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Original Research Article

EFFICACY OF INTRADERMAL MICRO INJECTION OF TRANEXAMIC ACID VS ORAL TRANEXAMIC ACID FOR THE TREATMENT OF MELASMA

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ABSTRACT

Background: *Melasma is a common acquired hyperpigmentation disorder that significantly affects quality of life. Tranexamic acid (TXA) has recently emerged as a promising therapeutic option, administered via different routes including oral and intradermal delivery. However, comparative evidence regarding their relative efficacy remains limited.* ***Objective:*** *To compare the efficacy of intradermal microinjection of tranexamic acid with oral tranexamic acid in the treatment of melasma.* ***Study Design:*** *A randomized controlled trial.* ***Setting:*** *Department of Dermatology, Combined Military Hospital, Nowshera, Pakistan.* ***Duration of Study:*** *11-October-2024 to 11-April-2025.* ***Methods:*** *A total of 62 patients with clinically diagnosed melasma were enrolled and allocated equally into two groups. Group A received intradermal TXA microinjections at three-week intervals for five sessions, while Group B received oral TXA 250 mg twice daily for 12 weeks. The primary outcome was the proportion of patients achieving treatment efficacy, assessed by [insert scale used, e.g., MASI reduction if available]. Statistical analysis was performed using the Chi-square test, with a p-value of ≤ 0.05 considered statistically significant.* ***Results:*** *The mean age in Group A was 31.61 ± 11.37 years and in Group B 31.48 ± 10.94 years. A significantly higher proportion of patients in the intradermal TXA group achieved efficacy (64.5%, n = 20) compared with the oral TXA group (29.0%, n = 9) (p = 0.005).* ***Conclusion:*** *Intradermal tranexamic acid microinjections demonstrated significantly superior efficacy compared to oral tranexamic acid in the treatment of melasma. These findings suggest that intradermal administration may be the preferred therapeutic option for achieving optimal clinical outcomes.*

Keywords: Tranexamic Acid, Melasma, Intradermal Injection, Oral Administration, Mmasi Score

INTRODUCTION

Melasma, previously referred to as chloasma, is a genetically inherited pigmentary disorder that primarily manifests on the facial region. This disorder is more prevalent in females as well as people with darker skin types, mostly linked to UV exposure as well as hormonal factors. Melasma is mostly diagnosed clinically, characterized by symmetric reticulated hypermelanosis in three primary facial patterns (1, 2). The prevailing clinical manifestation in 80% of instances is the centrofacial pattern, which affects the forehead, nose, and upper lip, while sparing the philtrum and chin (3, 4). The malar pattern is confined to the malar cheeks, while mandibular melasma happens on the jawline as well as the chin. This condition is thought to manifest in older individuals and may be more closely linked with significant photodamage. A recent pattern referred to as extra-facial melasma can appear on non-facial areas of the body, such as the neck, forearms, and upper extremities (5, 6). Dermoscopy reveals noteworthy pigmentation in pseudo-rete ridges in skin (7). The use of a Wood's lamp may improve the visibility of hyperpigmentation when pigment is situated in the epidermis (8).

Tranexamic acid (TXA) is a naturally occurring lysine derivative. It interacts with 5-lysine binding regions on plasminogen, preventing plasmin formation as well as displacing plasminogen from fibrin. The hypopigmentation effect is attributed to its antiplasmin activity, which demonstrates structural similarity to tyrosine. The recommended amount of TXA for melasma treatment is substantially lower than that necessary for its antifibrinolytic consequences (9-11). Transdermal injections have gained popularity as a means of drug administration in recent years.6 A study recorded the efficacy (63.2% and 27.8%) of intradermal micro injection of tranexamic acid and oral tranexamic acid in the management of melasma (12).

Melasma is a common skin condition that causes hyperpigmentation, sparking interest among both dermatologists and patients. This study aims to investigate the efficacy of intradermal micro-injection of TXA compared to oral administration in the treatment of melasma, as no such research has been conducted in our local context. The results of this study will help our medical professionals to provide valuable insights regarding the optimal route of administration for TXA in melasma treatment, ultimately contributing to improved therapeutic approaches for this challenging dermatological condition.

