ID Design Press, Skopje, Republic of Macedonia Open Access Macedonian Journal of Medical Sciences. **Special Issue: Vietnamese Dermatology** https://doi.org/10.3889/oamjms.2019.053 eISSN: 1857-9655 *Clinical Science* 



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

Phuong Pham Thi Minh<sup>1</sup>, Loan Pham Thi<sup>1</sup>, Anh Tran Lan<sup>1,2</sup>, Thuong Nguyen Van<sup>1,2</sup>, Hung Le Van<sup>1,2</sup>, Van Tran Cam<sup>1</sup>, Marco Gandolfi<sup>3</sup>, Claudio Feliciani<sup>3</sup>, Francesca Satolli<sup>3</sup>, Michael Tirant<sup>4,5</sup>, Aleksandra Vojvodic<sup>6</sup>, Torello Lotti<sup>4</sup>

<sup>1</sup>National Hospital of Dermatology and Venereology, Hanoi, Vietnam; <sup>2</sup>HaNoi Medical University, Hanoi, Vietnam; <sup>3</sup>Unit of Dermatology, University of Parma, Parma, Italy; <sup>4</sup>University of Rome G. Marconi, Rome, Italy; <sup>5</sup>Psoriasis Eczema Clinic, Melbourne, Australia; <sup>6</sup>Department of Dermatology and Venereology, Military Medical Academy of Belgrade, Belgrade, Serbia

#### **Abstract**

Citation: Thi Minh PP, Pham Thi L, Tran Lan A, Nguyen Van T, Le Van H, Tran Cam V, Gandolfi M, Feliciani C, Satolli F, Tirant M, Vojvodic A, Torello Lotti T. Early Treatment with Imiquimod 5% Cream of Periungual Warts in Vietnam: The Poorer, The Better. Open Access Maced J Med Sci. https://doi.org/10.3889/oamjms.2019.053

Keywords: Imiquimod; Periungual warts

\*Correspondence: Marco Gandolfi. Unit of Dermatology, University of Parma, Parma, Italy. E-mail: marco.gandolfi5@gmail.com

**Received:** 02-Jan-2019; **Revised:** 16-Jan-2019; **Accepted:** 17-Jan-2019; **Online first:** 25-Jan-2019

Copyright: @ 2019 Phuong Pham Thi Minh, Loan Pham Thi, Anh Tran Lan, Thuong Nguyen Van, Hung Le Van, Van Tran Cam, Marco Gandolfi, Claudio Felicani, Francesca Satolli, Michael Tirant, Aleksandra Vojvodic, Torello Lotti. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

Funding: This research did not receive any financial

Competing Interests: The authors have declared that no competing interests exist

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  $\leq$  25 mm²), moderate (25 mm² < total lesion area  $\leq$  50 mm²), severe (total lesion area > 50 mm²). The outcome was evaluated at the 4<sup>th</sup> and the 8<sup>th</sup> week. The result was graded as excellent (complete clearance), good ( $\geq$  50% clearance) and poor (< 50% clearance).

**RESULTS:** The total area of the wart lesion got decreased significantly from the beginning to the  $4^{th}$  and the  $8^{th}$  week (36.7 mm² vs 16.8 mm², p = 0.0001 and 16.8 mm² vs 8.8 mm², 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  $\pm$  14.1 months vs 22.3  $\pm$  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  $\pm$  13.8) and 21 males (aged 27.3  $\pm$  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  $\leq$  25 mm<sup>2</sup>), moderate (25 mm<sup>2</sup> <total lesion area  $\leq$  50 mm<sup>2</sup>), severe (total lesion area  $\geq$  50 mm<sup>2</sup>).

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).

1

Open Access Maced J Med Sci.

## Results

The warts condition before the treatment was mild in 21 patients (52.5%) (the total lesion area  $\leq$  25 mm²), moderate in 8 patients (20.0%) (25 mm² < total lesion area  $\leq$  50 mm²) and severe in 11 patients (27.5%) (total lesion area > 50 mm²). The duration of disease was 13.5  $\pm$  15.0 months.

