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A SPLIT-FACE COMPARATIVE STUDY OF INTRADERMAL INJECTION OF TRANEXAMIC ACID VERSUS PLATELET-RICH PLASMA IN THE TREATMENT OF MELASMA

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ABSTRACT

Objectives: To study and compare the efficacy of intradermal injection of tranexamic acid versus platelet-rich plasma in the treatment of melasma using modified melasma area and severity index (mMASI) and to evaluate the side effects of both treatments. **Methods:** A split-face comparative study was conducted on 40 patients with bilateral symmetrical melasma at SMS Medical College, Jaipur. Right side of the face received intradermal tranexamic acid injections while the left side of face received platelet-rich plasma (PRP) injections. Patients were evaluated at baseline, 4, 8 weeks using mMASI scores, subjective assessment, and photographic evaluation. Follow-up was done at 12, 16 and 20 weeks. **Findings:** Both treatments showed significant improvement in melasma severity. PRP demonstrated superior efficacy with mean mMASI reduction from 5.03 at baseline to 1.93 at 12 weeks (61.6% improvement) compared to tranexamic acid which reduced from 5.08 to 2.73 (46.3% improvement). PRP showed better sustained improvement with lesser recurrence during follow-up period. Both treatments were well-tolerated with minimal adverse effects including transient erythema, pain, and burning sensation. **Novelty:** This is the split-face comparative study evaluating intradermal tranexamic acid versus PRP in melasma treatment in the Indian population, providing direct comparison of two emerging minimally invasive therapeutic modalities with extended follow-up assessment.

INTRODUCTION

Melasma is a common acquired hypermelanosis characterized by symmetric brown patches predominantly affecting the face, particularly in women of reproductive age. The condition affects approximately 10-15% of pregnant women and 10-25% of women taking oral contraceptives, with a higher prevalence in individuals with darker skin phototypes (Akhtar et al. 2021). While melasma is asymptomatic, it causes significant psychological distress and impacts quality of life due to cosmetic disfigurement.

The pathogenesis of melasma involves multiple factors including ultraviolet radiation exposure, hormonal influences, genetic predisposition, and increased melanocyte activity. Traditional treatments include topical depigmenting agents such as hydroquinone, tretinoin, and corticosteroids, which often provide limited efficacy and may cause side effects with prolonged use (Bandyopadhyay et al. 2009).

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Recent therapeutic advances have focused on minimally invasive procedures. Tranexamic acid, a synthetic antifibrinolytic agent, has shown promising results in melasma treatment through its anti-inflammatory and anti-melanogenic properties (Ebrahimi and Naeini 2014). Platelet-rich plasma (PRP), containing various growth factors and cytokines, has emerged as a novel therapeutic option with regenerative and anti-inflammatory effects (Garg and Thami 2021).

Despite growing interest in these treatments, comparative studies evaluating their relative efficacy remain limited, particularly in the Indian population. This study aimed to provide a direct split-face comparison of intradermal tranexamic acid versus PRP in melasma treatment.

MATERIALS AND METHODS

Ethical Approval

The study protocol was approved by the Research Review Board and Ethics Committee of SMS Medical College and Attached Group of Hospitals, Jaipur, Rajasthan, India.

Study Design and Setting

This was an analytic interventional study conducted from March 2022 to March 2025 at the Department of Dermatology,

Venereology, and Leprosy, SMS Medical College, Jaipur, Rajasthan. An additional two months were allocated for data compilation, statistical analysis, and report preparation.

Study Population

Patients aged 18–50 years diagnosed with melasma attending the dermatology outpatient department were enrolled after providing written informed consent. Patients satisfying the inclusion and exclusion criteria were included.

Inclusion Criteria

- Patients diagnosed with melasma attending the dermatology OPD.
- Both males and females aged between 18 and 50 years.
- Willingness to provide written informed consent.

