

COMPARATIVE ASSESSMENT OF INTRADERMAL TRANEXAMIC ACID AND GLYCOLIC ACID PEEL IN REDUCING mMASI SCORES AMONG MELASMA PATIENTS

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ABSTRACT

Background: Melasma is a common acquired hyperpigmentation disorder with variable therapeutic responses. Glycolic acid peels are an established adjunctive treatment for melasma, while intradermal tranexamic acid shows promising efficacy but requires further validation.

Objective: To compare the efficacy and safety of intradermal TXA injections versus 50% GA peels in patients with melasma.

Methods:

Results: The overall mean mMASI score significantly decreased from 7.90 ± 2.00 at baseline to 3.56 ± 2.01 at follow-up ($p < 0.001$). In the TXA group, mMASI reduced from 8.23 ± 1.74 to 2.33 ± 0.93 , whereas in the GA group, it decreased from 7.57 ± 2.23 to 4.80 ± 2.06 ($p < 0.001$ for both). The reduction was greater in the TXA group. Both treatments were well tolerated, with mild and transient adverse effects such as erythema, pain, and burning sensation.

Conclusion: Both intradermal TXA and GA peels are effective and safe for melasma management. Intradermal TXA demonstrated comparatively superior efficacy and higher patient satisfaction. However, larger multicentric studies with longer follow-up are required to validate these findings.

KEYWORDS: Melasma, Tranexamic acid, Glycolic acid peel, mMASI, Hyperpigmentation, Dermatology, Pigmentary disorders.

INTRODUCTION

Melasma is a chronic, relapsing pigmentary disorder characterized by irregular, symmetrical brownish macules and patches over sun-exposed areas of the face, particularly the cheeks, forehead, upper lip, and nose [1–5]. Its multifactorial pathogenesis—encompassing ultraviolet (UV) radiation, hormonal influences, genetic predisposition, vascular alterations, and inflammatory processes—contributes to its persistent and treatment-resistant nature, often necessitating multimodal therapeutic approaches [6–10].

The global prevalence of melasma varies widely (1–50%) depending on ethnicity, skin phototype, and environmental exposure [11, 12]. It predominantly affects women of reproductive age (female:male $\approx$ 9:1), especially individuals with Fitzpatrick skin types IV–VI residing in tropical regions [13–15]. In addition to cosmetic disfigurement, melasma significantly impairs quality of life and psychosocial well-being.

At the molecular level, UV radiation stimulates melanocyte activity, while hormonal factors such as estrogen, progesterone, and melanocyte-stimulating hormone enhance melanogenesis [16]. Vascular proliferation mediated by vascular endothelial growth factor (VEGF) further sustains pigmentation [17]. Additionally, oxidative stress [18], inflammation [4], and activation of the plasminogen–plasmin pathway [19, 20] disrupt melanocyte homeostasis, leading to persistent hyperpigmentation. Clinically, melasma presents in centrofacial, malar, or mandibular patterns and may be classified histologically as epidermal, dermal, or mixed [21]. Diagnostic tools such as Wood’s lamp examination aid in determining pigment depth and guiding therapeutic decisions [21–23]. Conventional management strategies focus on reducing pigmentation and preventing recurrence [24, 25]. The hydroquinone–retinoid–corticosteroid triple combination remains the gold standard [26, 27]; however, concerns regarding adverse effects have prompted the exploration of safer alternatives, including azelaic acid, kojic acid, arbutin, niacinamide, and vitamin C [26–28]. Procedural interventions such as chemical peels, lasers, and microneedling are frequently employed to enhance therapeutic outcomes [29, 30].

Among chemical peels, glycolic acid (GA), an alpha-hydroxy acid derived from sugarcane, is widely used due to its exfoliative action and ability to inhibit melanogenesis [31]. Nevertheless, its use in darker skin types is limited by the risk of irritation and post-inflammatory hyperpigmentation. In contrast, tranexamic acid (TXA), a synthetic lysine analogue, offers a targeted mechanism by inhibiting the plasminogen–plasmin pathway, thereby reducing melanocyte activation, angiogenesis, and inflammation [32, 33]. Intradermal administration of TXA enhances localized drug delivery while minimizing systemic exposure.

Previous studies utilizing the Modified Melasma Area and Severity Index (mMASI) have demonstrated significant pigment reduction with both GA peels and TXA-based therapies [34]. While several studies have highlighted the tolerability of GA peels [35] and the efficacy of TXA in various formulations [36], as well as potential synergistic effects with adjunctive therapies [37, 38], direct comparative evidence evaluating both modalities in real-world clinical settings remains limited, particularly in Indian populations with minimal prior treatment exposure.