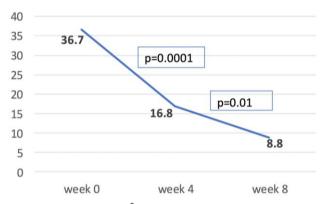


Figure 1: Wart area (in mm<sup>2</sup>) change by the time

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

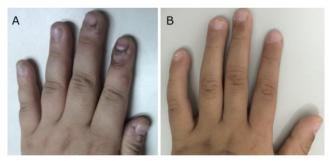


Figure 2: Periungual warts before (A) and after (B) treatment with imiguimod 5 % cream

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)	Р	Wart severity at the beginning					Treatment before imiquimod				В
				Severe		Mild/ moderate		Р	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.

## References

- 1. Herold M, Nielson C, Longo MI. Isotretinoin and Candida immunotherapy for recalcitrant warts in solid organ transplant recipients. Dermatologic therapy. 2018:e12803. <a href="https://doi.org/10.1111/dth.12803">https://doi.org/10.1111/dth.12803</a> PMid:30536495
- 2. Tosti A, Piraccini BM. Warts of the nail unit: surgical and nonsurgical approaches. Dermatologic Surgery. 2001; 27(3):235-9. https://doi.org/10.1097/00042728-200103000-00004
- 3. Wang Y, Abel K, Lantz K, Krieg AM, McChesney MB, Miller CJ. The Toll-like receptor 7 (TLR7) agonist, imiquimod, and the TLR9 agonist, CpG ODN, induce antiviral cytokines and chemokines but do not prevent vaginal transmission of simian immunodeficiency virus when applied intravaginally to rhesus macaques. Journal of virology. 2005; 79(22):14355-70.

https://doi.org/10.1128/JVI.79.22.14355-14370.2005 PMid:16254370 PMCid:PMC1280235

- 4. Grussendorf-Conen EI, Jacobs S, Rübben A, Dethlefsen U. Topical 5% long-term imiquimod treatment of cutaneous warts resistant to standard therapy modalities. Dermatology. 2002; 205(2):139-45. https://doi.org/10.1159/000063909 PMid:12218229
- 5. Kim MB, Ko HC, Jang HS, Oh CK, Kwon KS. Treatment of flat warts with 5% imiquimod cream. Journal of the European Academy of Dermatology and Venereology. 2006; 20(10):1349-50. https://doi.org/10.1111/j.1468-3083.2006.01709.x PMid:17062069
- 6. Hengge UR, Esser S, Schultewolter T, Behrendt C, Meyer T, Stockfleth E, Goos M. Self-administered topical 5% imiquimod for the treatment of common warts and molluscum contagiosum. British Journal of Dermatology. 2000; 143(5):1026-31. https://doi.org/10.1046/i.1365-2133.2000.03777.x PMid:11069514
- 7. Ahn CS, Huang WW. Imiquimod in the treatment of cutaneous warts: an evidence-based review. American journal of clinical dermatology. 2014; 15(5):387-99. <a href="https://doi.org/10.1007/s40257-014-0093-5">https://doi.org/10.1007/s40257-014-0093-5</a> PMid:25186654
- 8. Kim SY, Jung SK, Lee SG, Yi SM, Kim JH, Kim IH. New

alternative combination therapy for recalcitrant common warts: the efficacy of imiquimod 5% cream and duct tape combination therapy. Annals of dermatology. 2013; 25(2):261-3. <a href="https://doi.org/10.5021/ad.2013.25.2.261">https://doi.org/10.5021/ad.2013.25.2.261</a> PMid:23717030 PMCid:PMC3662932

9. Micali G, Dall'Oglio F, Nasca MR. An open label evaluation of the efficacy of imiquimod 5% cream in the treatment of recalcitrant subungual and periungual cutaneous warts. Journal of dermatological treatment. 2003; 14(4):233-6.

https://doi.org/10.1080/09546630310016763 PMid:14660271

10. Soni P, Khandelwal K, Aara N, Ghiya BC, Mehta RD, Bumb RA. Efficacy of intralesional bleomycin in palmo-plantar and periungual warts. Journal of cutaneous and aesthetic surgery. 2011; 4(3):188. <a href="https://doi.org/10.4103/0974-2077.91250">https://doi.org/10.4103/0974-2077.91250</a> PMid:22279384 PMCid:PMC3263129