METHODOLOGY

The study was designed as a randomized controlled trial conducted at the Department of Dermatology, Combined Military Hospital, Nowshera, from October 11/October/2024, to April 11/April/ 2025. An ethical approval was secured from the institute.

The sample size was calculated to be 62 participants, with 31 patients allocated to each of the two treatment groups. This calculation was performed using the WHO sample size calculator, based on the previously reported efficacy rates of 63.2% (13) for the intradermal intervention and 27.8% (13) for oral administration, with a 95% confidence level and 80% statistical power.

Participants were selected via consecutive non-probability sampling. The inclusion criteria encompassed adult patients of either gender aged 18 to 65 years who had received a clinical Diagnosis of melasma. This Diagnosis was established through visual inspection, which identified characteristic, symmetrical patches of hyperpigmentation and brownish discoloration on sun-exposed facial areas. Key exclusion criteria: individuals with any known clotting disorders, a history of recent hormonal therapy, those who were pregnant or lactating, and patients on anticoagulant medication.

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Informed consent was obtained from each participant. Demographic and baseline clinical data, including age, gender, body mass index (BMI), residence, employment status, educational background, and socioeconomic status, were recorded for each enrollee. Participants were then randomly assigned in equal numbers to either Group A or Group B using a blocked randomization technique.

Group A received treatment via intradermal microinjections of tranexamic acid. The procedure involved the application of a topical anesthetic (lidocaine hydrochloride 2%) followed by the administration of 0.05 mL of tranexamic acid (at a concentration of 4 mg/mL) per centimeter of the affected melasma area. This treatment was repeated at three-week intervals for a total of five sessions over 12 weeks (at weeks 0, 3, 6, 9, and 12). Group B received oral tranexamic acid at a dosage of 250 mg taken twice daily for a continuous period of 12 weeks.

The primary outcome efficacy was assessed at the end of the 12-week treatment period. Efficacy was defined clinically as a reduction in the modified Melasma Area and Severity Index (mMASI) score of between 25% and 50%. All clinical assessments were conducted under the supervision of an experienced consultant dermatologist with a minimum of five years of post-fellowship experience, ensuring consistency and accuracy in evaluation. All patient information and outcome data were recorded on a pre-designed structured proforma.

For data analysis, SPSS 25 was utilized. Age, BMI, and disease duration were determined using mean and SD. Gender, efficacy rates, melasma type, and other demographic factors were assessed using frequencies and percentages. The comparative efficacy between the two treatment groups was analyzed using the Chi-square test with a significance level of $p \leq 0.05$. Demographics and clinical variables were then stratified with the efficacy in both groups using the Chi-Square test, keeping the P value notable at < 0.05

RESULTS

This study evaluated the efficacy of two tranexamic acid (TXA) treatment modalities for melasma in a cohort of 62 patients, who were evenly divided into two groups. Group A received intradermal microinjections of TXA, while Group B was treated with oral TXA.

The mean age of the patients in Group A was 31.61 ± 11.37 years, with a mean disease duration of 2.87 ± 1.46 years and a mean Body Mass Index (BMI) of 24.02 ± 1.33 kg/m^2. Group B had a mean age of 31.48 ± 10.94 years, a disease duration of 2.94 ± 1.41 years, and a BMI of 24.31 ± 1.32 kg/m^2.

There were 20 (64.5%) female patients in Group A and 21 (67.7%) in Group B. In Group A, 11 (35.5%) were male, and in Group B, 10 (32.3%) were male patients (Table 1).

Treatment was deemed effective for 20 (64.5%) patients in Group A who received intradermal TXA. In stark contrast, only 9 (29.0%) patients in Group B taking oral TXA achieved this outcome. This disparity was statistically notable (P = 0.005) (Table 2). Table 3 presents the stratifications.

