Original Article

Efficacy of Oral Apremilast in The Treatment of Alopecia Areata, at The Tertiary Care Hospital, Karachi

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ABSTRACT

Background: Alopecia Areata (AA) presents a significant challenge in dermatology due to its unpredictable nature and psychological impact. Recent studies have focused on oral Apremilast, a phosphodiesterase 4 inhibitor, for its potential efficacy in treating AA.

Objective: This study aims to assess the efficacy of oral Apremilast in treating alopecia areata at a tertiary care hospital in Karachi.

Methods: A randomized controlled trial was conducted in the Department of Dermatology at Jinnah Postgraduate Medical Centre, Karachi, from August 2022 to June 2023. The study enrolled 85 patients exhibiting various symptoms of AA. Apremilast was administered orally at 30 mg twice daily, following a 5-day initial titration dose. The Severity of Alopecia Tool (SALT score) was employed to measure treatment effectiveness at the outset, 6 weeks, and 12 weeks. Data analysis was executed using SPSS version 23.

Results: Participants had an average age of 28.34 years (SD = 4.20), with a gender distribution of 51 women (60.0%) and 34 men (40.0%). The study demonstrated a significant decrease in SALT Scores from 62.42 ± 5.17 to 41.53 ± 13.44 at Week 12 (mean difference: 20.89, 95% CI: 17.86 to 23.92, p-value: 0.0001), indicating a notable reduction in AA severity. Oral apremilast was found to be effective in treating AA in 80.0% of patients.

Conclusion: The study concludes that oral Apremilast significantly reduces the severity of alopecia areata, as evidenced by the decline in SALT Scores from baseline to Week 12. These findings suggest that oral Apremilast may serve as a viable alternative treatment for AA, deserving further clinical exploration.

Keywords: Alopecia Areata, Apremilast, Efficacy, Randomized Controlled Trial, SALT Score

INTRODUCTION

Alopecia Areata (AA), characterized by abnormal hair growth cycles and immune cells infiltration around hair follicles[1], is a condition where patients typically experience the sudden onset of one or more distinct, circular or ring-shaped bald patches, ranging from 1 to 4 cm on the scalp. This condition is marked by the presence of "exclamation-mark" hairs- broken, short hairs that taper near the scalp[2-3] and may also manifest as nail pitting in some cases[4]. AA can affect any hair-bearing area, most commonly the scalp, eyebrows, eyelashes, and beard, exhibiting patchy or diffuse patterns of hair loss[5]. In extreme cases, it leads to total scalp hair loss (alopecia totalis) or complete body hair loss (alopecia universalis)[6]. Predominantly an immune-mediated disease, its exact pathogenesis remains elusive[7]. While hair regrowth is possible, the prognosis of AA is unpredictable, with about eighty percent of patients experiencing spontaneous recovery[8].

For mild cases, counseling on disease characteristics and adopting a "wait and see" approach is often advised[9]. Factors such as early onset, extensive and prolonged disease, and concurrent autoimmune disorders like atopy, autoimmune thyroid disease, and vitiligo portend a poorer prognosis[10]. The impact of AA on physical appearance can lead to significant psychological distress, manifesting as social phobia, anxiety, and depression[10]. Treatment modalities vary, including steroids (intra-lesionally, topically, or systemically), topical retinoids, systemic immune-modulating drugs, photo-chemotherapy, contact immunotherapy, anthralin, calcineurin inhibitors, minoxidil, dermatographia wigs, and hypnotherapy[11-12].

Recently, Apremilast, an oral phosphodiesterase 4 (PDE4) inhibitor, emerged as a promising treatment for various inflammatory skin conditions, including AA and psoriasis. By inhibiting interferon-gamma, a cytokine implicated in AA, Apremilast offers a novel

approach to managing this condition(12). The current study delves into the efficacy of oral Apremilast in AA treatment. Utilizing the Severity of Alopecia Tool (SALT) Score to standardize assessment, the study aims to ascertain whether Apremilast can effectively manage AA. This research contributes to developing evidence-based treatments for AA, potentially offering a new avenue for improving the lives of those afflicted by this challenging condition.

MATERIAL AND METHODS

In the study undertaken by the Department of Dermatology at Jinnah Postgraduate Medical Centre, Karachi, from August 2022 to June 2023, a methodical approach was employed to evaluate the efficacy of oral Apremilast in treating Alopecia Areata. The research team implemented a non-probability consecutive sampling strategy, incorporating 85 patients determined through the W.H.O sample size calculator, based on an expected efficacy of 26.7%(21) and a 95% confidence level.

