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Original Article

Comparison of Efficacy of 5% Tranexamic Acid vs 20% Azelaic Acid in Patients of Melasma

Fasiha Mushtaq[1]*, Riaz Khan Marwat[2], Maria Saleem[2], Anum Khan[3], Sara Khan[1], Huma Imran[1]

[1]PG Dermatology, Pakistan Institute of Medical Sciences (PIMS) Islamabad Pakistan.

[2]Professor Dermatology, Pakistan Institute of Medical Sciences (PIMS) Islamabad Pakistan.

[3]Senior Registrar Dermatology, Pakistan Institute of Medical Sciences (PIMS) Islamabad Pakistan.

Corresponding Author: Fasiha Mushtaq, PG Dermatology; Email: Fasiha_awan@yahoo.com

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ABSTRACT

Background: Melasma is a significant cosmetic concern globally, affecting individuals across various ethnic backgrounds, particularly in South Asian populations. The condition's etiology is complex, involving genetic, hormonal, and environmental factors such as sun exposure. Despite numerous treatment options, melasma remains challenging to manage effectively. Recent studies have explored the efficacy of tranexamic acid and azelaic acid, both of which target the melanin synthesis pathway but through different mechanisms.

Objective: The aim of this study was to compare the effectiveness of topical 5% tranexamic acid versus 20% azelaic acid in the treatment of melasma, with a focus on changes in the Melasma Area and Severity Index (MASI) scores.

Methods: This prospective comparative study was conducted at the Dermatology department of PIMS Hospital, Pakistan, over six months from August 2023 to January 2024. A total of 200 patients with melasma were enrolled and randomly assigned to two groups: Group A received 5% tranexamic acid cream, and Group B received 20% azelaic acid cream, both applied twice daily. Inclusion criteria included men and women aged 18 to 50 years with a diagnosis of melasma for at least six months. Pregnant women, patients with a history of Systemic Lupus Erythematosus (SLE) or Discoid Lupus Erythematosus (DLE), and those on hormonal therapy were excluded. The primary outcome measure was the change in MASI scores from baseline to the end of the study period. Data were analyzed using SPSS Version 25.

Results: The study found significant differences in treatment efficacy between the two groups. Group A (tranexamic acid) showed a reduction in MASI scores from 7.94 ± 1.88 at baseline to 5.50 ± 1.61 post-treatment. Group B (azelaic acid) demonstrated a decrease from 8.21 ± 1.96 to 5.89 ± 1.49. The proportion of patients experiencing excellent response was higher in Group A (36.0%) compared to Group B (19.0%), with a statistically significant difference in overall treatment efficacy ($P<0.0001$).

Conclusion: Topical 5% tranexamic acid was more effective than 20% azelaic acid in improving MASI scores in patients with melasma. This study supports the inclusion of tranexamic acid as a preferable treatment option for melasma, offering a promising alternative for those not responding to conventional therapies.

Keywords: Melasma, Tranexamic Acid, Azelaic Acid, Treatment Efficacy, MASI Score, Dermatology.

INTRODUCTION

Melasma is a prevalent dermatological condition distinguished by brown or gray-brown patches on the face, more frequently affecting women, especially those with darker skin types (1). This chronic and acquired condition is not congenital but develops over time and is notably more common during pregnancy (2,3). The incidence of melasma during pregnancy varies across different populations, with a study in Pakistan reporting a prevalence of 46% among pregnant women (4). The condition is closely associated with hormonal changes, and pregnancy-related hormonal fluctuations are known to trigger or exacerbate melasma in some women (5). The exact cause of melasma remains poorly understood, attributed to a combination of genetic, hormonal, and environmental factors (6). This complexity makes melasma sometimes resistant to treatment, with certain cases only partially responding to various therapeutic interventions (7).

Journal of Health and Rehabilitation Research 2791-156X JHRR

The treatment landscape for melasma includes a range of options, with tranexamic acid (TXA) and azelaic acid being notable for their potential efficacy. TXA, originally an antifibrinolytic agent, has been found to offer benefits in treating melasma by inhibiting melanocyte activation and reducing melanin production. Studies have documented positive outcomes with TXA, noting reductions in pigmentation and improvements in the appearance of melasma lesions (13,14). Azelaic acid, another key agent in melasma management, is valued for its ability to target melanin synthesis effectively. The objective of this study is to compare the efficacy of topical 5% tranexamic acid versus 20% azelaic acid in patients with melasma, aiming to provide valuable insights into the comparative effectiveness of these treatments (15,16). This comparison is crucial for advancing the understanding of treatment options for melasma, guiding clinicians in optimizing therapeutic strategies for this challenging and multifaceted skin condition.