In this context, the present study aims to comparatively evaluate the efficacy and safety of intradermal TXA and 50% GA peels in patients with melasma. In addition to clinical outcomes, the study incorporates patient satisfaction and treatment tolerability to provide a more comprehensive assessment of therapeutic effectiveness. Such an approach may contribute to the development of individualized and evidence-based management strategies for melasma.

METHODOLOGY

Study Setting and Duration

The study was conducted in the Outpatient Department of Dermatology, Venereology, and Leprosy. The department's standardized clinical infrastructure ensured uniform procedures and consistent patient monitoring throughout the study period. The study was carried out over 14 months (December 2023–February 2025), encompassing patient recruitment, intervention, follow-up, and data analysis.

Study Design

This was a prospective, randomized, interventional comparative clinical study designed to evaluate the efficacy and safety of intradermal tranexamic acid (TXA) versus 50% glycolic acid (GA) peels in the management of melasma. The study was conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

Although the sample size was modest, it was considered adequate for a preliminary comparative clinical evaluation. The study was open-label in nature, and no blinding was performed, which may introduce observer bias.

Study Population and Eligibility

50 clinically diagnosed melasma patients were enrolled after obtaining written informed consent.

Inclusion criteria: Participants aged 18–60 years of either gender.

Exclusion criteria: Prior melasma treatment within one month, hypersensitivity to study agents, photosensitivity, facial irritation, active infection, keloid tendency, bleeding disorders, anticoagulant use, pregnancy, lactation, or concurrent hormone therapy.

Sample Size Determination

The sample size was estimated using the formula $N = 4pq/d^2$, assuming a prevalence (p) of 2%, a confidence level of 95%, and an absolute precision (d) of 6%. The calculated minimum sample size was 20.9, which was increased to 50 participants (25 per group) to improve comparative analysis and account for potential dropouts. However, the relatively small sample size may limit the generalizability of the findings.

Intervention and Randomization

Group A: Intradermal Tranexamic Acid (TXA)

After cleansing and application of topical anesthesia (lidocaine–prilocaine), a patch test using 0.1 ml TXA (100 mg/ml) was performed. Under aseptic conditions, multiple intradermal microinjections were administered over affected areas at a dose of 0.1 ml/cm², with a maximum of 2 ml per session.

Group B: 50% Glycolic Acid Peel

Following a negative patch test, 50% glycolic acid was applied uniformly over the affected area for 1–3 minutes or until the appearance of mild erythema. The peel was then neutralized using cold water or sodium bicarbonate solution.

Post-Treatment Care and Follow-Up

Both groups received treatment sessions at two-week intervals. Patients were followed up monthly for a duration of three months. All participants were advised to use broad-spectrum sunscreen (SPF ≥50), avoid excessive sun exposure, and maintain skin hydration with mild cleansers and moisturizers to ensure uniform post-procedure care.

Data Collection and Outcome Measures

Clinical evaluation was performed at baseline and at each follow-up visit. Standardized clinical photographs were captured under identical lighting conditions to ensure consistency.

Primary outcome:

- Reduction in modified Melasma Area and Severity Index (mMASI) scores between baseline and follow-up, and comparison between the two treatment groups

Secondary outcomes:

- Patient-reported satisfaction
- Safety and tolerability assessed by recording adverse effects such as erythema, burning, desquamation, and post-inflammatory hyperpigmentation

Data Management and Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 26. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as frequencies and percentages.

- Student's *t*-test was used for comparison of continuous variables
- Chi-square test was applied for categorical variables
- Pearson's correlation coefficient was used to assess associations

A *p*-value < 0.05 was considered statistically significant. In addition, effect size and 95% confidence intervals were calculated to enhance the robustness and interpretability of the statistical findings.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of medical college. Written informed consent was obtained from all participants prior to enrollment. The study adhered to ethical principles ensuring patient confidentiality, safety, and compliance with institutional and international research guidelines.

RESULTS AND OBSERVATIONS

Demographic Characteristics of the Study Population

Age and Gender Distribution

As shown in **Table 1** and **Figure 1(A)**, most participants were aged 26–35 years (40.0%) and 36–45 years (40.0%), with a mean age of 34.6 ± 7.9 years. **Table 2** and **Figure 1(B)** demonstrate a female predominance (82.0%), consistent with known epidemiological trends. Combined age–gender analysis (**Table 3**, **Figure 1(C)**) showed a significant association ($\chi^2 = 12.872$, $P = 0.005$), with females predominantly in the 26–45-year group.