The patient cohort ranged from 20 to 50 years, encompassing diverse genders, all presenting with symptoms of alopecia areata. Exclusion criteria were meticulously set to ensure the validity of the results. Patients with prior diagnoses of connective tissue disorder, vasculitis, seropositive and seronegative arthritis, psoriasis, history of systemic agent treatments, secondary skin infections, severe hematological abnormalities, dermatological conditions affecting alopecia assessment, contraindications to oral Apremilast, and those who were pregnant or lactating were systematically excluded from the study.

The primary tool for assessing hair growth was the Severity of Alopecia Tool (SALT) score. This involved a detailed calculation of hair loss percentages in four key regions of the scalp: vertex (40%), right profile (18%), left profile (18%), and posterior (24%). The percentages were aggregated to form a composite SALT score. Assessments were conducted at the outset of the study, and subsequently at 6 and 12 weeks, with the scoring system ranging from 0 (re-growth ≤10%) to 4 (re-growth >75%).

To quantify the treatment's effectiveness, pre- and post-study images of patients were analyzed, and SALT scores were meticulously calculated. Success was defined as achieving over 75% hair growth after 12 weeks of treatment compared to the baseline. Clinical comparisons were systematically conducted at each visit, starting from the Baseline and followed by evaluations at 6 and 12 weeks. For the statistical analysis, the data was entered and processed using SPSS version 23. Descriptive statistics were used to calculate the mean and standard deviation for age and SALT score, while frequency and percentages were determined for gender and efficacy. Furthermore, a univariate analysis was carried out at a 5% significance level, ensuring a comprehensive and statistically robust evaluation of the treatment's efficacy. This methodological rigor was aimed at generating reliable, evidence-based insights into the effectiveness of oral Apremilast in treating Alopecia Areata.

RESULTS

In this comprehensive study conducted at Jinnah Postgraduate Medical Centre, the average age of participants was 28.34 years, with a standard deviation of 4.20, and the age range fell within a 95% confidence interval between 27.34 and 29.25 years. At the commencement of the study, the severity of alopecia areata, as gauged by the SALT score, was notably high, averaging at 62.42 with a standard deviation of 5.17. This initial severity was confined within a 95% confidence interval of 61.31 to 63.54.

As the study progressed to the 6-week mark, a discernible decrease in the SALT score was observed, lowering to an average of 58.60. This change, accompanied by a standard deviation of 5.91 and a confidence interval ranging from 57.33 to 59.87, marked a significant initial response to the oral Apremilast treatment. The downward trend in the SALT score was more pronounced at the 12-week checkpoint, where it fell to an average of 41.53, with a broader standard deviation of 13.44 and a confidence interval spanning from 38.63 to 44.43.

The study's demographic composition included 34 men and 51 women, representing 40.0% and 60.0% of the participants, respectively. This gender distribution was crucial in understanding the differential responses to the treatment. Remarkably, 80.0% of the participants exhibited successful treatment of alopecia areata with oral Apremilast, underscoring the potential healing benefits of this medication in this specific patient group.

Further analysis revealed a significant reduction in SALT Scores over the course of the study. The average score dropped from 62.42 to 58.60 by the 6-week interval, with a mean difference of 3.82, and continued to decrease to 41.53 by week 12, with a mean difference of 20.89. These results were statistically significant, with p-values of 0.0001 at both intervals, indicating a substantial and enduring improvement in the severity of alopecia areata.

An intriguing aspect of the study was the correlation between age, gender, and treatment effectiveness. Older participants showed a more pronounced response to treatment, with an average age of 29.28 years among those who responded effectively, compared to 24.59 years in those who did not. This suggests a potential link between age and positive therapeutic outcomes. Gender differences were also evident, with a higher percentage of females (56.5%) showing efficacy compared to males (23.5%). Conversely, a smaller proportion of females (3.5%) exhibited no efficacy, in contrast to males (16.5%). These observations, supported by a p-value of 0.0001, highlight the significance of age and gender in the effectiveness of oral Apremilast treatment for alopecia areata.