MATERIAL AND METHODS

This prospective comparative study was conducted in the Dermatology department of PIMS Hospital, Pakistan, over a period of six months from August 2023 to January 2024. The research aimed to evaluate the efficacy of 5% tranexamic acid versus 20% azelaic acid in patients with melasma. Utilizing the WHO calculator for sample size determination, a total of 200 individuals were selected, divided equally into two groups to ensure statistical significance at a 5% level with a power of 80%. The test value of the population mean was set at 26.60, with an anticipated population mean of 4.94 and a population standard deviation of 7.55.

The study welcomed both married and unmarried men and women aged between 18 and 50 years who had been suffering from melasma for at least six months. However, pregnant women, patients with a history of Systemic Lupus Erythematosus (SLE) or Discoid Lupus Erythematosus (DLE), and those undergoing oral contraceptive pills (OCPs) or hormonal therapy were excluded to maintain the integrity of the results and minimize external variable impacts.

Following the approval of the hospital's ethical committee, in line with the Declaration of Helsinki for ethical principles for medical research involving human subjects, the study commenced. Patients visiting the Dermatology Outpatient Department (OPD) at PIMS Hospital were screened for eligibility and enrolled upon meeting the inclusion criteria. Informed consent was obtained from all participants, thoroughly explained in their native language to ensure comprehension.

Participants were then allocated into two distinct groups; Group A received a 20% azelaic acid treatment applied twice daily, while Group B was treated with 5% tranexamic acid cream, also applied twice daily. All participants were advised to use sunscreen during daylight hours to protect against UV radiation, a known exacerbating factor for melasma. Follow-up visits were scheduled on a monthly basis, during which the Melasma Area and Severity Index (MASI) scores were recorded to assess the progression or regression of the condition. Data collected throughout the study were analyzed using the Statistical Package for the Social Sciences (SPSS) Version 25.

RESULTS

The study delineated the baseline characteristics and treatment outcomes of two groups of participants, each comprising 100 individuals, who were subjected to different treatments for melasma. The revised graph effectively displays the distribution of participants by marital status and gender across two groups in the study. Group A consists of 70 married and 30 unmarried participants, with a gender ratio of 20 males to 80 females. In contrast, Group B includes 58 married and 42 unmarried participants, with 15 males and 85 females. This visualization clearly differentiates between the groups for both marital status and gender, highlighting a higher proportion of females in both groups, which reflects the gender predisposition of melasma. The use of side-by-side bars allows for an easy comparison between Group A and Group B, emphasizing the differences and similarities in their demographic composition.

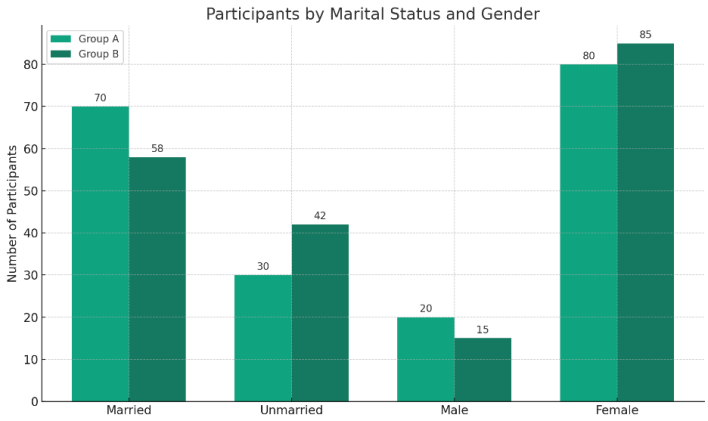

Figure 1 Gender and Marital Status

According to Table 1, the average age of participants in Group A was 32.26 years with a standard deviation of 8.21, while Group B had a slightly higher average age of 33.74 years with a standard deviation of 7.69. The duration of illness prior to the commencement of the study averaged 2.51 years in Group A and 2.88 years in Group B, indicating a somewhat longer period of melasma affliction in the latter group. Interestingly, both groups reported an identical average duration of sun exposure at 3.89 days, albeit with a marginal difference in standard deviation.

Journal of Health and Rehabilitation Research JHRR

The Melasma Area and Severity Index (MASI), utilized to assess the severity of melasma, demonstrated notable pre-treatment and post-treatment scores. Initially, Group A participants had an average MASI score of 7.94, which decreased to 5.50 following treatment. Similarly, Group B participants began with an average MASI score of 8.21, which was reduced to 5.89 after treatment. These outcomes underscore the efficacy of both treatments in mitigating the severity of melasma, albeit with a slightly more pronounced effect observed in Group A.

