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Evaluation of Efficacy and Safety of Oral Cyclosporine in the Treatment of Severe Alopecia Areata

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Abstract

Background: One of common forms of scaring hair loss is alopecia. Alopecia is an autoimmune disorder that is characterized by relapsing and remitting episodes of non scaring hair loss. Several treatment options are nowadays available to be prescribed to patients with alopecia areata including local and systemic corticosteroid therapy, immune suppressant agents and contact immunotherapy. Nonetheless, none of these agents have been 100 % effective in eradication of the disease totally and some agents are associated with intolerable side effects. Therefore, dermatologists are continuously searching for new agents and modalities in order to get better response and less sided effects.

Aim of the Study: The current study was planned and conducted to evaluate the efficacy and safety of oral cyclosporine in treating alopecia areata.

Patients and Method: This study included 35 patients with alopecia areata. The study was conducted at the dermatology unit, Al-Diwaniyah Teaching Hospital, Al-Diwaniyah Province, Mid-Euphrates Region of Iraq. The study started on June the 2nd 2018 and extended to June the 2nd 2019. The study was approved by the institutional ethical approval committee and included a verbal consent was obtained from each participant following full demonstration of the aim and procedures of the study. Every patient has received a daily dose of oral cyclosporine (3 mg/kg) for a period in the range of 2 to 12 months. Variables included in the current study were age, gender, type of alopecia areata, duration of disease, duration of treatment and treatment response. Outcome in the end of the study included clinical response and main side effects.

Results: Following treatment with oral cyclosporine, 28 patients (80 %) had satisfactory response and 7 patients (20 %) had unsatisfactory response. Treatment response was not correlated to age, gender, disease duration or type of disease ($P > 0.05$). There were unremarkable adverse effects in association with oral cyclosporine use.

Conclusion: oral cyclosporine is effective and safe mode of treatment in patients with alopecia areata

Key words: *Cyclosporine, alopecia areata, Iraq*

Introduction

In modern dermatological practice, hair loss may be broadly classified into scaring and non scaring hair loss [1]. Scaring hair loss is characterized by loss of hair follicles, whereas, non scaring hair loss is characterized by preservation of hair follicles [(1,2)]. One of common forms of scaring hair loss is alopecia [(3-5)]. Alopecia is an autoimmune disorder that is characterized by relapsing and remitting episodes of non scaring hair loss [(6-8)]. Clinically it is classified into several forms according to the distribution of hair loss [1]. Patchy involvement of scalp is commonly referred to as multifocal alopecia, the one which involves all scalp hair is called alopecia totalis, while the type that involves all body hair is called alopecia universalis [(9-11)].

The immunological basis of disease was made clear during the last 60 years owing to the discovery of several immune cells and humeral agents in close association with the disease [1]. The prevalence rate of alopecia areata has been estimated to fall between 0.1% and 0.2 %,

whereas, the lifetime incidence has been claimed to be approximately 2 % [1]. The data about gender variation in disease incidence are conflicting with some reports referring to a higher incidence among females [12], while others have reported higher incidence rate in association with male gender [5]. There are no reported suggestions about ethnic predilection [13].The onset of the disease can happen at any age; however, the majority of cases are seen before 40 and the mean age of onset has ranged from 25 to 36 [14]. The disease is often severe when being encountered in child age group [15].

Familial clustering and the occurrence of disease in patients with positive family history and twins more often than general population suggest a strong genetic contribution in the causation of this dermatological disorder [1]. Moreover, the disease happens in association with a number of autoimmune disorders such as systemic lupus erythematosus, thyroid disorders and rheumatoid arthritis [14]. A physical environmental trigger has rarely been identified, but a number of psychological triggers have been linked to the onset of disease such as emotional or physical stress [14].

Several treatment options are nowadays available to be prescribed to patients with alopecia areata including local and systemic corticosteroid therapy [16], immune suppressant agents [17] and contact immunotherapy [1]. Nonetheless, none of these agents have been 100 % effective in eradication of the disease totally and some agents are associated with intolerable side effects [17]. Therefore, dermatologists are continuously searching for new agents and modalities in order to get better response and less sided effects.

Oral cyclosporine has been regularly tested as a mode of treatment of alopecia areata by a number of researchers during the last three decades but the results were controversial [18-20]. Due to lack of consensus in the available published articles regarding the efficacy and safety of oral cyclosporine in treating alopecia areata and because of the rarity of national data with regard, the current study was planned and conducted in Al-Diwaniyah province, Mid-Euphrates region of Iraq to evaluate the efficacy and safety of oral cyclosporine in treating alopecia areata.

Patients and Method

This cohort study included 35 patients with alopecia areata. The study was conducted at the dermatology unit, Al-Diwaniyah Teaching Hospital, Al-Diwaniyah Province, Mid-Euphrates Region of Iraq. The study started on June the 2nd 2018 and extended to June the 2nd 2019. The study was approved by the institutional ethical approval committee and included a verbal consent was obtained from each participant following full demonstration of the aim and procedures of the study. Every patient has received a daily dose of oral cyclosporine (3 mg/kg) for a period in the range of 2 to 12 months. Variables included in the current study were age, gender, type of alopecia areata, duration of disease, duration of treatment and treatment response. Outcome in the end of the study included clinical response and main side effects.

