

# Comparison of Efficacy of Oral Tranexamic Acid Versus Glycolic Acid Peels in the Treatment of Melasma

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## ABSTRACT

**Objective:** To compare the efficacy of oral tranexamic acid versus glycolic acid peels in the treatment of epidermal and mixed-pattern melasma.

**Methodology:** A total of 88 patients, aged 20 to 50 years, diagnosed with epidermal or mixed-pattern melasma, were assigned to two treatment groups based on their treatment choice or eligibility criteria. Group A received oral tranexamic acid (250 mg twice daily), and Group B underwent 50% glycolic acid peels every two weeks for 12 weeks. MASI scores were recorded at baseline and at 12 weeks to assess the extent of improvement, and side effects were monitored.

**Results:** The baseline MASI score for all patients was 14.74 (SD = 3.09). At 12 weeks, the mean MASI score significantly decreased to 2.45 (SD = 1.70). Both groups showed substantial improvements in MASI scores. Group A had a mean MASI score of 15.5 at baseline, which reduced to 3.2, while Group B showed a mean reduction from 14.9 to 4.8. Statistical analysis revealed no significant difference in efficacy between the two treatments (p-value = 0.05).

**Conclusion:** Both oral tranexamic acid and glycolic acid peels are effective in treating melasma, with comparable results. Future studies with larger sample sizes and longer follow-up are recommended to assess long-term outcomes and potential combination therapies.

**Keywords:** Glycolic acid peels; MASI score; Melasma; Oral tranexamic acid; Treatment efficacy

### Authors' Contribution:

<sup>1,2</sup>Conception; Literature research; manuscript design and drafting; <sup>1,2</sup>Critical analysis and manuscript review; <sup>1,2</sup>Data analysis; Manuscript Editing.

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## Introduction

Melasma is a frequent, persistent, hyperpigmentary disease, which occurs mostly in women, particularly women of reproductive age. It is distinguished by the existence of brownish symmetrical spots which mostly occur in sun-exposed regions of the face such as the cheeks, forehead, upper lips and the chin.<sup>1</sup> This not only presents a cosmetic problem but also a major psychological problem to a patient. Although several treatment choices are available, melasma is not easily treatable since it is recurrent with the side

effects of traditional treatment being quite possible. Conventional therapeutic interventions, e.g., hydroquinone, retinoid, etc. have their advantages but do not produce long-term effects or have side effects, e.g., skin irritation.<sup>2,3</sup> In addition to this, non-topical therapies, such as chemical peels and laser therapies are effective but have risks of complications such as post-inflammatory hyperpigmentation (PIH).<sup>4,5</sup> Consequently, new more effective and safe methods of treatment are being sought.

The oral Tranexamic Acid (TXA) has been discovered to be a new therapeutic intervention in treating melasma in the recent years especially because of its antifibrinolytic activity that affects the melanogenesis cycle. This drug suppresses plasminogen/plasmin and lowers the activity of melanocytes and production of melanin. Oral TXA has proven to be successful particularly in those cases that are not susceptible to the standard treatments and with less side effects when compared to the other systemic treatments.<sup>67</sup> On the other hand, glycolic acid peels have been used as an exfoliating agent to decrease hyperpigmentation by shedding the upper dermis of the skin thereby enhancing the re-growth of new skin which is clearer.<sup>8</sup> Glycolic acid peels may be good agents in pigmentation reduction, but they may need consistent applications to actually make significant changes and may not be absolutely safe, including skin irritation.<sup>9</sup>

Oral TXA dental complicity with glycolic acid peels can possibly have a synergistic effect, which can yield more extensive outcomes in melasma therapy. Nevertheless there is no direct comparison of these two-treatment modalities, namely, their effectiveness in the treatment of various patterns of melasma, i.e. epidermal and mixed patterns.<sup>10</sup> Although there is research indicating that the two treatments are useful in the reduction of melasma, more research is required on which modality is more helpful to patients with certain types of melasma.<sup>511</sup> Melasma is determined by several factors that are genetically, hormonally and environmentally dependent such as long-term exposure to sun. The disorder is mostly seen in women of dark skin types and mostly Fitzpatrick skin types III to V.<sup>12</sup> Melasma can be classified into three types depending on the depth of pigmentation, epidermal, dermal, and mixed-pattern melasma. Epidermal melasma is also superficial pigmentation in nature that is generally susceptible to treatment with topical agents such as glycolic acid peels. Conversely, dermal melasma has deeper pigmentation, and this could need deeper

treatments; that is, the use of lasers or the use of systemic agents like oral TXA.<sup>9</sup>

