

Comparing the Efficiency of Elidel Cream and Elidel Accompanied With Tretinoin Cream in Treatment of Alopecia Areata

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Background: Alopecia areata is a disorder causing local or total body hair loss. Various therapeutic modalities have been used for the treatment of this disease; however, none of them were completely effective.

Objectives: In this study, we compared the efficacy of topical Elidel alone and Elidel accompanied with tretinoin in the treatment of alopecia areata.

Patients and Methods: This randomized controlled clinical trial was performed on patients with alopecia areata in Rasoul-e Akram Hospital in Tehran, Iran, from 2010 to 2011. Patients in the Elidel group applied Elidel 1% cream twice a day. The second group received 1% Elidel in the mornings and 0.05% tretinoin in the evenings. The results compared after three months of treatment.

Results: A total of 80 patients were randomly allocated to two treatment groups. The mean age of the patients was 21.8 ± 3.9 and 21.6 ± 4.4 years in the Elidel and Elidel plus tretinoin groups, respectively ($P = 0.879$). There were 26 males (65%) in the Elidel and 24 (60%) male patients in Elidel plus tretinoin groups ($P = 0.481$). In The Elidel group, the complete cure was observed in eight patients (20%), relative cure in 14 (35%), no change in 10 (25%), and disease aggravation in 8 (20%) cases; in the Elidel plus tretinoin group, the complete cure was reported in 18 patients (45%), relative cure in 12 (30%), no change in 8 (20%), and disease aggravation in 2 (5%) ($P = 0.048$) cases. The cure rate in both groups significantly changed in comparison to the previous findings ($P < 0.001$).

Conclusions: Our study showed that the combined use of Elidel and tretinoin was more effective than Elidel alone.

Keywords: Alopecia Areata; Elidel Cream; Tretinoin

1. Background

Alopecia areata is a disorder causing noncicatricial local or total body hair loss (1, 2). The prevalence of alopecia areata is about 150 cases per 100000 general populations. The pathophysiologic cause of alopecia is related to autoimmune disorders including the T-lymphocyte autoimmune responses against hair follicles antigens (1-4). Therefore, various therapeutic methods, which are basically immunosuppressive therapeutic methods such as systemic or pulse therapy with corticosteroids, applied for the treatment of this disorder (5-8). In addition, the application of the other therapies including topical stimulators such as 2, 2 butyl ester scuaric acid and diphen-cyprone as well as hair growth stimulators such as minoxidil (9-12) have not had any appropriate therapeutic response so far. Therefore, researchers intended to evaluate the novel therapeutic modalities without systemic complications. The therapeutic effects of retinoids have been evaluated on numerous dermatologic diseases and most of the studies have supported their effectiveness with fewer complications (13).

2. Objectives

We aimed to compare the synergistic therapeutic effect of topical tretinoin and Elidel versus topical Elidel alone.

3. Patients and Methods

This randomized controlled clinical trial was performed on the patients with alopecia areata who were referred to dermatology clinics of Rasoul-e Akram Hospital in Tehran, Iran, during 2010-2011. The inclusion criteria were patchy types of alopecia areata, without any scar in scalp area, 18 to 25 years of age, one to four lesions on the scalp, and lesion diameter of 1.5 to 6 cm. Pregnant or lactating women, patients with ophiasis and nail changes, cases with history of treatment and those with allergic reactions to Elidel or tretinoin were excluded from this study.

Convenience sampling was done and all patients with inclusion criteria were enrolled in the study until reaching the calculated sample size. Patients were randomly allocated to two groups using simple random number tables. Type I error was 5%, type II error was 20%, and es-

timated cure rates in Elidel group and Elidel plus tretinoin group were 40% and 70%, respectively. According to our calculations, each group comprised of 40 patients. Firstly, written informed consents were obtained from the patients who met the inclusion criteria. Then, the first patient was randomly allocated to the Elidel group and the second one to the Elidel plus tretinoin group by drawing lots. Topical Elidel 1% cream was applied twice a day (in the mornings and evenings) in the Elidel group. In the second group, patients applied 1% Elidel cream in the mornings and 0.05% tretinoin in the evenings. Both groups had to use medication for three months. The responses to treatment were defined as follow: complete cure, similar of hair density in alopecia areas and intact areas; relative cure, growth of thin terminal hairs with less density in comparison to the intact areas by about 50%; no change, no hair growth in the area without enlargement and/or lack of developing new lesions; and aggravation of lesions, increase in diameter or number of lesions. At the end of study, the results were compared in both groups. We used SPSS version 15 (SPSS Inc. Chicago, IL, USA) for statistical analysis. Frequency and rates for qualitative variables, median, mode, mean and standard deviation of quantitative variables calculated. Chi-square test was used to compare the rates while student t-test was used to compare the means of statistical analysis. P value < 0.05 was considered as statistically significant.

4. Results

We enrolled 80 patients in our study and randomly allocated them to two 40-patient groups of Elidel and Elidel plus tretinoin groups. The mean age of the patients was 21.8 ± 3.9 and 21.6 ± 4.4 years in Elidel and Elidel plus tretinoin groups, respectively. The mean age difference between the two groups was not significant ($P = 0.88$). There were 14 female (35%) and 26 male (65%)

patients in Elidel group whereas, 16 cases in Elidel plus tretinoin group were female (40%) and 24 were male (60%). The comparison of these rates showed no statistically significant difference between the study groups ($P = 0.48$). The mean number of primary lesions was 2.8 ± 1 in Elidel group and 2.4 ± 0.9 in Elidel plus tretinoin group, which showed no statistically significant differences between the groups ($P = 0.18$). Table 1 shows the results of treatment in the study groups according to the patients' gender. This table shows that there was a statistically significant difference between the study groups in all of the patients as well as male and female patients ($P = 0.048$). The treatment rate in both groups significantly changed ($P < 0.001$ in both groups).