Data were transferred into an SPSS (version 23) spread sheet and presented as mean, standard deviation, range, number and percentage. Mann Whitney U test was used to study difference in mean between two groups, while, Chi-square otr Yates correction were carried out to assess association between any two categorical variables. The level of significance was considered at $P \leq 0.05$.

Results

The currents cohort study was based on the inclusion of 35 Iraqi patients with alopecia areata. The mean age of enrolled patients was 23.69 ±10.03 years and the age range was from 10 to 40 years; most of the cases were above 15 years of age, as shown in table 1. The study included child age group cases that accounted for 10 (28.6 %), but none of patients was above 40. According to gender, the study included 24 (68.6 %) males and 11 (31.4 %) females with a male to female ratio of 1:2.18. According to type of alopecia, patients were categorized into 12 (34.3 %), 20 (57.1 %) and 3 (8.6 %) as multifocal, totalis and universalis, respectively, as shown in table 1.

Following treatment with oral cyclosporine, 28 patients (80 %) had satisfactory response and 7 patients (20 %) had unsatisfactory response. Treatment response was not correlated to age, gender, disease duration or type of disease ($P > 0.05$), as shown in table 2. There were unremarkable adverse effects in association with oral cyclosporine use.

Table 1: General characteristics of the study sample

Characteristic	Value
Age (years)	
Mean ±SD	23.69 ±10.03
Range	10 - 40
<15, n (%)	10 (28.6 %)
15-40, n (%)	25 (71.4 %)
Gender	
Male, n (%)	24 (68.6 %)
Female, n (%)	11 (31.4 %)
Male: Female'	1:2.18
Duration of disease	
Mean ±SD	5.71 ±2.62
Range	2 - 11
Type	
Multifocal, n (%)	12 (34.3 %)
Totalis, n (%)	20 (57.1 %)
Universalis, n (%)	3 (8.6 %)

n: number of cases; SD: standard deviation

Table 2: The treatment response according to disease characteristics of patients with alopecia areata

Characteristic	Satisfactory n = 28	Unsatisfactory n = 7	P
Mean age ±SD (years)	22.96 ±9.97	26.57 ±10.53	0.432 †
Male / Female	21/7	3/4	0.237 ¥
Mean duration of disease ±SD (years)	5.43 ±2.54	6.86 ±2.79	0.285 †
Multifocal / Totalis / Universalis	9 / 17 / 2	3 / 3 / 1	0.659 €

n: number of cases; SD: standard deviation; †: Mann Whitney U test; ¥: Yates correction; €: Chi-square test

Discussion

The pathophysiology of alopecia areata has been linked to immune basis a long time ago and anti-immune treatment whether local of systemic steroids or immune suppressant agents have extensively tested in treating the disease; however, complete satisfactory response has been never reached in daily dermatological practice [1]. Therefore, there is always a need to search for new modalities in treatment approach especially if one takes into consideration the psychological trauma and poor quality of life experienced by victims who never get improved [21].

Cyclosporine is unusually practiced in our country when dealing with alopecia areata; however, reports from all over the world have encouraged its use in such dermatologic autoimmune disease [18,20]. Nevertheless, the rate of successful remission and safety of the drug has been frequently questioned, despite the bulk of data supporting its efficient and safe use [19]. For that reason, we in the current study included 35 patients with alopecia areata aiming at exploring the efficacy and safety of oral cyclosporine in alopecia areata and found satisfactory response in 80 % of cases. Side effects were negligible especially when one takes into consideration the relatively low dose of the drug (3 m/kg/day).

Several previous studies have found comparables results [18-20]. For instance Açıkgöz et al., [20] described significant hair growth in about 50 % of enrolled cases; however, they mentioned that 3 patients have discontinued the drug because of intolerable side effects. Açıkgöz et al., have stated that they reach a dose of 6 mg /kg in some patients which is probably the cause behind intolerable side effects. Jang et al., have shown that the response of patients to oral cyclosporine was significantly better than that of oral betamethasone and that side effects were much less in association with cyclosporine use [18]. Indeed, the findings of the latter study support the findings of the current study in that oral cyclosporine if an efficient safe treatment modality for alopecia areata. In one review it has been stated that the success rate of oral cyclosporine was in the range of 25 to 76.6 % and that side effects may limit its use [19].

In conclusion, it is better to wait for future more research work to make clear consensus about the value

of oral cyclosporine in patients with alopecia areata; nonetheless and based on our observation and previous reports oral cyclosporine appears to be effective and safe mode of treatment in patients with alopecia areata

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under Department of pharmacology and therapeutics, Faculty of medicine, University of Kufa, Najaf ,Iraq and all experiments were carried out in accordance with approved guidelines.

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