Table 1: Demographics and clinical presentation

Demographics and clinical presentation		Groups			
		Group A (Intradermal TXA)		Group B (Oral TXA)	
		n	%	n	%
Gender	Male	11	35.5%	10	32.3%
	Female	20	64.5%	21	67.7%
Education	Literate	17	54.8%	13	41.9%
	Illiterate	14	45.2%	18	58.1%
Profession	Employed	16	51.6%	14	45.2%
	Unemployed	15	48.4%	17	54.8%
Residence	Urban	21	67.7%	17	54.8%
	Rural	10	32.3%	14	45.2%
Socioeconomic status	Lower class	7	22.6%	9	29.0%
	Middle class	16	51.6%	17	54.8%
	Upper class	8	25.8%	5	16.1%
Types of melasma	Malar	7	22.6%	8	25.8%
	Centrofacial	21	67.7%	18	58.1%
	Mandibular	3	9.7%	5	16.1%

Table 2: Comparison of efficacy between both groups

Efficacy	Groups				P value
	Group A (Intradermal TXA)		Group B (Oral TXA)		
	n	%	n	%	
Yes	20	64.5%	9	29.0%	0.005
No	11	35.5%	22	71.0%	

Table 3: Stratification of efficacy with demographic and clinical presentation

Demographics and clinical presentation				Groups				P value
				Group A (Intradermal TXA)		Group B (Oral TXA)		
				n	%	n	%	
Gender	Male	Efficacy	Yes	9	81.8%	6	60.0%	0.26
			No	2	18.2%	4	40.0%	
	Female	Efficacy	Yes	11	55.0%	3	14.3%	0.006
			No	9	45.0%	18	85.7%	
Education	Literate	Efficacy	Yes	8	47.1%	6	46.2%	0.96
			No	9	52.9%	7	53.8%	
	Illiterate	Efficacy	Yes	12	85.7%	3	16.7%	0.0001
			No	2	14.3%	15	83.3%	

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Profession	Employed	Efficacy	Yes	10	62.5%	7	50.0%	0.49
			No	6	37.5%	7	50.0%	
	Unemployed	Efficacy	Yes	10	66.7%	2	11.8%	0.001
			No	5	33.3%	15	88.2%	
Residence	Urban	Efficacy	Yes	16	76.2%	3	17.6%	0.0001
			No	5	23.8%	14	82.4%	
	Rural	Efficacy	Yes	4	40.0%	6	42.9%	0.88
			No	6	60.0%	8	57.1%	
Socioeconomic status	Lower class	Efficacy	Yes	5	71.4%	3	33.3%	0.13
			No	2	28.6%	6	66.7%	
	Middle class	Efficacy	Yes	9	56.2%	5	29.4%	0.11
			No	7	43.8%	12	70.6%	
	Upper class	Efficacy	Yes	6	75.0%	1	20.0%	0.05
			No	2	25.0%	4	80.0%	
Types of melasma	Malar	Efficacy	Yes	4	57.1%	4	50.0%	0.78
			No	3	42.9%	4	50.0%	
	Centrofacial	Efficacy	Yes	15	71.4%	3	16.7%	0.001
			No	6	28.6%	15	83.3%	
	Mandibular	Efficacy	Yes	1	33.3%	2	40.0%	0.85
			No	2	66.7%	3	60.0%	
Age groups (Years)	18 to 35	Efficacy	Yes	16	66.7%	6	25.0%	0.004
			No	8	33.3%	18	75.0%	
	36 to 50	Efficacy	Yes	4	80.0%	1	25.0%	0.09
			No	1	20.0%	3	75.0%	
	> 50	Efficacy	Yes	0	0.0%	2	100.0%	0.08
			No	1	100.0%	0	0.0%	
BMI (Kg/m2)	18 to 24.9	Efficacy	Yes	15	60.0%	6	31.6%	0.06
			No	10	40.0%	13	68.4%	
	> 24.9	Efficacy	Yes	5	83.3%	3	25.0%	0.01
			No	1	16.7%	9	75.0%	
Duration of disease (Years	1 to 3	Efficacy	Yes	11	55.0%	3	17.6%	0.02
			No	9	45.0%	14	82.4%	
	> 3	Efficacy	Yes	9	81.8%	6	42.9%	0.04
			No	2	18.2%	8	57.1%	