Exclusion Criteria

- Coagulation disorders or current use of anticoagulants.
- Known hypersensitivity to tranexamic acid, PRP, or vehicle components.
- Pregnant and lactating women.
- Use of medication known to induce pigmentation (e.g., minocycline, hydroxychloroquine, clofazimine, oral contraceptives).
- Presence of inflammatory facial dermatoses, keloids, or other pigmentary disorders.
- Recent melasma treatment within the past 4 weeks.
- Presence of systemic infections such as septicaemia, HIV, Hepatitis B or C.

Sample Size

Based on previous literature (IG Abd El Raouf et al., 2023), a sample size of 40 patients per group was calculated to detect a significant difference in mean mMASI score reduction with 80% power and 5% alpha. To account for a 20% dropout rate, the sample size was increased to 48 patients per group.

Interventions

Tranexamic Acid Injection

Tranexamic acid was prepared at a concentration of 4 mg/mL by diluting 4 mg from a 100 mg/mL vial with normal saline to make 1 mL. After applying a topical anesthetic under occlusion for 30 minutes, intradermal injections of tranexamic acid (0.05 mL) were administered at 1 cm intervals on the right side of the face, with a maximum dose of 2 mL (8 mg) per session. Injections were given at baseline, 4 weeks, and 8 weeks.

Platelet-Rich Plasma (PRP) Preparation and Injection

Venous blood (8-10ml) was collected aseptically into ACD vials. Samples were centrifuged at 1500 rpm for 12 minutes, then at 2500 rpm for 5 minutes. The platelet-rich plasma was then activated by adding 0.1 mL calcium chloride per 0.9 mL plasma. Following topical anesthesia for 30 minutes under occlusion, PRP (2 mL) was injected intradermally at 1 cm intervals into the left side of the face using a 31-gauge needle at baseline, 4 weeks, and 8 weeks.

Patient Instructions

Patients were instructed to avoid applying any topical agents other than sunscreen (SPF 30), which was to be applied every 4 hours during daylight throughout treatment and follow-up.

Outcome Assessment

- The severity of melasma was assessed at baseline, weeks 4, 8, 12, 16, and 20 using the modified Melasma Area and Severity Index (mMASI).
- Clinical photographs were taken under standardized conditions with consistent camera settings, lighting, and patient positioning and independently evaluated by a blinded observer.
- Patient subjective improvement was recorded using a Likert scale:

  1=1–25%improvement

  2=26–50% improvement

  3=51–75% improvement

  4 = 76–100% improvement
- Adverse events were monitored and recorded at each visit.
- Patients lost to follow-up after two contact attempts or who voluntarily withdrew were excluded from final analysis.
- The primary outcome was complete lesion resolution, defined as absence of pigmentation and restoration of normal skin markings.

Modified MASI (mMASI) Score Calculation

mMASI was calculated as

$0.3\times A(f)\times D(f)+0.3\times A(lm)\times D(lm)+ 0.3\times A(rm) \times D(rm) +0.1 \times A(c)\times D(c)$, where A = area and D = darkness of melasma at forehead (f), left malar (lm), right malar (rm), and chin (c).

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using appropriate statistical software. Quantitative variables are presented as mean ± standard deviation (SD), and qualitative variables as frequencies and percentages. Independent samples t-test was used to compare quantitative data between groups, while Chi-square test compared qualitative variables. Statistical significance was set at $p \leq 0.05$.

RESULTS

Demographic Characteristics

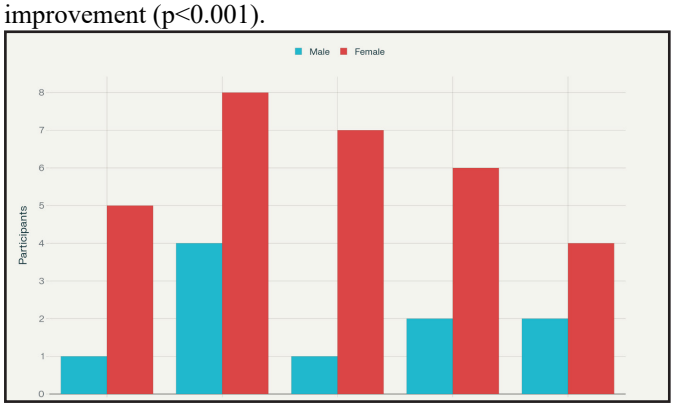
A total of 40 patients completed the study, comprising 10 males (25%) and 30 females (75%) with a mean age of 29.5±5.38 years. The majority were married (52.5%), vegetarian (72.5%), and from rural backgrounds (62.5%). Melasma predominantly involved both forehead and malar regions (65%), with severe pigmentation observed in 52.5% of cases. Most patients (45%) had disease duration of 1-2 years. Positive family history was present in 25% of patients, exclusively in females ($p<0.001$).

