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ATTENUATED CYCLOSPORINE AS A MAINTENANCE TREATMENT FOR INDIVIDUALS WITH MODERATE TO SEVERE CHRONIC PLAQUE PSORIASIS

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ABSTRACT

Background: Psoriasis is a chronic, inflammatory, systemic illness that mostly affects the skin and joints and lowers the quality of life for those who have it. Many psoriasis patients experience significant flare-ups of their condition often, necessitating ongoing systemic treatment. Limited information is available in the literature about the assessment of systemic maintenance therapy's ability to prevent recurrent flare-ups in psoriasis patients.

Aim: The purpose of this study was to evaluate the safety and effectiveness of weekend cyclosporine treatment (WCT) as a maintenance therapy for individuals with moderate to severe chronic plaque psoriasis in order to avoid recurrent flare-ups of the condition.

Methods: In this study, 44 psoriasis patients who had experienced at least three frequent flare-ups of their condition within the previous 12 months and were receiving weekend cyclosporine treatment (Group I) were compared to 44 age and gender-matched controls who were not receiving weekend cyclosporine treatment or any other systemic maintenance therapy (Group II).

Results: Group I showed an aggravation of the illness in 18.2% (n=8) of the individuals, which was substantially less than Group II, where 95.5% (n=42) of the subjects showed an exacerbation (p-value = 0.00). Subjects in Group I experienced considerably fewer overall exacerbations than those in Group II (p=0.00). 9.1% (n=8) of research participants had adverse effects such as myalgia (n=2), minor gingival hyperplasia (n=2), and acneiform eruptions (n=4), whereas Group II experienced six occurrences, including headache in two and acneiform eruptions in four.

Conclusion: In addition to being an efficient and secure form of maintenance therapy for psoriasis patients, the current study finds that weakened cyclosporin treatment for psoriasis reduces the frequency of disease exacerbations.

Keywords: weekend cyclosporine treatment, psoriasis, cyclosporine, and psoriasis maintenance therapy

INTRODUCTION

Psoriasis is a chronic, inflammatory condition that mostly manifests in the skin and joints of those who have it. Psoriasis's clinical manifestation and progression are unclear, and many patients experience worsening of their condition. Although there are a number of well-established treatment techniques for causing remission in psoriasis patients, there is a dearth of information in the literature about the effectiveness and safety of various strategies for maintaining remission and preventing the disease's typical flare-ups.[1]

One of the most popular treatments for causing a quick remission in patients with moderate to severe psoriasis is oral cyclosporin (CYC). Several cyclosporin regimens have been employed to induce and maintain remission in psoriasis

patients. However, prolonged and continuous use of cyclosporin treatment has been linked to a number of negative consequences, including the risk of nephrotoxicity, necessitating its cessation when remission is achieved.2

When cyclosporins or other systemic treatments are stopped, psoriasis patients frequently experience an exacerbation of their condition, which may be upsetting for both patients and medical professionals. There haven't been many attempts at weekend cyclosporin medication regimens and tactics to keep moderate to severe chronic plaque psoriasis in remission. As a psoriasis maintenance treatment, WCT (Weekend Cyclosporine Therapy) involves giving cyclosporin twice a week.3

According to findings from earlier research, cyclosporin medication administered continuously and on weekends is equally effective at preventing exacerbations in psoriasis patients. According to other research in the literature, psoriasis patients who received weekend cyclosporin medication experienced a longer relapse period than those who received a placebo. The frequency of exacerbations in people prior to starting cyclosporin was not reported in these investigations, which evaluated individuals with chronic plaque psoriasis.4

In the therapeutic setting, weekend cyclosporin medication may be appropriate as maintenance treatment for certain psoriasis patients who have a propensity for repeated flare-ups.

In order to prevent recurrent flare-ups of moderate to severe chronic plaque psoriasis, the current research sought to evaluate the safety and effectiveness of WCT (weekend cyclosporine treatment) as a maintenance therapy.

MATERIALS AND METHODS

In order to prevent recurrent flare-ups of moderate to severe chronic plaque psoriasis, the current retrospective study sought to evaluate the safety and effectiveness of WCT (weekend cyclosporine treatment) as maintenance therapy. The research participants came from the Institute's Department of Dermatology. Before participating in the study, all participants and school officials gave their verbal and written informed consent.