These findings compare one of the patients' conditions before and after treatment with Elidel and tretinoin. According to Table 1, complete and relative cure rates were reported in 22 cases (55%) in Elidel group and in 31 patients (75%) in Elidel plus tretinoin group. The comparison of these rates showed a significant difference between these groups ($P = 0.03$). No serious complication was reported by patients in Elidel group whereas adverse effects were reported in 18 cases (45%) in Elidel plus tretinoin group (6 females and 12 males, $P < 0.001$). These side effects included severe erythema and burning resulting in dose reduction in 12 cases and treatment continued by administration of antihistamines and the therapy was stopped in six patients to eliminate the side effects.

5. Discussion

Up to now, numerous studies have been conducted on treatment of alopecia areata and many of those researches have compared the efficacy of different topical agents on hair regrowth (14-20). In a comparative study of topical 0.05% tretinoin, topical betamethasone dipropionate lotion, and 0.25% dithranol paste, satisfaction was reported by 55% of patients who were treated with topical tretinoin

Table 1. Treatment in Different Genders ^a

Investigated Group	Aggravation of Lesions	Without Changes	Relative Cure	Complete Cure	Sum	P Value
Males						
Elidel	2 (14.3)	4 (28.6)	6 (42.9)	2 (14.3)	14 (100)	0.274
Elidel-Tretinoin	0 (0)	4 (25)	6 (37.5)	6 (37.5)	16 (100)	
Females						
Elidel	6 (23.1)	6 (23.1)	8 (30.8)	6 (23.1)	26 (100)	0.202
Elidel-Tretinoin	2 (8.3)	4 (16.7)	6 (25)	12 (50)	24 (100)	
Total						
Elidel	8 (20)	10 (25)	14 (35)	8 (20)	40 (100)	0.048
Elidel-Tretinoin	2 (5)	8 (20)	13 (30)	18 (45)	40 (100)	

^a Data are presented as No. (%).

in comparison with 70% and 35% of cases who were respectively underwent topical steroid and dithranol therapy (14). In a randomized bilateral half-head comparison, at least 50% hair regrowth on treated sites was reported in only 12% of patients who were treated with 1% bexarotene gel; mild irritation was a common side effect among the studied patients (15).

In an open study, cosmetic response was observed in 25% of patients with severe alopecia areata who were treated with 0.5% to 1.0% anthralin cream (16). In another study, the combination of 5% minoxidil and 0.5% anthralin was used to treat 51 patients with severe alopecia areata and only 11% of patients achieved cosmetically acceptable hair regrowth (17). In another study, 61% of patients using 0.1% betamethasone valerate foam showed more than 75% hair regrowth while only 27% of patients who underwent treatment with 0.05% betamethasone dipropionate lotion had the same rate of regrowth (18). Folliculitis is a common side effect of topical corticosteroids; however, telangiectasia and atrophy may rarely develop. The reported relapse rate was 37% to 63% (19, 20). In spite of these studies, there has not yet been any study comparing the efficacy of Elidel plus tretinoin creams with Elidel alone. Therefore, we designed this study to compare these two therapeutic modalities. According to our results, there were no differences between the two groups regarding their gender; therefore, these two variables were not confounders in our study. The clinical findings indicated that the pretreatments characteristics were similar to some extent and it seems that there was no significant difference in clinical condition of the patients. It indicated that post treatment results were not related to patients' pretreatment clinical conditions. According to the results of the present study, therapeutic response rates in both groups were significantly higher after treatment in comparison to the pretreatment ones and both therapeutic modalities had resulted in complete or relative cure rate in more than 50% of the patients. However, therapeutic response was more acceptable in Elidel plus tretinoin group; i.e. higher rate of complete cure and fewer aggravated lesions were observed in this group. The comparison of two therapeutic modalities regarding the patients' gender showed no significant differences. The main reason of these finding might be the small sample size. Nevertheless, it seems that therapeutic outcomes were better in both male and female patients in the Elidel plus tretinoin group.

This study showed that tretinoin was significantly associated with more side effects; although these adverse events have not been serious, three patients withdrew because of the side effects. In these cases, treatment continued after controlling and eliminating their complications. Although this study was a randomized controlled clinical trial, it has some limitations. Further studies with larger sample size are recommended to achieve more accurate results. In conclusion, both therapeutic modalities including Elidel alone and Elidel with tretinoin were

effective in the treatment of alopecia areata; however, the comparison of these two therapeutic modalities showed that Elidel plus tretinoin was significantly more effective than Elidel alone. In addition, although tretinoin side effects are not serious, its side effects are very common.

Authors' Contributions

Study concept and design: Aziz Jalali, Mobasher, Analysis and interpretation of data: Mobasher, Rabbani, Ahmadi Jazi. Drafting of the manuscript: Mobasher, Ahmadi Jazi. Critical revision of the manuscript for important intellectual content: Aziz Jalali, Mobasher, Rabbani, Ahmadi Jazi, Statistical analysis: Mobasher, Ahmadi Jazi.

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