Oral TXA has been found to be promising in the management of epidermal and mixed-pattern melasma. It has been discovered that TXA does not only lessen pigmentation but also lessens the relapses of melasma.<sup>13</sup> This is unlike glycolic acid peels which in many cases are not effective in deeper pigmentations such as those observed in dermal or mixed-pattern melasma but are very useful in epidermal melasma.<sup>4</sup> What still is lacking though is an in-depth research that compares the two treatments directly on certain patterns of melasma, particularly the use of both therapies together.

This research aims at comparing the effectiveness of oral TXA and glycolic acid peels in treating epidermal and mixed-pattern melasma with emphasis on their impact on MASI scores, skin side effects and patient adherence.

## Methodology

It was an Interventional Study, which was carried out in the tertiary care hospital, Peshawar, between January 25, 2019, and July 25, 2019. The duration of the study was six months.

The online sample size calculator was used to compute the sample size using the Kelsey method. The sample size was be 88 (44 patients in each of the two groups). This was computed using a two sided significance of 95, power of 80 and odds ratio of 9.5. The ratio of exposing to non-exposing was 1:1 where 33 percent exposed patients were supposed to have desired outcome and 5 percent unexposed patients were supposed to have desired outcome.<sup>14</sup>

The sample included adults between 20-50 years and were diagnosed with epidermal or mixed-pattern melasma. Informed consent taken from patients. The exclusion criteria comprised patients that were hypersensitive to TXA or glycolic acid, those with a history of thromboembolic disorders, pregnant or lactating, other simultaneous skin

diseases or systemic conditions that influenced pigmentation, e.g., thyroid disorders.

Patients in the study were assigned to two treatment groups based on their treatment choice or eligibility criteria. Group A received oral TXA at a dosage of 250 mg twice daily. Group B received 50% glycolic acid peels twice a month. Both treatments were administered by a qualified dermatologist with at least five years of clinical experience.

After every two weeks the 12-week studies were planned as follow-up visits. Clinical assessment was done at every visit and photographs were captured to record melasma development. The severity and the extent of the melasma in every one of the patients at the baseline and in the follow-up visits were measured through the Melasma Area and Severity Index (MASI) score. These visits were also recorded in side effects and patient reported outcomes.

The main finding of the research was the decrease of MASI score which is a scale to determine the severity of melasma by pigmentation in the forehead, right malar, left malar and chin. The secondary outcome was the evaluation of the side effects (gastrointestinal discomfort, or skin irritation) during the treatment.

The statistical analysis was done using Statistical Package of social sciences (SPSS) version 25. Descriptive statistics, means, and standard deviations were used to summarise the population and clinical characteristics. The importance of differences between the two groups was determined with the help of independent samples t-tests on continuous variables and chi-square tests on categorical variables. The cut-off point was taken as p-value below 0.05.

**Ethical approval** was obtained from ethical and research committee of the Hayatabad Medical Complex, Peshawar (Ref No. 089/HEC/PICO/18) dated 08 August, 2018.

## Results

The population size of the study was 88 patients, of which Group A (n=44 patients) were given the oral of TXA and Group B (n=44 patients) was the glycolic acid peels. The demographics of patients showed the equal representation of both genders in the two groups. The age distribution was between 20-49 years with most of the patients between the age bracket of 20-40 years. All patients were measured on the baseline MASI score, which is an indicator of the severity of the melasma at the start of the research.

The 12-week MASI and baseline scores were analysed in all patients (table:1). The average baseline MASI was 14.74 (standard deviation = 3.09) thus showing a moderate to severe level of melasma in all the patients. By the time (12 weeks), the mean MASI score had significantly reduced to 2.45 (standard deviation = 1.70), which showed a significant improvement in the two treatment study groups.