Table 1 Baseline Characteristics and Treatment Outcomes

Variables	Group A (n=100)	Group B (n=100)
Age (Years)	32.26 ± 8.21	33.74 ± 7.69
Duration of Illness (Years)	2.51 ± 0.94	2.88 ± 1.00
Duration of Sun Exposure (Days)	3.89 ± 1.2	3.89 ± 1.14
MASI Score (Pre-treatment)	7.94 ± 1.88	8.21 ± 1.96
MASI Score (Post-treatment)	5.50 ± 1.61	5.89 ± 1.49

Table 2 Stratification of Both Groups Based on Efficacy and Gender

Variables	Group A	Group B	P-Value
Efficacy			
Poor Response	20 (20.0%)	61 (61.0%)	0.000
Good Response	44 (44.0%)	20 (20.0%)	
Excellent Response	36 (36.0%)	19 (19.0%)	
Gender			
Male	20 (20.0%)	15 (15.0%)	0.35
Female	80 (80.0%)	85 (85.0%)	

Stratification based on efficacy and gender, as depicted in Table 2, further elucidates the response to treatment within each group. A significant disparity in treatment efficacy was observed, with 20% of Group A participants experiencing a poor response compared to 61% in Group B, a difference that was statistically significant (P-value=0.000). Conversely, Group A demonstrated a higher proportion of good and excellent responses at 44% and 36%, respectively, compared to Group B's 20% (good response) and 19% (excellent response). This disparity highlights the superior effectiveness of the treatment administered to Group A in managing melasma.

The gender distribution within the study cohorts revealed that both groups predominantly comprised female participants, with Group A having 80% and Group B 85% female participants. The male participants constituted 20% of Group A and 15% of Group B, with a P-value of 0.35, indicating no significant difference in gender distribution between the two groups.

DISCUSSION

Melasma, a widespread cosmetic concern, affects individuals across various ethnicities, with a notable prevalence in South Asian countries, including Pakistan. This condition's etiology is multifaceted, encompassing genetic predispositions, hormonal fluctuations, and sun exposure, which collectively contribute to its complex pathogenesis (17,18). Addressing this dermatological challenge necessitates a multifaceted treatment approach, given its resistance to singular treatment modalities. The study under discussion embarked on a comparative analysis of the efficacy of 5% tranexamic acid versus 20% azelaic acid in the treatment of melasma, inspired by the emerging interest in tranexamic acid as a novel therapeutic agent in this domain.

The findings from this study highlighted a divergent response to treatment between the two groups: Group A, treated with tranexamic acid, demonstrated a significantly lower rate of poor response (20.0%) and higher rates of good (44.0%) and excellent responses (36.0%), in stark contrast to Group B, treated with azelaic acid, which exhibited a higher poor response rate (61.0%) and lower rates of good (20.0%) and excellent responses (19.0%). The statistical significance of these differences, underscored by a P-value of 0.00, clearly favored tranexamic acid over azelaic acid in treating melasma. These observations align with previous studies, such as those by Sayyida Komal et al. (19) and Fahmida Malik (20), which also reported superior outcomes with tranexamic acid, both in monotherapy and in combination with other treatments, compared to azelaic acid.

Journal of Health and Rehabilitation Research 2791-156X JHRR

Moreover, Nasrin Saki's controlled trial (21) lends further support, illustrating the rapid onset of action of intradermal tranexamic acid compared to 2% hydroquinone, albeit with comparable long-term efficacy. This body of evidence collectively situates tranexamic acid, particularly its intradermal administration, as a more effective alternative to azelaic acid in the management of melasma (22). The study's demographic findings reveal a predominance of married female participants, underscoring the influence of hormonal factors, such as those associated with pregnancy and contraceptive use, on melasma development. The role of UV radiation in exacerbating this condition further highlights the multifactorial nature of melasma and the importance of comprehensive treatment strategies that address these underlying factors. Both azelaic and tranexamic acid have mechanisms of action that target key aspects of melasma's pathogenesis, with the former inhibiting tyrosinase activity and the latter reducing melanin production through its antifibrinolytic properties (15,22).

Reflecting on the study's strengths, the comparative design and the significant sample size contribute to the robustness of the findings. However, the study is not without limitations. The exclusion of pregnant women and individuals on hormonal therapy, while reducing potential confounders, may limit the generalizability of the findings to all individuals with melasma. Furthermore, the reliance on topical applications of the treatments does not fully explore the potential of systemic administration routes, which could offer alternative therapeutic benefits.

CONCLUSION

In conclusion, the study corroborates the efficacy of 5% tranexamic acid as a superior treatment for melasma compared to 20% azelaic acid, as evidenced by the improvement in MASI scores. These findings, supported by existing literature, advocate for the integration of tranexamic acid into the therapeutic arsenal against melasma. Future research should aim to explore the long-term efficacy and safety profiles of tranexamic acid, potentially in combination with other treatments, to optimize melasma management strategies. Additionally, investigating the efficacy of tranexamic acid across diverse demographic groups would enhance the understanding of its role in treating this challenging condition.

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Journal of Health and Rehabilitation Research 2791-156X JHRR

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