A comparison between systemic psoralen plus ultraviolet A therapy and topical clobetasol in the treatment of vitiligo

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Background: Topical corticosteroids and oral psoralen plus ultraviolet A radiation (PUVA therapy) are two common treatment methods for vitiligo. The aim of this study was to compare the efficacy, complications and patterns of repigmentation of these two methods.

Methods: This prospective randomized clinical trial was conducted from July 2007 to October 2008. Patients with disseminated vitiligo were divided into two groups. PUVA therapy was administered in one group and topical clobetasol was used in the other group. Results were recorded in 4 categories and therapeutic findings and complications were compared after 24 weeks.

Results: Among 37 participants in the PUVA therapy group, 18 (48.6%) patients achieved marked and 14 (37.8%) patients showed good repigmentation. Similarly, among 35 participants in the clobetasol group, 6 (17.1%) patients showed marked and 8 (22.8%) patients showed good repigmentation. Treatment complications were observed in 16.2% of the participants in PUVA group and 28.6% of the participants in clobetasol group. The patterns of repigmentation were different in the two groups.

Conclusion: PUVA showed better therapeutic effects, and did not cause significant complications. Therefore, it could be used as one of the first line medications in the treatment of vitiligo.

Keywords: clobetasol, phototherapy, PUVA, vitiligo

INTRODUCTION

Vitiligo is a common disorder which causes great cosmetic problems for patients; therefore, its proper management is highly important. It approximately affects 0.5-2 percent of the world’s population. This disease usually starts in childhood or adolescence but may occur at any age. Both sexes are equally affected, and the maximum incidence is between ages 10 -30.

There are various treatments for this disease, but two most common ones are oral psoralen plus ultraviolet A radiation (PUVA therapy), and topical corticosteroids. Each mode of treatment has its own complications. In a study in Saudi Arabia, 32 patients were treated with PUVA and the overall response rate was 59.4%. In Filipino, 25 patients with vitiligo lesions were treated with topical clobetasol propionate cream. After six months of treatment, 22 of the 25 patients showed at least 90% repigmentation. Since PUVA therapy and topical clobetasol are two routine treatment modalities for vitiligo in Iran but their efficacy has not been compared yet, we decided to compare the efficacy and complications of these methods.

PATIENTS AND METHODS

This study was conducted as a prospective randomized comparative clinical trial in the outpatient clinic of the Department of Dermatology, Imam Khomeini Hospital, Ahwaz, south of Iran from...
July 2007 to October 2008. The diagnosis of vitiligo was made by two experienced dermatologists on the basis of the patients’ history and the typical clinical features. The study was approved by ethics committee of Ahwaz Jondishapour University of Medical Sciences.

**Inclusion criteria**

Patients aged 14 years or more who were diagnosed with disseminated vitiligo with 10 - 30 percent of body surface involvement by two expert dermatologists were included in the study.

Patients must not have received any treatments at least one month prior to the visit.

**Exclusion criteria**

Patients with history of previous cardiac, renal, or hepatic diseases, photosensivity or diseases such as porphyria, systemic lupus erythematosus, skin cancer or history of previous skin malignancy, segmental vitiligo, and pregnant or lactating women were excluded from the study.

**Study Protocol**

Patients who met the above-mentioned criteria and were willing to participate in the study were selected and randomly divided into two groups. Group 1 was assigned to receive PUVA therapy and group two received topical steroid. Randomization was made using a random number table. A written informed consent was obtained from each patient before initiating the study. After obtaining the history and physical examination, a photograph of the lesions was taken, a questionnaire was completed and a schematic picture of the lesions was drawn. Laboratory tests including liver and renal function tests, antinuclear antibody and thyroid function tests were measured. Group 1 consisted of 38 patients, all of whom received PUVA therapy (Waldman W UV-7001 K, Germany) on alternate days, 2 sessions per week. In this group before starting the treatment, an eye examination was performed by an expert ophthalmologist. All patients were advised to wear UVA-block sunglasses during the day if they were outdoors. Two hours before exposure to radiation, patients received 0.6 mg/kg oral psoralen. UVA radiation was started with 2–3 Joul/cm² according to the Fitzpatrick’s skin type of the patients and increased by 0.5 Joul/cm² per session. Group 2 consisted of 42 patients, all of whom received topical steroid. Topical steroid was prepared by dissolving 30 grams of 0.05% clobetasol propionate cream in Isopropyl alcohol and delivering the volume to 100 milliliters. The patients had to use it on the affected skin topically, two times per day. Treatments continued for 24 weeks. Clinical evaluation was made at day 1, and every 4 weeks thereafter by two board certified dermatologists blinded to treatment modalities. Improvement was categorized as marked (> 75% repigmentation), good (50-75% repigmentation), moderate (25-50% repigmentation) and poor or no improvement (< 25% repigmentation). Comparisons were made using Chi-square (K²) and Fisher’s exact test and significance was set at the p<0.05 level.