Measure	MASI Score at Baseline	MASI Score at 12 Weeks
Count	88	88
Mean	14.74	2.45
Standard Deviation	3.09	1.70
Minimum	10.00	0.00
25th Percentile	12.00	1.00
Median	15.00	3.00
75th Percentile	17.00	4.00
Maximum	20.00	5.00

Both the treatment groups had significant improvement in MASI scores, with the oral TXA group having slightly more reduction.

Comparing scores of the two groups there was no statistically significant difference in the efficacy of the two treatment modalities after 12 weeks of follow-up.

Treatment Group	Mean MASI Score at Baseline	Mean MASI Score at 12 Weeks	p-value
Oral Tranexamic Acid	15.5	3.2	0.148
Glycolic Acid Peels	14.9	4.8	

This indicates that although the two treatments were effective in terms of reducing the severity of melasma, the level of efficacy was not statistically significant.

Additional analysis was done to determine whether there was any age factor that affected the effectiveness of the treatments. Figure 1 indicates the correlation between the age and the decrease in MASI scores at 12 weeks. The findings show that younger and older patients reacted the same when subjected to both methods and no significant tendency that age influenced the outcome was recorded.

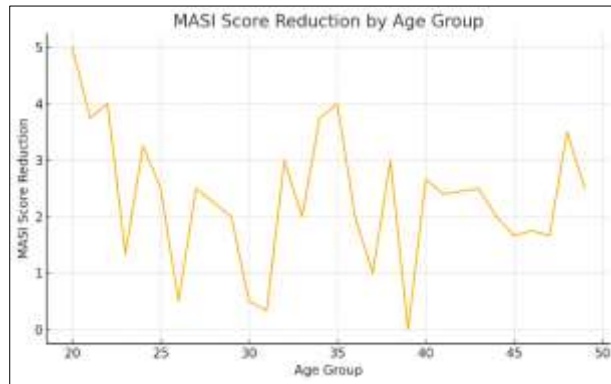


Figure 1: MASI Score Reduction by Age Group

Comparison of the MASI scores at baseline and 12 weeks with regard to the age group indicates that there is a little difference in the response to treatment. Nevertheless, there was no particular age group that was always performing better than the others. The summary of the results is presented in Table 3 below, which shows the average decrease in the MASI scores, per the treatment, in different age groups.

Age Group	Mean MASI Score at Baseline	Mean MASI Score at 12 Weeks	Average Reduction
20-29	14.85	3.12	11.73
30-39	15.00	3.00	12.00
40-49	14.70	2.45	12.25

The patients showed good tolerance towards both the treatments. Oral TXA group complained of slight stomach pain such as nausea, but these were short-term without the need to withdraw drugs. The erythema and skin irritation were also mild in the glycolic acid peel group. No serious side effects were mentioned, and no dropouts in the group of complications related to the treatment were reported.

## Discussion

The objective of the present study was to compare the effectiveness of oral TXA and glycolic acid peels in epidermal and mixed-pattern melasma treatment. The number of allocated patients was 88 who were divided into two treatment groups: Group A was given oral TXA (250 mg two times a day), and Group B was given 50% glycolic acid peels twice every 12 weeks. The two therapies yielded significant changes in the MASI and the mean score of the MASI at the baseline was 14.74 and 2.45 at 12 weeks. Although the Oral TXA had a higher reduction in MASI scores. The difference between the two treatments was not found statistically (p-value = 0.148). Both therapies were tolerated and minimal and short term side effects recorded in the two groups.

The current study provides a comparatively new approach to the technique of dealing with melasma and compares oral TXA and glycolic acid peels, in particular, in terms of epidermal and mixed-pattern issues. Though previous studies have evaluated each of the modalities individually, the present report is one of the few studies which involve carrying out a direct comparative study in a Pakistani cohort,

specifically with reference to its therapeutic effectiveness in each of the individual melasma phenotypes. This study contributes to the body of existing literature in order to compare two available therapeutic options at the same time. The novelty of the methodology is not limited to the local setting and thus, conforms to the growing global interest in alternative interventions of melasma. Although similar studies have been conducted in other countries, including the United States, Europe, and other countries in Asia, the present study stands out by comparing oral TXA and glycolic acid directly to each other in the form of peels in a Pakistani population.