Primary Outcome - mMASI Scores

Both treatment modalities demonstrated statistically significant improvement in mMASI scores over time. At baseline, mean mMASI scores were comparable between groups (Tranexamic acid: 5.08±1.539 vs PRP: 5.03±1.486, p=0.173).

PRP showed superior efficacy with mean mMASI reduction

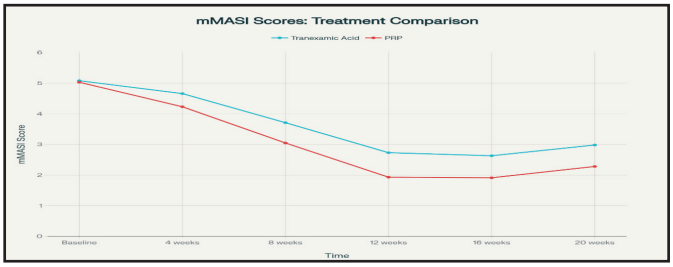
from 5.03±1.486 at baseline to 1.93±0.98 at 12 weeks, representing 61.6% improvement. Tranexamic acid showed reduction from 5.08±1.539 to 2.73±0.98, representing 46.3% improvement (p<0.001).

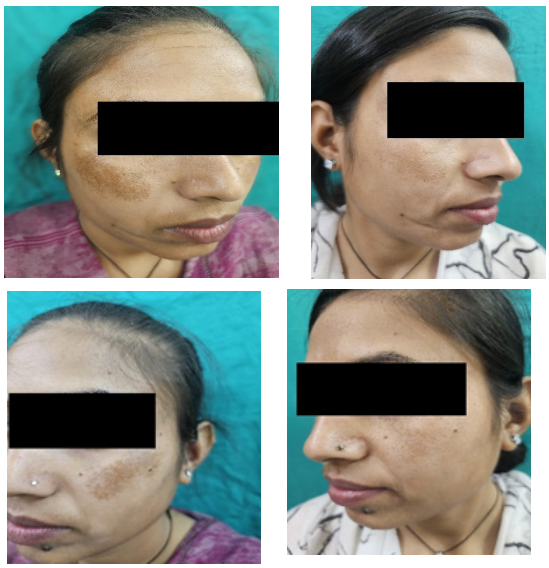


During follow-up period, PRP maintained better sustained improvement. At 20 weeks, mean mMASI scores were 2.28±1.26 for PRP versus 2.98±1.17 for tranexamic acid (p<0.001), indicating lesser recurrence with PRP treatment.

Table 1. Mean mMASI Scores Comparison

Time Point	Tranexamic Acid (Mean±SD)	PRP (Mean±SD)	P-Value
Baseline	5.08±1.539	5.03±1.486	0.173
4 weeks	4.66±1.503	4.23±1.413	<0.001
8 weeks	3.71±1.23	3.047±1.221	<0.001
12 weeks	2.73±0.98	1.93±0.98	<0.001
16 weeks	2.63±0.95	1.91±1.06	<0.001
20 weeks	2.98±1.17	2.28±1.26	<0.001





Before treatment After treatment Before treatment After treatment

Secondary Outcomes

Subjective Patient Assessment

PRP demonstrated significantly superior patient satisfaction at all time points. At 12 weeks, mean subjective scores were 2.53±0.679 for PRP compared to 2.13±0.607 for tranexamic acid (p<0.001). The difference remained statistically significant through 16 weeks but converged at 20 weeks (p=0.785).

