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ORIGINAL ARTICLE

Efficacy and Safety of Combination of Mometasone Furoate 0.1% Cream and Adapalene 0.1% Gel in Alopecia Areata.

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ABSTRCT

Background: Alopecia areata (AA) is an autoimmune disease characterized by non-cicatricial hair loss. No definitive therapy currently exists for AA. Despite widespread use of topical corticosteroids in AA, the success of these agents is controversial. Thus, the aim of this study was to evaluate the efficacy and safety of the mometasone furoate 0.1% cream plus adapalene 0.1% gel in treatment of AA.

Methods: A cohort study on alopecia areata patients from the outpatient clinic of Dermatology, Venereology and Andrology Department, Faculty of Medicine, Zagazig University Hospitals in the period from June 2018 to February 2019. This study included 40 patients of alopecia areata of both sexes with chronic recurring disease not responding to other lines of treatments. Patients were treated with combination of Adapalene 0.1 gel and mometasone furoate 0.01 cream (Elocon). Patients used this combination by themselves at home for 6 months, they were advised to apply a layer of adapalene gel on the diseased area followed immediately by Elocon cream once daily at night. Elocon is applied alone in the morning. The response was assessed by the "Severity of Alopecia Tool Score". Patients were assessed photographically every 2 weeks for 6 months. Side effects were recorded.

Results: We found that 35% patients showed 100% response, 5% patient showed 75% response and 60% patients showed no hair regrowth. As regarding side effects, 85% of the patients showed side effects, but no patient was lost. As regarding side effects, 85% of the patients showed side effects, in the form of erythema in 60% of cases, irritation in 85% of cases and telangiectasia in 25% of cases, there was no patient drop out.

Conclusion: Combined use of adapalene gel and mometasone furoate cream is favorable modality of AA treatment only for mild cases with SALT score > 20%. It can be applied easily by the patient at home. Side effects were mild and well tolerated.

Keywords: Alopecia Areata, Adapalene, Mometasone.

INTRODUCTION

Alopecia areata (AA) is an organ-specific autoimmune disease characterized by non-cicatricial hair loss in hair, beard, moustache, eyebrows, eyelashes, chest, back, and extremities. Lesions of AA often resolve spontaneously, but the disease may progress to loss of all scalp hair (alopecia totalis) or to total loss of scalp and body hair (alopecia universalis). AA is a common disease, affecting about 1% of the population [1] Male and females are affected equally and the prevalence is almost the same for all ethnic groups. Many theories were implicated in pathogenesis of AA, such as an autoimmune lymphocytic attack to the hair, genetic basis, and environmental factors, but the precise etiology of AA is still obscure. The pathologic features of AA lesions is characterized by perifollicular and intrafollicular mononuclear cell infiltrates, directed at the anagen hair bulbs. The infiltrate is composed predominantly of activated CD4(+) and CD8(+) T cells, together with macrophages and Langerhans cells [2]. A variety of treatment modalities for AA are available, including topical, intralesional, and systemic steroids; topical immunotherapy; anthralin; minoxidil; photochemotherapy; and systemic agents such as cyclosporine, methotrexate, sulfasalazine, and biologics. However, no definitive therapy currently exists for AA [3].

Topically, intralesionally or systemically corticosteroids are the most commonly used agents in the treatment of AA. Despite widespread use of topical corticosteroids in AA, the success of these agents is controversial. In several studies it is reported that topical corticosteroid treatment is not effective when used alone and not superior to the placebo; but in some other studies, successful results were obtained in AA with topical corticosteroids [2,4].

Adapalene is a synthetic, third-generation topical retinoid analogue derived from naphthoic acid. Adapalene is one of the essential agents of acne treatment because of its anti-inflammatory effects and its ability to block key pathophysiologic mechanisms in the development of acne. Although there have been many studies showing the efficacy of adapalene in acne treatment, there is no study that reports its efficacy in alopecia areata or androgenetic alopecia, in contrast to other topical retinoids tretinoin and bexarotene [5].

The present study was aimed to evaluate the efficacy and safety of the mometasone furoate 0.1% cream plus adapalene 0.1% gel in treatment of AA.

