Safety and Efficacy of Phototoxic Doses of Ultraviolet A for Treatment of Alopecia Areata

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Abstract

Background: Alopecia areata (AA) is a disease of the hair follicles with multifactorial etiology and a strong component of autoimmune origin. A number of treatments can induce hair growth in alopecia areata but none has been shown to alter the course of the disease. The high rate of spontaneous remission makes it difficult to assess efficacy, particularly in mild forms of the disease. The present study aims at determining the efficacy and safety of using the phototoxic doses of ultraviolet A (UVA) after application of topical 8-methoxypsoralen in the treatment of extensive and resistant cases of AA.

Patients and Methods: 20 patients receiving phototoxic doses of UVA after topical application of psoralen (test therapy group). Each patient was treated for 3 months and followed up for additional 3 months.

Results: At 3 months, patients receiving phototoxic doses of PUVA showed a mean SALT reduction of –46.01% ± 30.65 from baseline [95% Confidence interval (CI): –60.35% to –31.66%]. Treatment success, defined as achievement of SALT change ≥75% in comparison to baseline, was achieved by 20% of patients. The mean cumulative dose achieved at the end of treatment was 100J/cm² ± 21.56 (range 40-120 J/cm²). At 6 months, patients receiving phototoxic doses of PUVA showed a mean SALT reduction of –55.32% ± 37.53 from baseline (95% CI: –72.88% to –37.75%).

Conclusion: The current study offers a proof that phototoxic regimen of PUVA exerts a safe and effective in the treatment of AA.

Key Words: Alopecia Areata (AA) – Phototoxic therapy – Psoralen ultraviolet A (PUVA) – Safety.

Introduction

ALOPECIA areata is a common, non-scarring, autoimmune disease that can affect any hair-bearing area. It is a lymphocyte cell-mediated inflammatory type of hair loss, but its pathogenesis is not fully understood. The disease can present as a single, well demarcated patch of hair loss, multiple patches, or extensive hair loss in a form of total loss of scalp hair alopecia totalis (AT) or loss of entire scalp and body hair alopecia universalis (AU) [1]. The choice of treatment depends on the extent of alopecia, patient age and general health, and on the patient's motivation for treatment.

Various therapeutic agents have been described for the treatment of AA, but none are curative or preventive [2]. Phototherapy in the form of topical psoralen and ultraviolet A (PUVA) has been a well documented therapy for AA [3]. The success of such therapy might be attributed to the immunosuppression caused by PUVA mediated by several mechanisms, including depletion of Langerhan's cells and their antigen presenting capacity. In addition, induction of apoptosis of T lymphocytes and decreasing production of several cytokines might be other mechanisms of action [4].

The efficacy of local and systemic PUVA was compared in 41 patients with various forms of the disease, with the best responses occurring in patients with localized hair loss, AT and AU forms had much poorer success rates. Overall, however, PUVA seemed a reasonable therapeutic option for AA patients resistant to other forms of treatment. Later, PUVA was reported effective in cases with multiple lesions [5], AA totalis or AA universalis undergoing either complete remission or improvement of around 90% after systemic PUVA [6,7] although three relapsed after therapy.

A Previous study optimistically demonstrated 90% hair regrowth in 53% of patients during treatment, but high relapse rates over up to 10 years of follow-up again led the authors to conclude that systemic PUVA should not normally be used for AA [2].
The aim of the current study is to determine the efficacy and safety of using the phototoxic doses of UVA after application of topical 8-methoxypsoralen (MOP) in the treatment of alopecia areata.

**Patients and Methods**

Twenty Patients complaining of AA of more than 2 months duration were recruited from the Dermatology OPC of Kasr Al-Aini Hospitals and assessed for eligibility to be enrolled in the study. A topical psoralen, 0.2% Methoxsalen (ammoidin) solution 0.03g/15ml was applied on the areas of alopecia 15 minutes before UVA exposure.

The initial UVA dose used was 6 J/cm² for skin types IV and V and 3J/cm² for skin type III. The dose increased according to the phototoxic reaction in the last session and the patient's response. The treatment was performed weekly until a phototoxic reaction was achieved, the sessions were stopped and the patient was instructed to rest until all signs of phototoxicity completely subsided.

