

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

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Abstract

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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 \pm 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 and 11 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 $84.39 \pm 17.03\%$, after 1-month treatment reduced to $65.10 \pm 26.29\%$, and decreased dramatically after 2-months treatment was $45.67 \pm 28.21\%$ after 3-months treatment was $29.97 \pm 29.67\%$. At the end of the study, the area of hair loss according to SALT was $24.19 \pm 29.42\%$ 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 \pm 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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