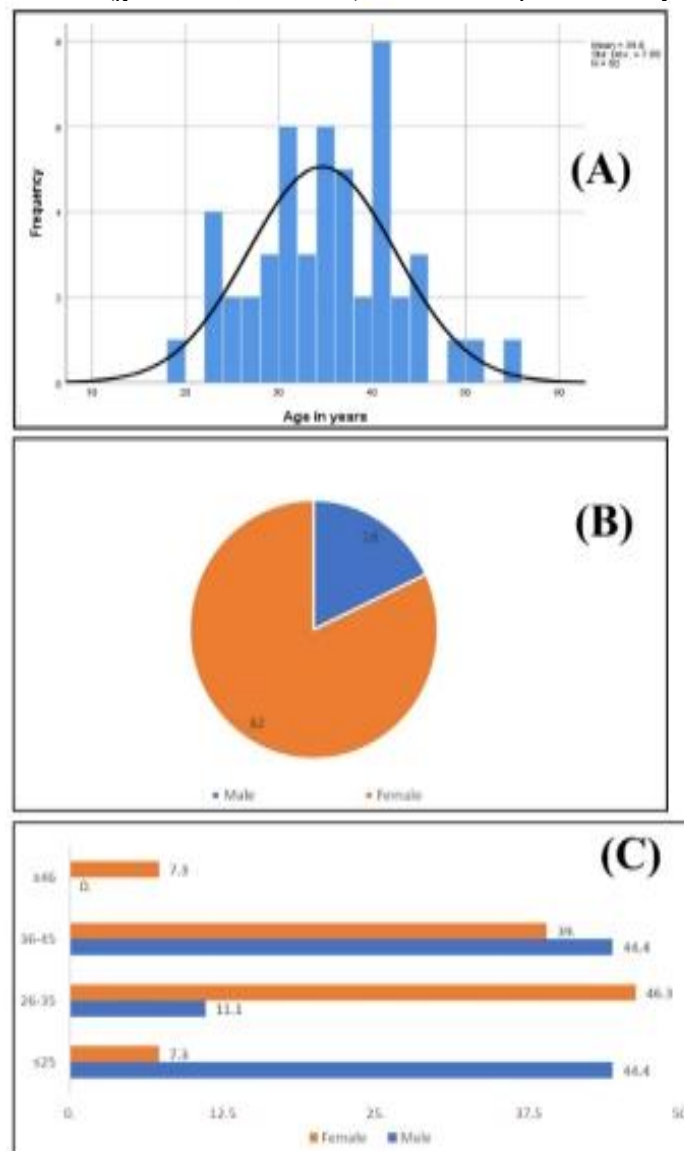


Figure 1 – Distribution of patients according to (A) age group, (B) gender, and (C) age group and gender.

Occupational and Clinical Profile

As presented in **Table 4** and **Figure 2(A)**, homemakers (48.0%) constituted the largest group, followed by skilled laborers (16.0%) and educators (12.0%). The centofacial pattern was most common (62.0%), followed by malar (36.0%) and mandibular (2.0%) (**Table 4**, **Figure 2(B)**).

Photoprotection was inadequate, with only 36.0% reporting sunscreen use (Table 5, Figure 2(C–F)). Most participants were treatment-naïve, with minimal prior topical, oral, or procedural interventions.