METHODS

The present study was carried at Dermatology, Venereology and Andrology Department, Faculty of Medicine, Zagazig University Hospitals in the period from June 2018 to February 2019. The present study included 40 patients with alopecia areata of both sexes with chronic recurring disease not responding to other lines of treatments as topically, intralesionally or systemically corticosteroids. After excluding patients with serious intercurrent medical illness, significant cardiovascular disease, localized scalp infections or inflammation, immunosuppressed patients, history of local or systemic therapy within 6 months or pregnancy.

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Patients were subjected to history taking regarding age, sex, family history, history of drug intake and alopecia areata onset, duration, course, location and number. All patients were subjected to general physical examination with specific attention to associated medical condition. Dermatological examination of the lesion(s) of hair loss including site, size and severity. Severity assessment by Severity of Alopecia Tool score (SALT score) [6]. The scalp is divided into the following 4 areas:

- Vertex: 40% (0.4) of scalp surface area.
- Right profile of scalp: 18% (0.18) of scalp surface area.
- Left profile of scalp: 18% (0.18) of scalp surface area.
- Posterior aspect of scalp: 24% (0.24) of scalp surface area.

Percentage of hair loss in any of these areas is percentage of hair loss multiplied by the percent of surface area of the scalp in that area. SALT score is the sum of percentage of hair loss in all above mentioned areas

Procedure

Patients were treated with combination of adapalene 0.1 gel (Adapalene) and mometasone furoate 0.01 cream (Elocon). Patients used this combination by themselves at home for 6 months. Patients were advised to apply a layer of adapalene gel on the diseased area followed immediately by Elocon cream once daily at night. Elocon is applied alone in the morning. After 6 months patients were assessed for side effects. The most common side effects were erythema, irritation and telangiectasia.

The study was photographically documented for results evaluation, using a digital camera with resolution 10 Mega Pixels (Canon ixus 175 digital camera). The photographs were taken at weeks 0 (at start of therapy), 2, 4, 6, 8 with 2 weeks interval and re-evaluated 24th week. Percentage hair regrowth was assessed with 6 grades according to Tiwary et al. [1]:

- A0 = no change or further loss of hairs
- A1 = 1–24% regrowth
- A2 = 25–49% regrowth
- A3 = 50–74% regrowth
- A4 = 75–99% regrowth
- A5 = 100% regrowth

STATISTICAL ANALYSIS

All data were collected, tabulated and statistically analyzed using SPSS 24.0 for windows (SPSS Inc., Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Quantitative data were expressed as mean ± SD (Standard deviation) for parametric and median and range for non-parametric data. Independent T test and Mann Whitney test were used to calculate difference between quantitative variables in two groups for parametric and non-parametric variables respectively. Kruskall-Wallius test was used to compare between more than two independent groups of non- normally distributed variables. Wilcoxon Signed Ranks Test between dependent two related samples. non normally distributed. All statistical comparisons were two tailed with

significance Level of P-value ≤ 0.05 indicates significant, p <0.001 indicates highly significant difference while, P> 0.05 indicates non-significant difference.

RESULTS

This study included 40 AA patients: 32 were males and 8 females, their age ranged from 5 to 50 with a mean of 27 ± 16 years. There were 85% patchy cases and 15% totalis. 65% patchy cases had 1 patch, 10% had 2 patches, 5% had 4 patches and 5% had 5 patches. The mean of disease duration was 28.8± 47 months (Table 1). There was a significant decrease in SALT score after treatment (p=0.008) (Figure 1). However, regarding response 35% patients showed 100% response, 5% patient showed 75% response and 60% patients showed no hair regrowth (Figure 2). As regarding side effects, 85% of the patients showed side effects, in the form of erythema (abnormal redness of the skin) in 60% of cases, irritation (a subjective feeling of inflammation described by the patient with no objective manifestation seen) in 85% of cases and telangiectasia (threadlike red lines or patterns on the skin) in 25% of cases, there was no patient drop out (Figure 3).

Table 1. Demographic & clinical data characteristics of all patients.

