 (+) in PsA delayed the time for conversion from plaque psoriasis into PsA.

Many types of research show the relationship between HLA-B27, HLA-Cw06, and PsA. HLA-B27 took high percentage in PsA and related to early onset of arthritis, spondylitis (spinal joint, sacroiliac joint), distal interphalangeal joint arthritis and uveitis,

affecting more frequently males and with poor prognosis; HLA-Cw06 involved the early onset of skin psoriasis, late arthritis, extensive cutaneous lesions, often happened in patients which positive family history for psoriasis. HLA-DR7 involved the progress of PsA. According to many scientists, HLA-DR7 and B22 are protective factors.

Alenius et al., [1] researched clinical signs and HLA in 88 PsA patients in Switzerland in which 25.7% of patients were HLA-B27 (+). Danafa et al., [2] researched the relationship between HLA and PsA in 158 PsA patients in which 15.8% patients were HLA-B27 (+).

Fitzgerald at al., [3] in 2015 showed that the rate of HLA-Cw06 (+) was 28.5%. Another research of Danafa et al., [2] showed the relationship between HLA and PsA in 158 PsA patients concluded that 12% of patients had HLA-Cw06 (+) and demonstrated the relationship between HLA-B27 and PsA.

Alenius and his associates found that healthy people with HLA-B27 (+) had a greater risk of PsA ($p = 0.017$).

This is the first study that analyses the HLA pattern of psoriatic patients in Vietnam and correlates with disease progression and therapeutic burden.

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Letter to the Editor

Quality of Life in Psoriasis Vietnamese Patients Treated with Metformin in Combination with Methotrexate

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Abstract

A cross-sectional study was performed on 48 psoriasis Vietnamese patients treated with metformin as an add-on for methotrexate and 48 psoriasis patients treated methotrexate alone. The mean PASI scores were 5.25 ± 5.72. Total QOL scores had a slight difference between patients treated metformin combined with methotrexate and methotrexate alone (62.32 ± 18.1 vs 60.91 ± 19.63). Combined therapy with metformin and methotrexate contributes to significantly improve the quality of life for patients with psoriasis.

Dear Editor,

Psoriasis is a chronic skin disease affecting social relations, psychological status, and daily activities. Quality of life (QOL) is increasingly recognised as an important outcome measure in psoriasis patients [1], [2]. Dermatologic treatment of psoriasis has become increasingly effective, sometimes even using complementary and alternative medicine (CAM), contributing to improve the QOL of patients [3] significantly. According to some studies showed that metformin is a logical add-on therapy for patients with psoriasis and metabolic syndrome treated with methotrexate. Evaluation of the quality of life of patients with psoriasis treated with metformin and methotrexate is important. A Metformin therapy combined with methotrexate has any impact on the QOL of patients with psoriasis?

A cross-sectional study was performed on 48 psoriasis patients treated with metformin as an add-on for methotrexate, and 48 psoriasis patients treated methotrexate alone. The severity of disease was calculated by the Psoriasis Area and Severity Index (PASI). These patients were interviewed with the short-form-36 (SF36) questionnaire to assess their quality of life.

The mean PASI scores were 5.25 ± 5.72. Total QOL scores had a slight difference between patients treated metformin combined with methotrexate and methotrexate alone (62.32 ± 18.1 vs

60.91 ± 19.63). Especially in two domains: Role-physical (59.4 ± 21.3 vs. 58.8 ± 25.2) and social functioning (62.5 ± 24.6 vs. 60.15 ± 25.5) (P < 0.01).

Metformin act through activation of adenosine monophosphate-activated protein kinase (AMPK) in extracellular signal-related kinase (ERK1/2) signalling pathway leading to cell cycle arrest and therefore inhibition of cell proliferation, the hallmark of psoriasis. AMPK activation not only inhibits iNOS, dendritic, T cell and monocyte/macrophage activation but also activates IL-10 and TGF-β, thereby exerting its anti-inflammatory action. The anti-proliferative and anti-inflammatory action of metformin might have resulted in improving the QOL of psoriasis patients [4], [5], [6], [7], [8].

In conclusion, there is a difference in the quality of life in psoriasis patients treated metformin as an add-on for methotrexate compared with patients treated methotrexate alone. Combined therapy with metformin and methotrexate contributes to significantly improve the quality of life for patients with psoriasis.

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