SALT score would be determined at baseline and each follow-up visit [8]. Percent change of SALT from baseline: For determination of efficacy. Treatment success, defined as effective sustained growth of hair in more than 75% of the affected area, was evaluated at the end of the study.

**Statistical analysis:** Data were coded and entered using the statistical package SPSS version 21. Data was summarized using mean ± standard deviation in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between variables over time were done using non-parametrical Friedman test and Wilcoxon test.

**Results**

Sixteen males (80%) and 4 females (20%) were included in this study, their age ranged from 10 to 60 years with a mean age 21.15 ± 17.7. The mean SALT score at baseline was 41.47 ± 23.62. Patients receiving phototoxic doses of PUVA showed a mean SALT reduction of –46.01% ± 30.65 from baseline [95% Confidence interval (CI): –60.35% to –31.66%] [(Table 1), Figs. (1,2)].
Table (1): Clinical data for the patients receiving phototoxic doses of UVA at 3 and 6 months following treatment.

<table>
<thead>
<tr>
<th></th>
<th>Before treatment (n=20)</th>
<th>After 3-months treatment (n=20)</th>
<th>After-6 months treatment (n=20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SALT Score (mean±SD)</td>
<td>41.47±23.62</td>
<td>24.4±20.95</td>
<td>21.42±24.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Percent of reduction of SALT score</td>
<td>-46.01±30.65</td>
<td>-55.32±37.53</td>
<td></td>
<td>0.121</td>
</tr>
<tr>
<td>Treatment success</td>
<td>4 (20%)</td>
<td>9 (45%)</td>
<td></td>
<td></td>
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As shown in Table (2), the mean number of phototoxic reaction in all patients within 3 months of therapy was 2.75 (range 2-5). The number of sessions needed to reach treatment success was 2.11. The mean cumulative dose achieved at the end of treatment was 100J/cm²±21.56 (range 40-120J/cm²).

Table (2): Doses in the phototoxic group at 3 months (end of treatment).

<table>
<thead>
<tr>
<th></th>
<th>Mean number of phototoxic reactions in</th>
<th>Mean cumulative dose (J/cm²)</th>
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<tbody>
<tr>
<td></td>
<td>All patients (n=20)</td>
<td>100±21.56</td>
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<tr>
<td></td>
<td>Ttt Success (n=4)</td>
<td>2.75</td>
</tr>
<tr>
<td></td>
<td>3 months</td>
<td>2.11</td>
</tr>
<tr>
<td></td>
<td>Ttt Failure (n=16)</td>
<td>3.27</td>
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Discussion

Although alopecia areata is one of the most common autoimmune diseases, the pathobiology of this chronic, relapsing hair-loss disorder is not fully understood, and the available therapies are disappointing [9]. In a trial to search for effective, safe modalities for the treatment of this distressful disorder, the use of PUVA in a phototoxic regimen has recently re-emerged with promising results [10].

The results achieved by the current study (45% of patients achieving excellent response >75% hair regrowth and 25% achieving good response >50% hair regrowth) appeared to be lower than that achieved by (85% good-excellent response) [10], but higher than that reported by another study (57% positive treatment response) [11].

The proposed efficacy of phototherapy in the treatment of AA could be attributed mainly to its immune-modulatory effect, which could occur via several mechanisms. AA is characterized by increase in the immunologic activity of Th1 cells and Th1-type cytokines are known to play a critical role in the pathogenesis of AA [2,12].

Moreover, it is known that phototherapy induces the disappearance of epidermal Langerhans cells and their decreased antigen-presenting capacity, apoptosis induction in T lymphocytes, and modulation of cytokine release, e.g. increasing production of interleukin (IL)-2, IL-1b, and IL-10 and decreasing IFN-γ production [13].

In the current study patients received an average total cumulative UVA dose of 100J/cm², in comparison to 42J/cm² [10] and 22J/cm² [11] owing to difference in the protocol. Even though we were higher in comparison to both other studies we were still in the "safe zone <1000J/life time" [14].

In conclusion: The current clinical trial serves as a proof for the efficacy and safety of the use of the phototoxic regimen of UVA in the treatment of AA.

References