**RESULTS**

A total of 80 patients with skin types ranging from III to V were enrolled in this study. Eight patients (1 from group 1; 7 from group 2) withdrew from the study. The most frequent causes of discontinuation were no response or disappointment from the treatment results. Seventy two participants, 42 females and 30 males (ages 14-60 with a mean age of 27.7 years old), completed the full therapy protocol. None of the patients had a history of autoimmune diseases (such as thyroid disorders, diabetes mellitus, alopecia areata, etc) but laboratory results showed abnormal thyroid tests in 2 participants. Nine individuals (11.25%) had a positive family history of vitiligo at least in one of their first-degree relationships and 12 (16.7%) participants had halo naevus. White hairs were seen on the skin lesions in 43 participants (53.75%). Regarding Fitzpatrick’s skin type of the patients, 37 patients (46.25%) had type III, 25 patients (31.25%) had type IV and 10 patients (12.25%) had type V. There were no significant differences between the two groups with respect to demographic and clinical characteristics (Table 1). After 6 months, 18 patients (48.6%) in group 1 showed marked and 14 patients (37.9%) showed good repigmentation, but none of the patients in this group showed poor or no repigmentation. Of 35 cases in group 2, who were treated with topical clobetasol, only six (17.1%) showed marked and
8 (22.9%) showed good repigmentation (Table 2). Statistical difference between the two groups was significant (P= 0.00). Six patients (16.21%) in the PUVA group and 10 patients (28.57%) in the clobetasol group suffered from drug complications (Table 3). The difference was significant (P <0.05).

The pattern of repigmentation was different in the two groups. In group 1, the predominant pattern of repigmentation was perifollicular but there was not pure marginal repigmentation of the lesions. In group 2, the first predominant pattern was perifollicular and the second was pure marginal (Table 4). The relationship between the presence of white hairs on skin lesions and the response to the treatment is shown in Table 5.

**DISCUSSION**

This study showed that after 6 months of treatment, PUVA therapy proved to be more effective than topical corticosteroids in creating repigmentation. This difference was statistically significant (P=0.00). About 48.6% of the patients who were treated with PUVA showed marked repigmentation, while only 17.1% of the patients in the clobetasol group showed the same result. In one randomized comparative study, the efficacy of topical clobetasol propionate cream 0.5% was compared to the use of topical psoralsin plus sunlight (PUVAsol) in the treatment of childhood vitiligo. Overall, clobetasol was significantly better than PUVAsol in achieving 75% repigmentation 4. The result of this study was different from ours, but this study was conducted on children and the responsiveness of vitiligo in children can be rather different than adults. In addition, the patients used sunlight instead of artificial UVA radiation. In a study in Saudi Arabia, 32 patients were treated with PUVA and the overall response rate was 59.4% 5. In our study, none of the 37 patients in PUVA therapy group showed less than 25% repigmentation and 48.6% showed marked improvement. In 101 children with vitiligo treated with moderate- to high-potency topical corticosteroids, 64% had repigmentation of the lesions but local steroid side effects were noted in 26% of them 7. In our study, 40% of the patients in the clobetasol group showed moderate or marked repigmentation, and 28.6% developed steroid side effects.