		Studied patients (N=40)
Age (years) Mean ± SD		27 ± 16
Male, n (%)		32 (80)
Disease duration (months) Mean ± SD		8 ± 7
Type of alopecia	**Totalis**	6 (15)
	Patchy	34 (85)
Number of lesions of patchy Mean ± SD		1.5 ± 1.2
Previous treatment, n (%)		10 (25%)
Baseline SALT Mean ± SD		31.5 ± 33.4
Post-treatment SALT Mean ± SD		27.3 ± 36

SALT, Severity of Alopecia Tool Score

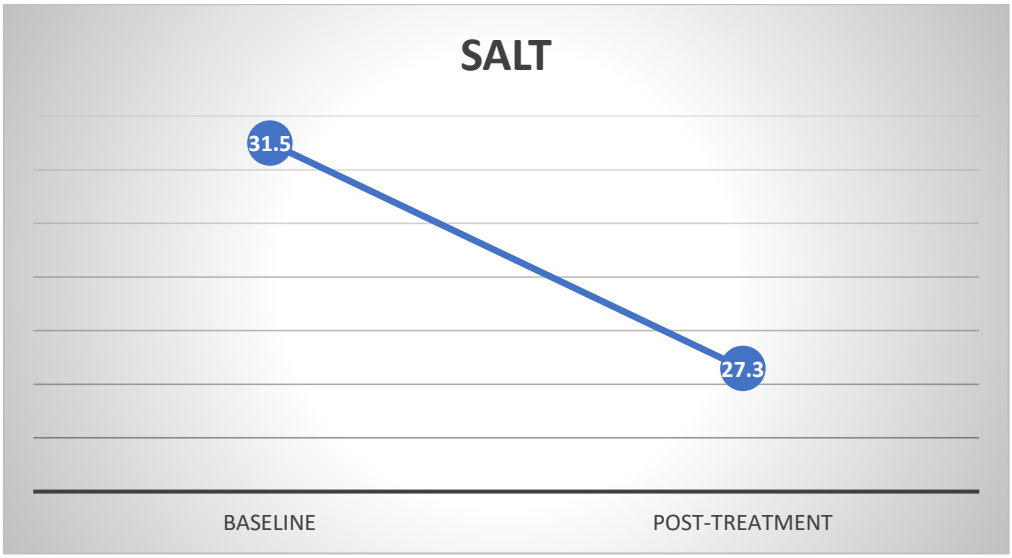

Figure 1. Change in SALT score before and after treatment.

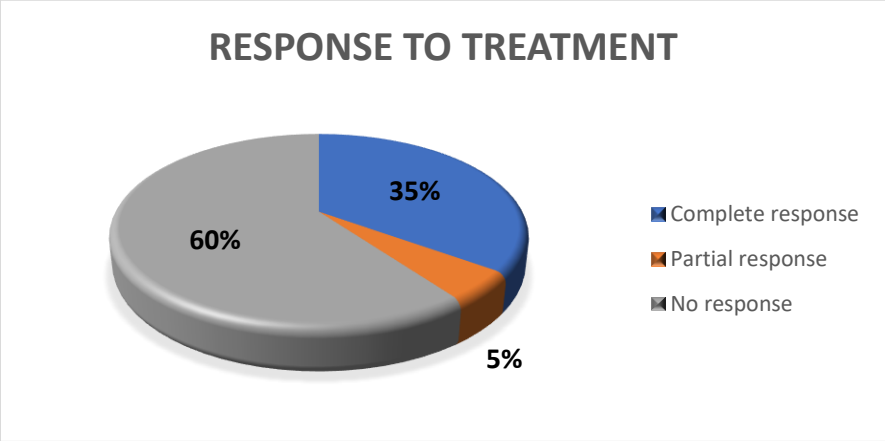

Figure 2. Frequencies of response to treatment

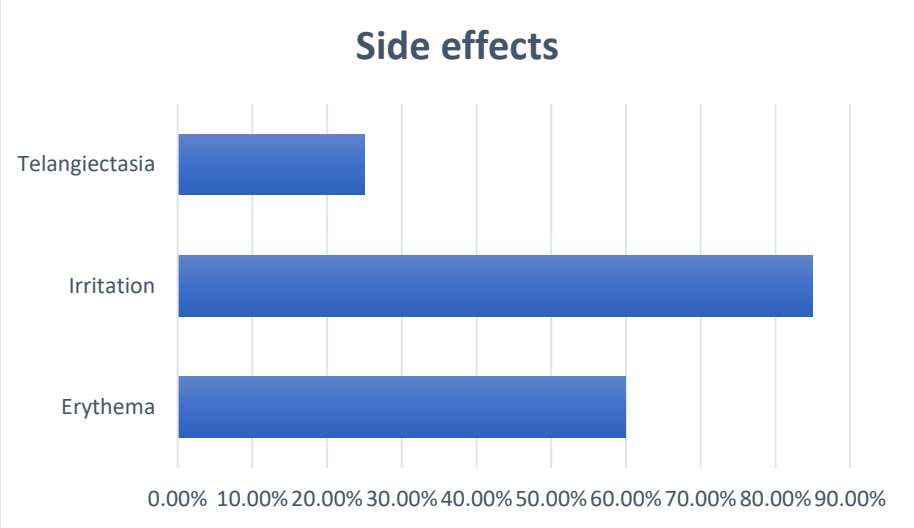

Figure 3. Side effects of the treatment among the studied patients.