Investigations, side effects, treatment plans, and severity scores were among the demographic and clinical data evaluated in research participants. These were updated and kept up to date in the institute's records at every visit by people receiving psoriasis therapy. The most prevalent systemic treatment for moderate to severe psoriasis was daily cyclosporin at a dosage of 3–5 mg/kg/day. Most participants had satisfactory clinical response with PASI-90 or PASI > 75 regarding disease control. Following a satisfactory clinical response, the daily cyclosporin dosage was reduced by around 1 mg every other week for the following 6–10 weeks until being discontinued.

In a subgroup of participants, daily CYC resulted in a 90% or more decrease in the psoriasis area and severity score (PASI-90). While few patients were treated without systemic medications, WCT was administered to a small number of interested participants with a history of frequent exacerbations at a dosage of 3-5 mg/kg/day administered twice a week. A daily cyclosporin was often initiated for clinical remission induction ≥ PASI-90, followed by tapering, for any individual on WCT experiencing a disease exacerbation without any systemic drug as maintenance treatment. The selection of CYC as a systemic drug for these participants' exacerbation therapy was based on their prior history of daily CYC response. For the first four weeks, subjects on WCT or daily CYC were routinely monitored every two weeks, and then every four weeks after that.

The clinical records of individuals with moderate to severe psoriasis were used to collect data. Subjects that met the inclusion criteria were included after screening. Clinical and demographic information was entered on pre-made structured proforma and evaluated retrospectively for each participant.

Participants in the study had to be at least eighteen years old, have been diagnosed with chronic plaque psoriasis for at least two years, be taking cyclosporin daily, and have experienced three or more exacerbations in the previous year, as indicated by a PASI of at least ten or a body surface area (BSA) of at least ten during exacerbations. According to the study's exclusion criteria, participants who were treated with systemic medications other than daily CYC for exacerbations during the MP were not allowed to participate.

Group I consisted of participants who were screened, treated with daily CYC at 3-5 mg/kg/day (induction phase), achieved clinical remission (≥ PASI 90), tapered and stopped CYC, and maintained WCT for at least 6 months as part of the maintenance phase. Group II consisted of participants who were in clinical remission (PASI ≥ 90) on daily CYC (IP), tapered and terminated, but did not begin WCT or any systemic medication for maintenance (MP). The subjects were matched by gender and age into two groups. Two groups that experienced an exacerbation during the maintenance phase were treated with daily CYC (3–5 mg/kg/day, which was reduced and terminated after reaching PASI > 90). During the induction and maintenance phases, two groups were permitted to use topical treatment and antihistamines as needed. When results were evaluated, the maintenance phase in two groups was defined as the length of the research. In both groups, the maintenance period lasted for at least six months. Each individual in both groups had their blood pressure,

lipid profile, renal and liver function tests, and complete blood count evaluated at baseline and follow-up. The number of psoriasis patients who experienced disease exacerbations and the total number of exacerbations throughout the maintenance phase were used to measure the results. An exacerbation during the maintenance phase was defined as PASI > 10 or involving 10% of the body surface area (BSA) during the MP. At every follow-up visit, all individuals were evaluated for side effects, such as hypertension and nephrotoxicity, in accordance with established practice.

ANOVA, the chi-square test, the student's t-test, Fisher's exact test, the Mann Whitney U test, and SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA) were used to statistically evaluate the data gathered from the research participants. A p-value of less than 0.05 was regarded as the significance level.

RESULTS

In order to prevent recurrent flare-ups of moderate to severe chronic plaque psoriasis, the current retrospective study sought to evaluate the safety and effectiveness of WCT (weekend cyclosporine treatment) as maintenance therapy.

In the current study, 44 psoriasis patients who had experienced at least three frequent exacerbations of their condition within the previous 12 months and were receiving weekend cyclosporine treatment (Group I) were compared to 44 age and gender-matched controls who were not receiving weekend cyclosporine treatment or any other systemic maintenance therapy (Group II). 48 participants who met the inclusion criteria were split between the two groups. Because the research individuals were included at the same time, the mean duration of the maintenance period in the two groups was 11.62±3.11 months.

Clinic-demographic information at baseline was similar between the two groups in terms of mean age, gender, duration of disease, mean weight, body surface area (BSA), mean exacerbation (n) in the year prior to the induction phase, and duration of the maintenance phase (p=0.74, 1.00, 0.25, 0.34, 0.56, 0.91, and 1 respectively) (Table 1).