Photographic Assessment

Independent photographic evaluation confirmed superior results with PRP treatment. At 12 weeks, mean photographic scores were 2.78±0.733 for PRP versus 2.23±0.620 for tranexamic acid (p<0.001). This significant difference was maintained throughout the study period including follow-up.

Table 2. Secondary Outcome Measures at 12 Weeks

Assessment Type	Tranexamic Acid (Mean±SD)	PRP (Mean±SD)	P-Value
Subjective	2.13±0.607	2.53±0.679	<0.001
Photographic	2.23±0.620	2.78±0.733	<0.001

Adverse Effects

Both treatments were well-tolerated with minimal side effects. Common adverse effects included:

Table 3. Adverse Effects Comparison

Side Effect	Tranexamic Acid n(%)	PRP n(%)	Clinical Significance
Erythema	30 (75%)	27 (67.5%)	Mild, transient
Pain	23 (57.5%)	19 (47.5%)	Injection-related
Burning	29 (72.5%)	7 (17.5%)	Moderate but temporary
Oedema	6 (15%)	6 (15%)	Minimal, temporary

PRP showed significantly lower incidence of burning sensation compared to tranexamic acid (17.5% vs 72.5%, p<0.001). All adverse effects were transient and resolved within 24-48 hours without intervention.

Statistical Analysis Summary

Paired t-tests revealed statistically significant differences favoring PRP at all post-treatment time points for mMASI scores (p<0.001). Secondary outcome measures consistently favored PRP with statistical significance maintained through 16 weeks. Both treatments showed significant improvement from baseline (p<0.05), but PRP demonstrated superior efficacy with better patient satisfaction and sustained results during follow-up period.

DISCUSSION

This split-face comparative study demonstrates the superior efficacy of intradermal PRP over tranexamic acid in melasma treatment. The findings align with previous studies reporting significant improvement with both modalities, while providing direct comparative evidence favoring PRP (Janney et al. 2019).

Our results align with previous prospective studies, such

as Karthikeyan et al. and the recent work by Rajalakshmi et al., where PRP led to greater improvement in melasma severity indices compared to TXA when used as intradermal injections. The underlying mechanism may be attributed to the higher concentration of growth factors and transforming growth factor beta (TGF-β1) in PRP, which modulate melanogenesis, angiogenesis, and dermal repair. TXA exerts its effect by inhibiting the plasminogen activation pathway, thereby reducing UV-induced melanogenesis, but the global improvement appears more modest and often plateaus over time.

The mechanism of action differs between treatments. Tranexamic acid acts through inhibition of plasminogen activation, reducing keratinocyte-melanocyte interaction and inflammation (Maeda and Naganuma 1998). PRP contains multiple growth factors including PDGF, TGF-β, and VEGF, which promote tissue regeneration, reduce inflammation, and potentially modulate melanogenesis through complex cellular interactions (Mehryan et al. 2014).

The superior efficacy of PRP may be attributed to its multifactorial mechanism involving growth factor-mediated tissue remodeling, anti-inflammatory effects, and improved dermal architecture. The sustained improvement observed with PRP during follow-up suggests more durable therapeutic effects compared to tranexamic acid.

Our results showed both treatments were safe with minimal adverse effects. The lower incidence of burning sensation with PRP compared to tranexamic acid may be related to the biocompatible nature of autologous plasma versus the synthetic compound.

Limitations

This study has several limitations including single-center design, relatively small sample size, and short duration of study. Longe-term studies with larger cohorts are needed to confirm these findings and assess durability of improvement.

CONCLUSION

Intradermal PRP demonstrates superior efficacy compared to tranexamic acid in melasma treatment, with greater improvement in mMASI scores, better patient satisfaction, and more sustained results during follow-up. Both treatments are safe and well-tolerated, making them viable alternatives to traditional topical therapies. PRP appears to be the preferred minimally invasive treatment option for melasma, though longe-term studies are warranted to establish optimal treatment protocols and assess long-term efficacy.

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