Various patterns of repigmentation in vitiligo lesions may develop with different treatment modalities. In one study, PUVA predominantly
exhibited a perifollicular pattern of repigmentation while steroids caused a diffuse type of repigmentation. In our study, patients receiving PUVA predominantly developed a perifollicular pattern of repigmentation and patients on clobetasol also showed perifollicular and/or marginal type of repigmentation predominantly. Because the dominant pattern of repigmentation in our patients was perifollicular, we expected that there should be a reverse relationship between the presence of white hairs on skin lesions and response to treatment but we did not find such a relationship. Perhaps this finding reflects the fact that clinical whitening of hairs on skin lesions does not necessarily indicate complete destruction of melanocytes in hair follicles; this must be confirmed by ultrastructural studies. In this study, the rate of complications was lower in the PUVA group than in the clobetasol group and it was statistically significant. Of 35 patients treated with topical clobetasol, 9 patients developed mild to moderate cutaneous atrophy (moderate in 3 and mild in 6 cases). In fact, one of the most important concerns with the use of potent topical steroids is cutaneous atrophy or striae. In this study, we tried to prevent this complication by diluting clobetasol cream in isopropyl alcohol (30 grams in 100ml). The irritant nature of isopropylic alcohol may also prevent skin atrophy. Only 2 patients in the PUVA group complained about erythema and burning sensation. Perhaps the lighter types of skin color in our patients and relatively low doses of PUVA were the reasons for the lower rate of adverse reactions to UVA. Long-term follow-up is necessary to assess chronic side effects in patients who receive PUVA therapy. Long term high-dose exposure to PUVA has been consistently observed to significantly increase the risk of squamous cell carcinoma.

One of the advantages of phototherapy is that it is done under the guidance and supervision of a physician; therefore, problems such as lack of patient’s cooperation largely decrease. There are some problems that limit the use of PUVA therapy. For example, the required equipment is only available in large cities and oral methoxalen can be scarce. The relatively high cost of treatment, when compared to topical corticosteroids, and the need to protect the eyes are additional problems. Another important limitation of this treatment is being time-consuming for the patients. Therefore, when the use of PUVA is impossible, in limited vitiligo, topical corticosteroids are relatively inexpensive, available and moderately effective. Furthermore, its consumption in specific groups such as children, pregnant and lactating women is also permitted and it does not have the limitations of PUVA. On the whole, the results of this study showed that PUVA therapy in patients with higher skin types was well tolerated with relatively good results and was more effective than topical corticosteroids without significant complications.

**REFERENCES**

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**Table 4. Patterns of repigmentation in vitiligo lesions**

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Perifollicular</th>
<th>Marginal</th>
<th>Diffuse</th>
<th>Perifollicular &amp; marginal</th>
<th>Perifollicular &amp; diffuse</th>
<th>Marginal &amp; diffuse</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PUVA</td>
<td>32 (86.5%)</td>
<td>0</td>
<td>0</td>
<td>5 (13.5%)</td>
<td>0</td>
<td>0</td>
<td>37</td>
</tr>
<tr>
<td>Clobetasol</td>
<td>12 (34.3%)</td>
<td>10 (28.6%)</td>
<td>5 (14.3%)</td>
<td>4 (11.4%)</td>
<td>1 (2.8%)</td>
<td>3 (8.6%)</td>
<td>35</td>
</tr>
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</table>

**Table 5. Repigmentation in skin lesions with white hairs**

<table>
<thead>
<tr>
<th>Treatment Group and number of patients</th>
<th>Marked (75%&lt;)</th>
<th>Good (51-75%)</th>
<th>Moderate (25-50%)</th>
<th>None or poor (25%&gt;)</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>PUVA (number of patients)</td>
<td>13 (54.2%)</td>
<td>8 (33.3%)</td>
<td>3 (12.5%)</td>
<td>0 (0%)</td>
<td>24</td>
</tr>
<tr>
<td>Clobetasol (number of patients)</td>
<td>3 (15.8%)</td>
<td>4 (21.1%)</td>
<td>10 (52.6%)</td>
<td>2 (10.5%)</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>16 (37.2%)</td>
<td>12 (27.9%)</td>
<td>13 (30.2%)</td>
<td>2 (4.7%)</td>
<td>43</td>
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</tbody>
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