Analyzing the clinical outcomes of the study participants, it was found that 18.2% (n=8) of those receiving weekend cyclosporin therapy experienced exacerbations during the maintenance phase, which was substantially less than the 95.5% (n=42) of those in the group not receiving weekend cyclosporin treatment. Six of the eight individuals in group I who experienced an exacerbation during the maintenance phase had just one exacerbation, whereas two of them experienced two.

Of the forty-two individuals in Group II who experienced exacerbations, fourteen had three exacerbations, ten had two, eight had four, four had five, and two had six. According to the study's findings, group I experienced considerably fewer exacerbations during the maintenance period (mean of 0.21±0.51 versus 2.93±1.41) than group II (p=0.00). At the conclusion of the maintenance phase, group II's body surface area was considerably larger than group I's (p=0.00).

In contrast to six events in Group II, which included headache in two and acneiform eruptions in four study participants, 9.1% of subjects in the weekend cyclosporin therapy group experienced adverse events, including myalgia (n=2), mild gingival hyperplasia (n=2), and acneiform eruptions (n=8). During the maintenance period, none of the subjects in either group experienced significant adverse events such as nephrotoxicity or severe hypertension that required stopping the medication.

DISCUSSION

In the current study, 44 psoriasis patients who had experienced at least three frequent exacerbations of their condition within the previous 12 months and were receiving weekend cyclosporine treatment (Group I) were compared to 44 age and gender-matched controls who were not receiving weekend cyclosporine treatment or any other systemic maintenance therapy (Group II). The current study's design was comparable to that used in earlier research by Ronzi G et al. (2011) and Garrido Colmenero C et al. (2015), where the authors similarly used a similar study design in their separate investigations.

According to the study's findings, 48 participants who met the requirements for inclusion were split between the two groups. Because the research individuals were included at the same time, the mean duration of the maintenance period in the two groups was 11.62±3.11 months. In terms of mean age, gender, duration of disease, mean weight, body surface area (BSA), mean exacerbation (n) in the year prior to the induction phase, and duration of the maintenance phase, the clinic-demographic data in the two groups were similar at baseline (p=0.74, 1.00. 0.25, 0.34, 0.56, 0.91, and 1 respectively).

These results were in line with the findings of earlier research by Golbari NM et al7 in 2018 and Nast A et al8 in et al in 2012, where the authors' demographic information for psoriasis individuals was similar to the findings of the current study.

Comparing the clinical outcomes of the study participants, it was found that 18.2% (n=8) of those receiving weekend

cyclosporin therapy experienced exacerbations during the maintenance phase, which was substantially less than the 95.5% (n=42) of those in the group not receiving weekend cyclosporin treatment. Six of the eight individuals in group I who experienced an exacerbation during the maintenance phase had just one exacerbation, whereas two of them experienced two.

Of the forty-two individuals in Group II who experienced exacerbations, fourteen had three exacerbations, ten had two, eight had four, four had five, and two had six. The findings of Mrowietz U et al. (2012) and Fernandes IC et al. (2013), who also reported a comparison of the clinical outcomes on WCT and non-WCT identical to the current study, were consistent with these results.

In addition, it was observed that the mean number of exacerbations during the maintenance phase was 0.21±0.51 as opposed to 2.93±1.41, which was considerably lower in Group I than in Group II (p=0.00).

At the conclusion of the maintenance phase, group II's body surface area was considerably larger than group I's (p=0.00). In contrast to six events in Group II, which included headache in two and acneiform eruptions in four study participants, 9.1% of subjects in the weekend cyclosporin therapy group experienced adverse events, including myalgia (n=2), mild gingival hyperplasia (n=2), and acneiform eruptions (n=8). During the maintenance period, none of the subjects in either group experienced significant adverse events such as nephrotoxicity or severe hypertension that required stopping the medication.

These results were consistent with the 2010 studies by Colombo D et al.11 and Colombo D et al.12, where the authors' reports of cyclosporin-related exacerbation episodes and adverse events were similar to the current study's findings.

CONCLUSION

Considering its limitations, the present study concludes that weakened cyclosporin treatment for psoriasis decrease the number of disease exacerbation along with being effective and safe method of maintenance therapy in psoriasis subjects. However, further longitudinal multi-institutional studies with larger sample size and longer monitoring are needed to reach a definitive conclusion.