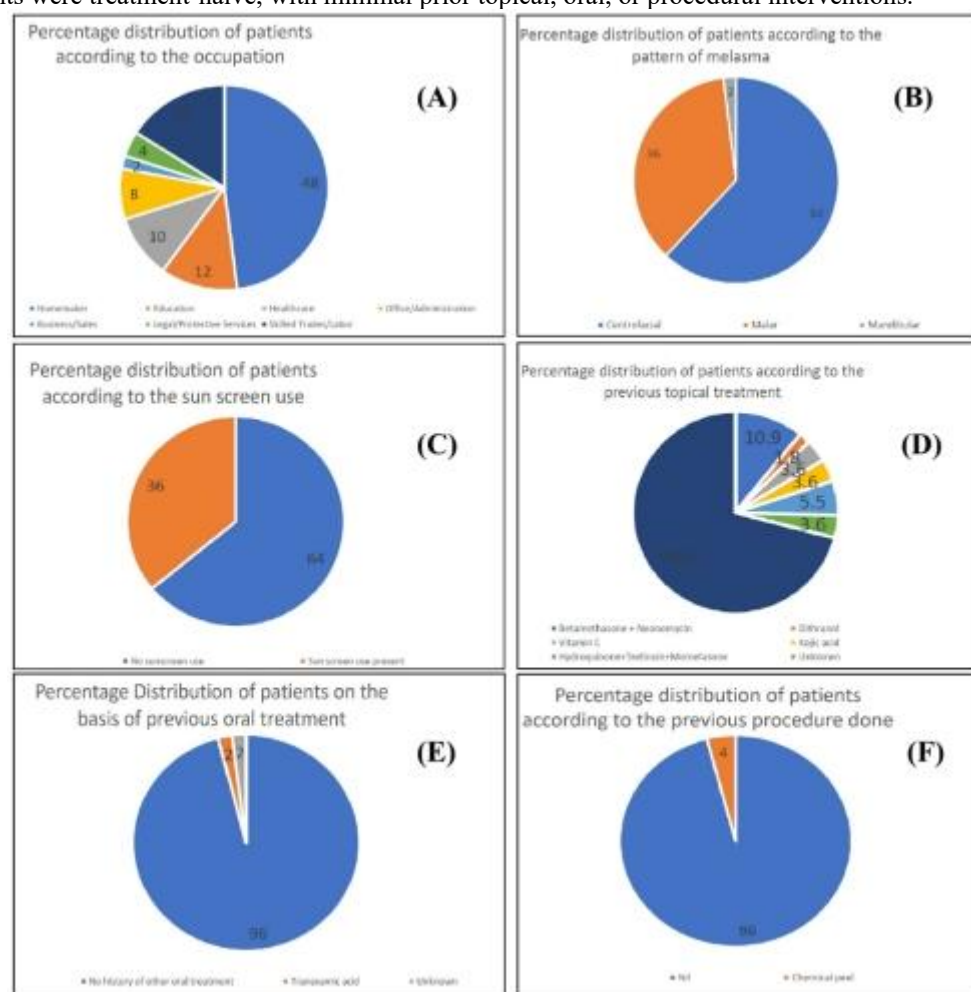


Figure 2 – Distribution of patients according to (A) occupation, (B) pattern of melasma, (C) sunscreen use, (D) previous topical treatment, (E) previous oral treatment, and (F) previous procedure done.

Treatment Distribution and Baseline Comparability

Participants were equally allocated to intradermal tranexamic acid (TXA) and glycolic acid (GA) peel groups (Table 6, Figure 3(A)). Mean age did not differ significantly between groups ($P = 0.501$) (Table 7, Figure 3(B)). Baseline characteristics were comparable ($P > 0.05$), ensuring unbiased comparison (Table 8).

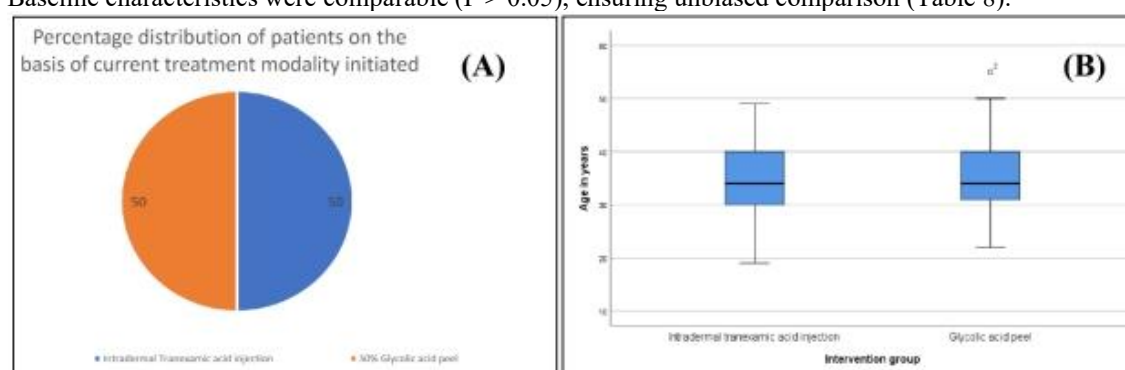


Figure 3 – (A) Distribution of patients based on treatment modality and (B) comparison of mean age across groups.

Therapeutic Outcomes

mMASI Score Improvement

As shown in **Table 9** and **Figure 4(A)**, the overall mean mMASI score significantly decreased from 7.90 ± 2.00 to 3.56 ± 2.01 . In the TXA group, scores reduced from 8.23 ± 1.74 to 2.33 ± 0.93 ($P < 0.001$) (**Figure 4(B)**), while in the GA group, scores decreased from 7.57 ± 2.23 to 4.80 ± 2.06 ($P < 0.001$) (**Figure 4(C)**). Between-group comparison (**Figure 4(D)**) showed a significantly greater reduction with TXA ($\Delta = 5.90 \pm 1.24$) compared to GA ($\Delta = 2.76 \pm 0.69$) ($P < 0.001$).

Effect Size and Confidence Interval Analysis

Effect size analysis demonstrated a very large overall treatment effect (Cohen's $d = 2.16$). Between-group comparison showed an extremely large effect favoring TXA ($d = 3.13$), while within-group effects were stronger for TXA ($d = 4.23$) than GA ($d = 1.29$). The 95% confidence interval for the mean difference (2.57–3.71) did not cross zero, confirming statistical significance and robustness of the findings.