The results of this study are consistent with various other works of other international researchers which have studied the therapeutic value of oral TXA and glycolic acid peels in the treatment of melasma. As an example, Agrawal et al. (2023) found that oral TXA greatly reduced the MASI scores of melasma patients, which is also similar to the strong pigimentary improvement observed at the 12-week intervention period in the current study.<sup>6</sup> In addition, Sahu et al. (2021) found that glycolic acid peels have shown a significant reduction in melasma severity which confirms the evidence found with the group in this study with glycolic acid.<sup>9</sup>

Conversely, the results of this study are opposite to the ones reported in previous studies that reported a statistically significant difference in treatment efficacy between oral TXA and glycolic acid peels. For example, Soundarya et al. (2021) stated that TXA was significantly better than glycolic acid peels in terms of the MASI score reduction and patient satisfaction.<sup>15</sup>

Various studies done in other countries other than Pakistan have tested the comparative efficacy of oral TXA and glycolic acid peels in the management of melasma. For example, a study done in India by Devi et al. revealed that oral administration of TXA resulted in better improvement in MASI score compared to topical administration.<sup>2</sup> Similarly, a study by Tiwary et al (2020) in the United States

found oral TXA to be useful for treating melasma, with similar results to more invasive procedures such as lasers.<sup>4</sup> These results are congruent with the current study, where improvements were found during intervention for both interventions though no statistically significant difference was found.

International studies have been conducted to look at the comparative efficacy of oral TXA and glycolic acid peels.

Melasma is a common dermatologic problem in Pakistan, which is mainly caused by extensive exposure to ultraviolet radiation and the extensive use of oral contraceptives in women of reproductive age. Experimental studies such as this, recent study by Khan et al. (2024), have discovered various methods of treating melasma - most particularly the hydroquinone and azelaic acid practices.<sup>5</sup> Nevertheless, further studies targeting systemic treatments such as oral TXA and their efficacy in the treatment of several types of melasma are needed. This research is of particular importance, as it supplements the literature from the region and has given evidence-based knowledge to clinicians in treating melasma in Pakistan.

A number of studies performed in the United States and Europe demonstrate the efficacy and safety of oral TXA for the reduction of hyperpigmentation.<sup>12,16</sup>

These results support our investigation that found both oral TXA and glycolic acid peels resulted in significant attenuation of severity of melasma. However, the fact that no statistically significant difference in efficacy was found between the two interventions in the present study is not consistent with findings reported in the literature, where one modality consistently was found to demonstrate better efficacy than the other.

Our results support the existing literature in terms of the safety and effectiveness of both interventions; however, the possibility of a divergent effect with long follow-up deserves further study.

Though this study has some important points, a few limitations have been identified. First, the study period was rather short (12 weeks); a long-term

follow-up would be necessary for a thorough evaluation of long-endpoints (e.g., long-term efficacy and relapses) related to the treatments under investigation. Secondly, while the sample size is enough for the first comparison, for more detailed results the power of the sample is not enough to detect minor differences in the therapeutic effectiveness of the two modalities. Future studies would do better if the study groups were larger and the study period longer. In addition, any studies related to combination agents; such as oral TXA administered concurrently with glycolic acid peels, or others such as ancillary modalities, might potentially be used to further improve therapeutic outcomes for melasma.

### Conclusion

While the oral TXA group showed a slightly greater reduction in MASI scores, the difference between the two treatments was not statistically significant, suggesting that both options are effective for managing melasma. Both treatments were well tolerated, with only mild, transient side effects observed.

The findings of this study support the conclusion that both oral TXA and glycolic acid peels are viable treatment options for melasma, with comparable efficacy. These results align with the study's objective of evaluating and comparing the effectiveness of these two therapies. Given the significant improvement observed in both groups, either treatment could be considered for patients with epidermal or mixed-pattern melasma.

For future research, it is recommended to conduct studies with larger sample sizes and longer follow-up periods to assess the long-term effects and recurrence rates of both treatments. Exploring combination therapies, such as oral TXA in conjunction with glycolic acid peels, may also be a promising direction to enhance treatment outcomes for melasma.

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