DISCUSSION

AA is an autoimmune disease that presents as non-scarring hair loss patches. The exact pathogenesis of AA and the molecular mechanisms that lead to hair loss are not fully understood yet. However, it is now well-established that AA is an autoimmune inflammatory disease evoked by environmental factors in genetically predisposed patients. The collapse of the physiological state of anagen hair follicles immunoprivilege leading to perifollicular T-cell infiltrates and increase in inflammatory chemokines and cytokines may contribute to the disease development [7].

Several types of treatment modalities have been tried but none of them has been proved to be a definitive and curative treatment for AA. Topical immunotherapy may be used in the management of severe AA with encouraging results, although the number of studies on long-term efficacy is low and data on relapse rates are lacking [8].

Adapalene improve the effect of mometasone furoate due to many factors. First, retinoids increase percutaneous absorption of mometasone furoate thus improved its efficacy. Second, retinoids have a role in the growth, differentiation and maintenance of hair [9]. Third, AA is known as an inflammatory disease and topical adapalene has some specific anti-inflammatory effects, so adapalene may suppress inflammation causing hair loss in AA. And lastly, adapalene has immunomodulatory effects and induce T-cell apoptosis which have crucial roles in the pathogenesis of AA [10].

This study aims to evaluate the efficacy and safety of the combination adapalene 0.1% gel and mometasone furoate 0.1% cream in the treatment of alopecia areata.

In our study patients were assessed clinically using SALT score and the mean of SALT score was 12.5%. In our study, we found that AT patients were 15%, while patchy cases were (mostly single 65% and multiple only 20%).

In the present study the response rate after 6 months of treatment with combination of adapalene gel and elocon cream was 35 % complete response, 5% partial response and 60% no response. This study

proved that patient characters and lesion character had no effect in the response.

However, Unal, [5] proved that higher regrowth rate in the group used combination of mometasone furoate cream and adapalene gel than that of group of mometasone furoate cream alone (90 % versus 71% respectively). Satisfaction of patients in combination group was better 85%. In Zaher et al. [4] study, 17 of 30 AA patches treated with mometasone furoate alone responsed to treatment (56.7%). According to the SALT scoring system for hair regrowth, there was a mean hair re-growth of 22.4 ± 20.64 % in the responding AA patches. Their results were better than ours because their cases only patchy cases with small patches.

Considering side effects of combination of adapalene and mometasone furoate in our study, 85% of the patients showed side effects, in the form of erythema in 60% of cases, irritation in 85% of cases and telangiectasia in 25% of cases. These side effects may be due to long use of treatment. These results disagreed with Zaher et al. [4] that reported that 58.8% AA patches (treated with mometasone furoate showed side effects either atrophy in 3 cases (17.6%) or erythema in 7 cases (41.2%). Unal, [5] reported no side effect of adapalene such as itching, pain, paresthesia, vesicle, erythema and edema, because the use of mometasone furoate may decrease the incidence of adapalene related side effect.

In the present study adapalene and mometasone furoate is effective for patchy AA with SALT score 10-20%. Also s side effects of mometasone furoate and adapalene were mild and more tolerated.

Though we have achieved great success with combination of adapalene gel and mometasone furoate cream and this study gives us new hope that these indeed may be a good treatment modality for AA. Furthermore, studies are needed to better understand the role of adapalene and mometasone furoate in alopecia areata and to validate the final results.

CONCLUSION

Treatment of AA using combination of mometasone furoate cream and adapalene gel is a promising, easy-to-use technique more than other traditional methods of AA treatment. Adapalene gel and mometasone furoate cream is favorable modality of AA treatment only for mild cases with SALT score > 20%. It can be applied easily by the patient at home. Side effects were mild and well tolerated.

conflict of interest: No

Personal financial

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