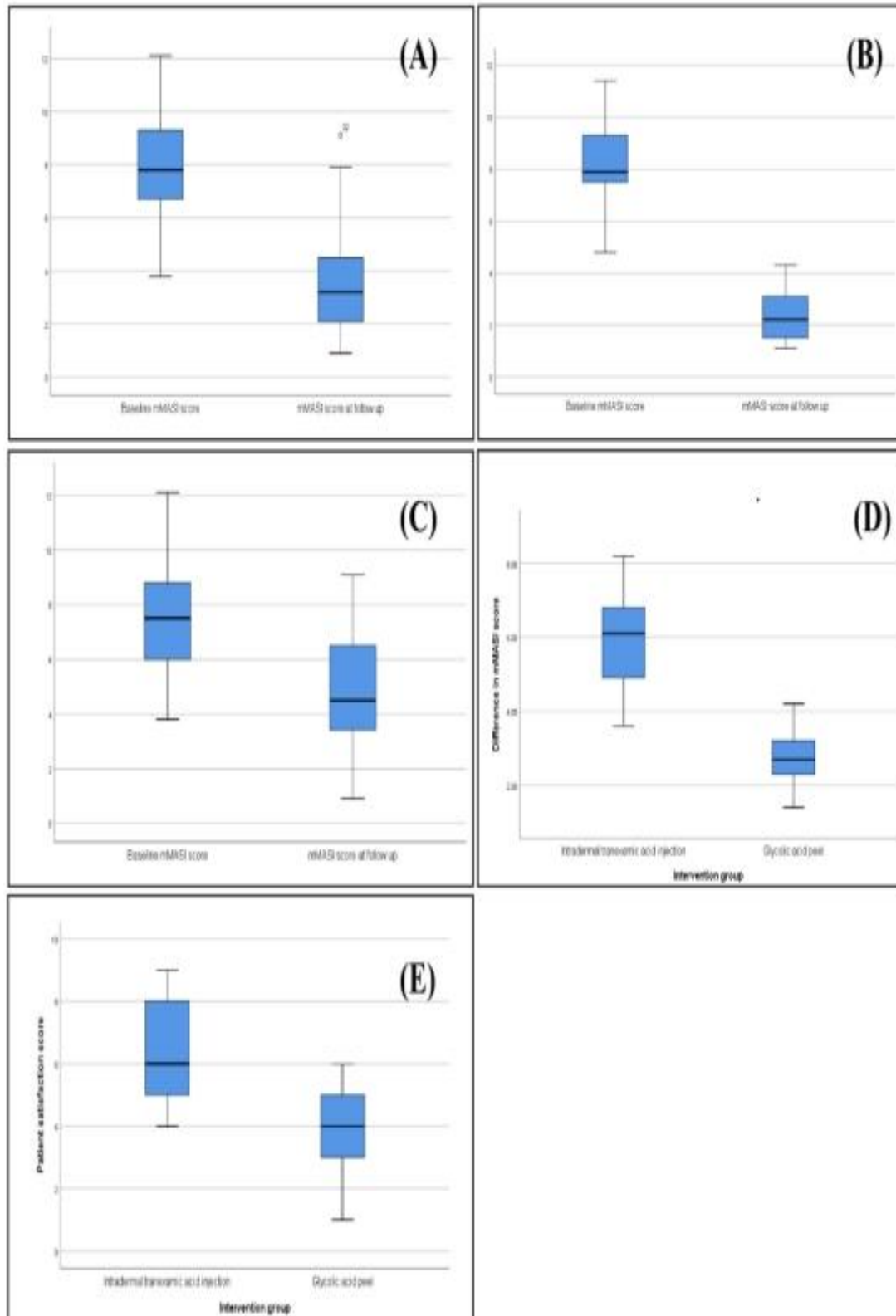


Figure 4 – (A) mMASI scores at baseline and follow-up, (B) TXA group comparison, (C) GA group comparison, (D) mean difference between groups, and (E) patient satisfaction.

Patient Satisfaction

Patients treated with TXA reported significantly higher satisfaction scores (6.36 ± 1.41) compared to the GA group (4.00 ± 1.44) ($P < 0.001$), as shown in **Figure 4(E)** and **Figure 5**.