REFERENCES

1. Touw C, Hakkaart-Van Roijen L, Verboom P, Paul C, Rutten F, Finlay A. Quality of life and clinical outcome in psoriasis patients using intermittent cyclosporin. Br J Dermatol 2001;144:967–72.
2. Chaidemenos G, Mourellou O, Avgoustinaki N, Papakonstantinou M, Karakatsanis G, Katsambas A. Intermittent vs. continuous 1-year cyclosporin use in chronic plaque psoriasis. J Eur Acad Dermatol Venereol 2007;21:1203–8.
3. Maza A, Montaudié H, Sbidian E, Gallini A, Aractingi S, Aubin F, et al. Oral cyclosporin in psoriasis: A systematic review on treatment modalities, risk of kidney toxicity and evidence for use in non-plaque psoriasis. J Eur Acad Dermatol Venereol 2011;25:19–27.
4. Lebwohl M, Ellis C, Gottlieb A, Koo J, Krueger G, Linden K, et al. Cyclosporine consensus conference: With emphasis on the treatment of psoriasis. J Am Acad Dermatol 1998;39:464–75.
5. Ronzi G, Moggio E, Grasso V, Roveda G, Carugno A, Alborghetti A, et al. Ciclosporina-A e week-end therapy nella psoriasi a placche: La nostra esperienza. Bollettino della Società Medico Chirurgica di Pavia 2011;124:217–25.
6. Garrido Colmenero C, Blasco Morente G, Tercedor Sánchez J. Oral cyclosporine weekend therapy: A new maintenance therapeutic option in patients with severe atopic dermatitis. Pediatr Dermatol 2015;32:551–2.
7. Golbari NM, Porter ML, Kimball AB. Current guidelines for psoriasis treatment: A work in progress. Cutis 2018;101:10–2.
8. Nast A, Boehncke WH, Mrowietz U, Ockenfels HM, Philipp S, Reich K, et al. S3–Guidelines on the treatment of psoriasis vulgaris. J Dtsch Dermatol Ges 2012;10:s1–s95.
9. Mrowietz U. Implementing treatment goals for successful long-term management of psoriasis. J Eur Acad Dermatol Venereol 2012;26: 12–20.
10. Fernandes IC, Torres T, Selores M. Maintenance treatment of psoriasis with cyclosporine A: comparison between continuous and weekend therapy. J Am Acad Dermatol 2013;68:341–2.

11. Colombo D, Cassano N, Altomare G, Giannetti A, Vena G. Psoriasis relapse evaluation with week-end cyclosporine A treatment: Results of a randomized, double-blind, multicenter study. Int J Immunopathol Pharmacol 2010;23:1143–52.
12. Colombo D, Flori L, Altomare G, Aste N, Sgarbi S. Clinical outcome evaluation following cyclosporine a treatment in moderate to severe psoriasis: a retrospective study. International Journal of Immunopathology and Pharmacology. 2010;23:363–7.

Characteristics	**Group I**	**Group II**	**p-value**
Mean age (years)	33.9±9.5	34.8±10.0	0.74
Gender			
Males	24	24	1.00
Females	20	20	
Disease duration (months)	50.6±12.2	54.6±11.6	0.25
Mean weight (kg)	66.7±7.4	68.5±5.2	0.34
BSA (baseline)	1.84±0.91	1.68±0.96	0.56
Mean Exacerbation (n) in last 1 year before induction phase	3.39±0.57	3.34±0.47	0.91
Maintenance phase duration (months)	11.62±3.11	11.62±3.11	1

Table 1: Baseline clinical and demographic data of two groups of study subjects at baseline before maintenance phase

Outcome parameters	**Group I**	**Group II**	**p-value**
Subjects with exacerbation during maintenance n (%)	8 (18.2)	42 (95.5)	**0.00**
Number of exacerbations during maintenance n (%)			
0	36 (81.8)	2 (4.5)	**<0.001**
1	6 (13.6)	4 (9.1)	
2	2 (4.5)	10 (22.7)	
3	0	14 (31.8)	
4	0	8 (18.2)	
5	0	4 (9.1)	
6	0	2 (4.5)	
Mean BSA at end of MP	1.96±1.50	4.05±2.08	**0.00**
Mean PASI at end of MP	2.91±2.12	5.39±2.38	**0.00**
Mean total exacerbation during MP	0.21±0.51	2.93±1.41	**0.00**
Adverse effects	4 (9.1)	0	0.47

Table 2: Outcomes in two groups of study subjects at the end of maintenance phase