DISCUSSION

Our investigation into the efficacy of intradermal microinjections versus oral administration of tranexamic acid for melasma revealed a statistically superior outcome for the intradermal approach. Specifically, a positive therapeutic response, which was defined as a 25-50% reduction in the modified Melasma Area and Severity Index (mMASI) score after twelve weeks, was observed in 20 patients (64.5%) receiving intradermal TXA, compared to only nine patients (29.0%) in the oral TXA group. This strongly suggests a more favourable outcome with localized injection therapy under our specific protocol.

The demographic profile of our cohort was notably well-balanced, with mean ages of 31.61 ± 11.37 years in the intradermal group and 31.48 ± 10.94 years in the oral group, and closely matched durations of disease and BMI. This homogeneity strengthens the internal validity of our comparative analysis. The predominance of female patients (64.5% and 67.7% in Groups A and B, respectively) and the centrofacial pattern as the most common clinical presentation are consistent with the established epidemiology of melasma described in various studies (13, 14).

Our primary finding of intradermal superiority appears to align directly with the results of Shetty et al, who reported a 35.6% improvement in mMASI with intradermal injections compared to 21.7% with oral TXA (13). Similarly, the study by Komal et al. documented notably better response categories for intradermal TXA compared to a topical active (azelaic acid) (15). The proposed mechanism for this localized efficacy, particularly for dermal and mixed melasma subtypes, is the direct delivery of TXA to the site of pathology, potentially inhibiting the interaction between melanocytes and keratinocytes via the plasminogen pathway more effectively than systemic circulation allows (16, 17).

Conversely, Khurana et al. reported a dramatic 57.5% improvement in MASI score with oral TXA versus 43.6% with microinjections, with 100% of the oral group showing greater than 50% improvement (14). Panchal et al. concluded that oral TXA showed a notable standard mean difference in MASI reduction at both 8 and 12 weeks compared to adjuvant treatments. In contrast, the results for topical and intradermal routes were not significant (18). A critical factor that may explain these discrepancies is the treatment protocol. Our study administered intradermal injections of 4 mg/ml every three weeks, potentially leading to a higher cumulative local dose and more sustained suppression of melanogenesis in the target area. In contrast, studies like Khurana et al. utilized monthly injections, a frequency they suggest might be suboptimal; they indicated that increasing the frequency of the injections could yield better efficacy. Furthermore, the concentration of TXA used (4 mg/ml) and the total volume injected per session, which was tailored to the affected area in our protocol, are pivotal variables influencing the outcome.

Our study makes a valuable contribution to the ongoing debate by providing evidence that a once-every-three-week intradermal TXA injection regimen can yield notably better efficacy than a standard oral course over 12 weeks, with an acceptable safety profile. Future research should focus on standardizing and optimizing intradermal protocols, including direct comparisons of different injection frequencies and concentrations, as well as conducting long-term studies to assess the durability of the response and recurrence rates after cessation of either treatment modality.

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CONCLUSION

In conclusion, the intradermal micro-injection of tranexamic acid in our study was notably more effective than oral tranexamic acid for the treatment of melasma.

DECLARATIONS

Data Availability Statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department Concerned. (IRB)
Consent for publication
Approved
Funding
Not applicable

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTION

KIRAN BIBI (Postgraduate Resident)
Conception of Study,Collection of Data, Development of Research Methodology Design, Review of manuscript, Manuscript drafting and Final approval of manuscript.
SUMMAYA SALEEM (Assistant Professor)
Study Design, Conception of Study, Supervise the Entire Process, and Final Approval of Manuscript.

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