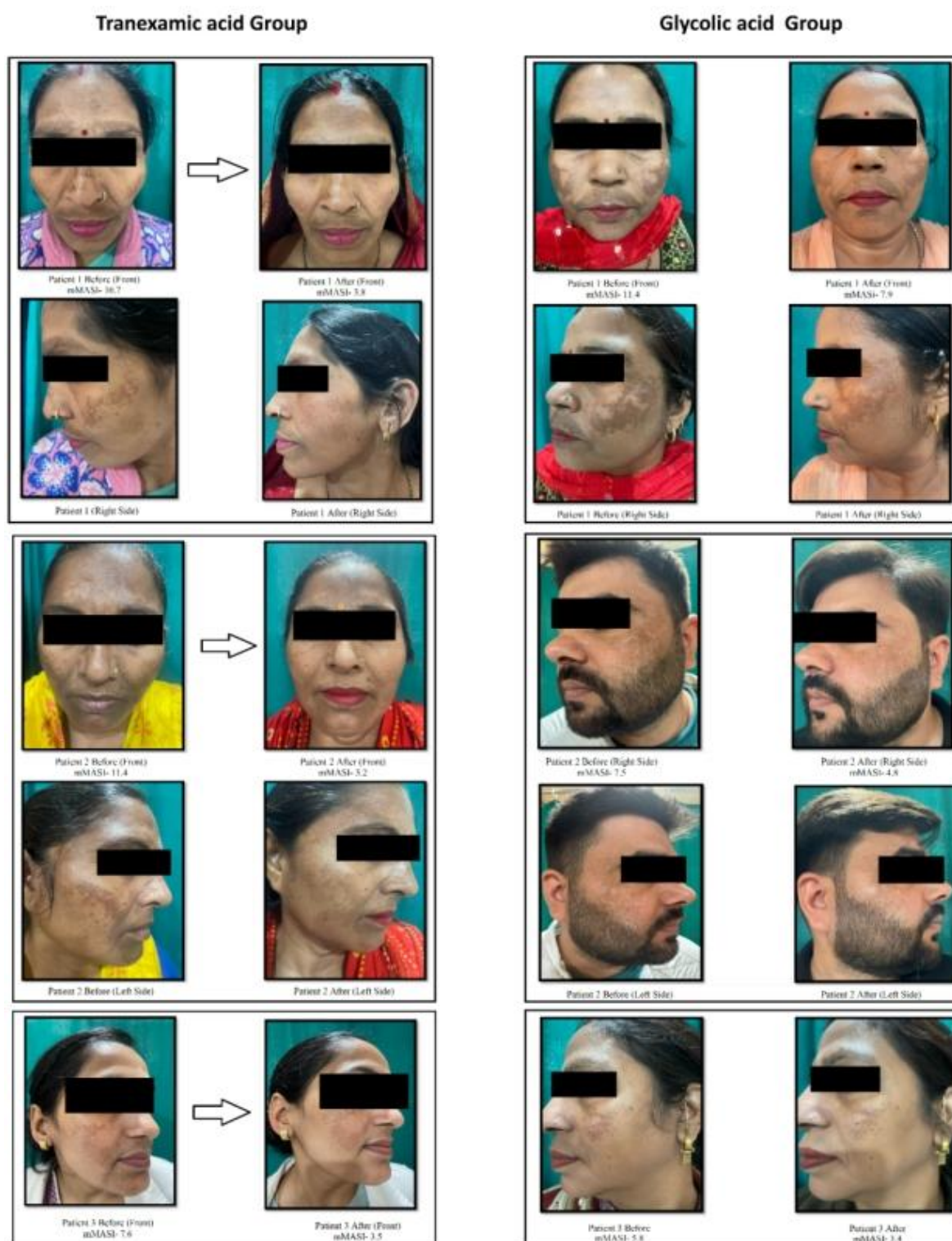


Figure 5: Effect of intradermal tranexamic acid and glycolic acid on patients

A

Adverse Effects

Adverse effects were mild and transient in both groups (**Table 10**). In the TXA group, pain and erythema (20% each) were most common, while the GA group showed burning (20%), erythema (16%), and itching (8%). No severe adverse events were observed, and most participants experienced no side effects.

Table 1 – Distribution of Patients According to the Age Group

S. No.	Age Group (in years)	No. of Patients	Percentage (%)
1	≤ 25	7	14.0
2	26–35	20	40.0
3	36–45	20	40.0
4	≥ 46	3	6.0

Total	—	50	100
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Table 2 – Distribution of Patients According to the Gender

S. No.	Gender	No. of Patients	Percentage (%)
1	Male	9	18.0
2	Female	41	82.0
Total	—	50	100

Table 3 – Distribution of Patients According to the Age Group and Gender

Age Group (in years)	Male N (%)	Female N (%)	Total N (%)
≤ 25	4 (44.4)	3 (7.3)	7 (14.0)
26–35	1 (11.1)	19 (46.3)	20 (40.0)
36–45	4 (44.4)	16 (39.0)	20 (40.0)
≥ 46	0 (0.0)	3 (7.3)	3 (6.0)
Total	9 (100.0)	41 (100.0)	50 (100.0)

Table 4 – Distribution of Patients According to Occupation and Pattern of Melasma

S. No.	Category	No. of Patients (N)	Percentage (%)
A. Occupation			
1	Homemaker	24	48.0
2	Education	6	12.0
3	Healthcare	5	10.0
4	Office/Administration	4	8.0
5	Business/Sales	1	2.0
6	Legal/Protective Services	2	4.0
7	Skilled Trades/Labor	8	16.0
	Total	50	100
B. Pattern of Melasma			
1	Centrofacial	31	62.0
2	Malar	18	36.0
3	Mandibular	1	2.0
	Total	50	100