Table I: Demographic Characteristics of Study Participants (n=85)

Variables	Mean±SD	95% C. I
Age in years	28.34 ± 4.20	27.34----29.25
Baseline SALT score	62.42 ± 5.17	61.31----63.54
06 weeks SALT score	58.60 ± 5.91	57.33----59.87
12 weeks SALT score	41.53 ± 13.44	38.63----44.43
Gender (%)		
Male	34 (40.0)	
Female	51 (60.0)	

Table II: Comparison of SALT Score Changes Over Time (n=85)				
Salt Scores	Baseline	Weeks	95% C. I	P-value
Baseline to Week-6	62.42 ± 5.17	58.60 ± 5.91	2.91----4.73	0.0001
Baseline to Week-12	62.42 ± 5.17	41.53 ±13.44	17.86----23.92	0.0001
Week-6 to Week-12	58.60 ± 5.91	41.53 ± 13.44	14.39----19.74	0.0001

Table III: Association of Age and Gender with Efficacy (n=85)					
Variables		Yes (n=68)	No (n=17)	95% C. I	P-Value
Age in years, Mean ± SD		29.28 ± 3.83	24.59 ± 3.53	2.65----6.73	0.0001
Gender	Male, *n* (%)	20 (23.5)	14 (16.5)	0.023----0.345	0.0001
	Female, *n* (%)	48 (56.5)	3 (3.5)		

DISCUSSION

This study provided an in-depth evaluation of oral Apremilast's role in treating Alopecia Areata (AA), a condition marked by hair loss and limited treatment options. The primary focus was to assess the impact of Apremilast on AA severity using the Severity of Alopecia Tool (SALT) score. The findings demonstrated significant improvement in SALT scores at baseline, 6 weeks, and 12 weeks, indicating a decrease in AA severity with oral Apremilast treatment over a 12-week period. The statistical significance of these results was affirmed by a p-value of less than 0.0001, suggesting a reliable therapeutic benefit. This reduction in SALT scores from an initial average of 62.42 ± 5.17 to 58.60 ± 5.91 at 6 weeks and further to 41.53 ± 13.44 at 12 weeks underscores the long-term efficacy of Apremilast in AA management.

The study's strength lies in its detailed observation of Apremilast's effects on patients with moderate to severe AA, particularly those unresponsive to prior treatments. The observed hair regrowth and patient satisfaction highlight Apremilast's potential as an alternative therapy. Parallel studies corroborate these findings, with Apremilast showing reduced disease activity and improved mental health outcomes for AA patients(13-14). Comparative analyses involving Apremilast, minoxidil, and corticosteroids revealed

a higher response rate despite increased side effects(15). However, concerns remain regarding the long-term safety and efficacy of Apremilast, especially given the incidences of tolerable but persistent side effects such as diarrhea, nausea, and upper respiratory tract infections(16).

The study also revealed that Apremilast could be an effective option for patients showing poor response to corticosteroids, suggesting its viability as a safer and more effective alternative for those unable to benefit from traditional treatments(17). While certain studies reported improvements in hair regrowth and mental health, highlighting the psychological impact of AA, the long-term safety profile of Apremilast necessitates further investigation(17-19). Continuous monitoring of patients is crucial due to the mild but recurrent side effects observed over prolonged treatment periods, although these are balanced by the positive outcomes associated with this medication(20-23).

Age and gender emerged as influential factors in treatment efficacy, underscoring the importance of considering these variables in clinical practice. The study's limitations stem from its single-arm trial design, which poses challenges in definitively attributing improvements to the treatment rather than other factors, due to the lack of a comparative therapy. A more extended follow-up period and a more comprehensive study design could enhance the understanding of Apremilast's impact.

Extending the duration of follow-up is essential for evaluating treatment outcomes more thoroughly, detecting potential relapses, and assessing long-term benefits and risks. This study adds to the growing body of evidence supporting oral Apremilast as a viable treatment for AA. However, to fully establish its effectiveness in treating AA, further extensive, randomized controlled trials with extended durations are needed. Such studies will be crucial in reinforcing the findings and addressing the current gaps in understanding the long-term effects of Apremilast in AA treatment.

CONCLUSION

In conclusion, the findings of this study suggested that oral Apremilast is an effective treatment for Alopecia Areata. The observed decrease in SALT Scores from the initial measurement to Week 12 signifies a noteworthy improvement in the severity of the condition. This evidence positions oral Apremilast as a compelling therapeutic option for Alopecia Areata, meriting further clinical research to confirm its efficacy and explore its potential as a standard treatment in this domain.

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