Table 5 – Distribution of Patients According to Sunscreen Use, Previous Treatments, and Procedures

S. No.	Variable	Category	No. of Patients (N)	Percentage (%)
1	Sunscreen Use	No sunscreen use	32	64.0
2		Sunscreen use present	18	36.0
		Total	50	100
1	Previous Topical Treatment	Betamethasone	6	10.9
2		Dithranol	1	1.8
3		Vitamin C	2	3.6
4		Kojic acid	2	3.6
5		Hydroquinone + Tretinoin + Mometasone	3	5.5
6		Unknown	2	3.6
7		Nil	39	70.9
		Total	55	100
1	Previous Oral Treatment	No history of other oral treatment	48	96.0
2		Tranexamic acid	1	2.0
3		Unknown	1	2.0
		Total	50	100
1	Previous Procedures Done	Nil	48	96.0
2		Chemical peel	2	4.0
		Total	50	100

Table 6 – Distribution of Patients According to the Current Treatment Modality Initiated

S. No.	Intervention	No. of Patients (N)	Percentage (%)
1	Intradermal Tranexamic Acid Injection	25	50.0

2	50% Glycolic Acid Peel	25	50.0
	<i>Total</i>	<i>50</i>	<i>100</i>

Table 7 – Comparison of Mean Age Across the Treatment Groups

Treatment Group	N	Mean Age (years)	SD	t-statistic	p-value
Intradermal Tranexamic Acid Injection	25	33.84	7.15	-0.677	0.501
50% Glycolic Acid Peel	25	35.36	8.64		

Table 8 – Baseline Characteristics of the Study Population and Their Association with Intervention Group

Variable	Category	Intradermal Tranexamic Acid Injection (n=30)	50% Glycolic Acid Peel (n=25)	Total (n=55)	P-value
<i>Sex</i>	Male	6 (66.7%)	3 (33.3%)	9 (100.0%)	0.269
	Female	19 (46.3%)	22 (53.7%)	41 (100.0%)	
<i>Occupation</i>	Homemaker	12 (50.0%)	12 (50.0%)	24 (100.0%)	0.333
	Education	2 (33.3%)	4 (66.7%)	6 (100.0%)	
	Healthcare	2 (40.0%)	3 (60.0%)	5 (100.0%)	
	Office/Administration	1 (25.0%)	3 (75.0%)	4 (100.0%)	
	Business/Sales	0 (0.0%)	1 (100.0%)	1 (100.0%)	
	Legal/Protective Services	2 (100.0%)	0 (0.0%)	2 (100.0%)	
	Skilled Trades/Labor	6 (75.0%)	2 (25.0%)	8 (100.0%)	
<i>Pattern</i>	Centrofacial	17 (54.8%)	14 (45.2%)	31 (100.0%)	0.336
	Malar	7 (38.9%)	11 (61.1%)	18 (100.0%)	
	Mandibular	1 (100.0%)	0 (0.0%)	1 (100.0%)	
<i>Sunscreen Use</i>	No	17 (53.1%)	15 (46.9%)	32 (100.0%)	0.556
	Yes	8 (44.4%)	10 (55.6%)	18 (100.0%)	
<i>Previous Topical Treatment</i>	Nil	22 (56.4%)	17 (43.6%)	39 (100.0%)	0.474
	Betamethasone	3 (50.0%)	3 (50.0%)	6 (100.0%)	
	Dithranol	1 (100.0%)	0 (0.0%)	1 (100.0%)	
	Vitamin C	2 (100.0%)	0 (0.0%)	2 (100.0%)	
	Kojic Acid	1 (50.0%)	1 (50.0%)	2 (100.0%)	
	Hydroquinone + Tretinoin + Mometasone	1 (33.3%)	2 (66.7%)	3 (100.0%)	
	Unknown	0 (0.0%)	2 (100.0%)	2 (100.0%)	
<i>Previous Oral Treatment</i>	No History of Other Oral Treatment	25 (52.1%)	23 (47.9%)	48 (100.0%)	0.353
	Tranexamic Acid	0 (0.0%)	1 (100.0%)	1 (100.0%)	
	Unknown	0 (0.0%)	1 (100.0%)	1 (100.0%)	
<i>Previous Procedure Done</i>	Nil	24 (50.0%)	24 (50.0%)	48 (96.0%)	1.000
	Chemical Peel	1 (50.0%)	1 (50.0%)	2 (100.0%)	

Table 9 – Descriptive Statistics for mMASI Scores at Baseline and Follow-up

Variable	N	Minimum	Maximum	Median	Mean	Standard Deviation
<i>Baseline mMASI score</i>	55	3.8	12.1	7.80	7.90	2.00
<i>mMASI score at follow-up</i>	55	0.9	9.1	3.20	3.56	2.01

Table 10 – Distribution of Patients According to the Adverse Effects Developed in Different Treatment Groups

S. No.	Adverse Effect	Intradermal Tranexamic Acid Group N (%)	Glycolic Acid Peel Group N (%)
1	Pain during injection / Burning	5 (20.0%)	5 (20.0%)
2	Erythema post-procedure / Erythema	5 (20.0%)	4 (16.0%)
3	Itching	—	2 (8.0%)
4	No side effects	15 (60.0%)	14 (56.0%)
<i>Total</i>		<i>25 (100.0%)</i>	<i>25 (100.0%)</i>

DISCUSSION

Melasma is a chronic, relapsing hypermelanosis that significantly impacts quality of life despite its benign nature [1,12,13]. Its multifactorial pathogenesis—driven by UV exposure, hormonal influences, and inflammatory and vascular mediators—leads to increased melanocyte activity and persistent pigmentation [5,7,9,10,29]. These mechanisms necessitate multimodal therapeutic approaches targeting melanogenesis, epidermal turnover, and dermal pathways [2,4,7,20,19,24,28].

The demographic profile of this study aligns with established epidemiological trends, with most patients aged 26–45 years and a marked female predominance, consistent with hormonal influences reported in earlier studies [3,7,9,10,29]. The high proportion of inadequate sunscreen use highlights the critical role of photoprotection as a modifiable risk factor [11,19]. The predominance of the centrofacial pattern further supports previous findings [22,31].

Intradermal tranexamic acid (TXA) demonstrated significant reduction in mMASI scores, which may be attributed to its inhibition of the plasminogen–plasmin pathway and subsequent reduction in inflammatory and angiogenic mediators such as prostaglandins and VEGF [36,38,47,37]. These findings are consistent with prior studies reporting the efficacy of TXA in melasma management [38]. The intradermal route likely enhances localized drug delivery, contributing to improved outcomes.

Glycolic acid (GA) peels also showed significant improvement, primarily through epidermal exfoliation and inhibition of tyrosinase activity [25,31]. The magnitude of improvement observed is comparable to earlier reports supporting GA as an effective option, particularly for epidermal melasma [25,31]. However, its relatively superficial mechanism may limit efficacy compared to therapies targeting deeper pathways.

Comparatively, TXA demonstrated greater reduction in mMASI scores, possibly due to its combined anti-inflammatory and antiangiogenic effects acting on both epidermal and dermal components [36]. The magnitude of this difference was further supported by effect size analysis, which demonstrated an extremely large between-group effect (Cohen's $d = 3.13$), indicating a substantial clinical advantage of TXA over GA in this cohort. Additionally, the overall treatment effect was very large ($d = 2.16$), with a higher within-group effect observed for TXA compared to GA. The 95% confidence interval for the mean difference (2.57–3.71) did not cross zero, confirming the precision and statistical robustness of the observed findings. These results reinforce the clinical relevance of TXA; however, they should be interpreted cautiously in view of the limited sample size and short follow-up duration. Similar observations have been reported in previous studies. However, these findings should be interpreted cautiously due to the limited sample size and short follow-up duration.

Both treatments were well tolerated, with only mild and transient adverse effects, consistent with earlier reports [25,31]. Higher patient satisfaction in the TXA group may reflect faster clinical improvement and minimal downtime.

The strengths of this study include its prospective design and objective outcome assessment. However, limitations such as small sample size, short follow-up, single-center design, and lack of blinding may affect generalizability and introduce bias. Future studies with larger cohorts, longer follow-up, and combination therapies (e.g., TXA with GA or laser modalities) are warranted. Additionally, incorporation of biochemical markers such as tyrosinase, plasmin, and VEGF may provide further mechanistic insights [2,4,36,38].

Future research could investigate the use of digital image-analysis methods alongside the Modified Melasma Area and Severity Index (mMASI) to improve the objectivity and reproducibility of pigmentation assessment. Research on deep-learning approaches for detecting and classifying oral mucosal lesions demonstrates the application of image-based analytical techniques in clinical assessment. However, these methods would require specific validation in melasma before they could be recommended for clinical use [39].

CONCLUSION

In conclusion, both intradermal tranexamic acid (TXA) and 50% glycolic acid (GA) peels demonstrated significant efficacy and acceptable safety profiles in the management of melasma. Intradermal TXA showed relatively greater reduction in mMASI scores and higher patient satisfaction, suggesting its potential as an effective minimally invasive therapeutic option. In contrast, GA peels remain a practical and accessible modality, particularly for epidermal melasma.

However, these findings should be interpreted with caution due to limitations including small sample size, short follow-up duration, and lack of blinding. Further large-scale, multicentric studies with longer follow-up and exploration of combination therapies are warranted to validate these results and optimize individualized treatment strategies.

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