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Original Research Article

A comparison of the effectiveness of intralesional tranexamic acid against platelet-rich plasma in the treatment of melasma

Manasha Karthikeyan, Govardhan Jagadeesh Kumar*, Indradevi Radhakrishnan

Department of Dermatology, Sri. Lakshmi Narayana Institute of Medical Sciences, Villianur Commune, Agaram, Kudappakkam, Puducherry, India

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***Correspondence:**
Dr. Govardhan Jagadeesh Kumar,
E-mail: Gopi3333@yahoo.com

ABSTRACT

Background: Melasma, derived from the Greek word "melas" meaning "black", manifests as an acquired, more or less symmetrical hypermelanosis of sun-exposed skin. This study aimed to compare and evaluate the efficacy and safety of intradermal injection of tranexamic acid and platelet-rich plasma in treating various types of melasma.
Methods: Conducted from June 2022 to December 2023 at the outpatient department of dermatology, Sri Lakshmi Narayana institute of medical sciences, Puducherry, this split-face prospective study involved 40 melasma cases. Tranexamic acid (4 mg/ml) was intradermally injected into the right side of the face, while PRP was injected into the left side. Improvement was assessed using the modified Melasma area severity index (MASI) grading system and dermoscopy, measuring disease severity and percentage of improvement before and after therapy on both sides of the face.
Results: The study comprised predominantly females (80%) aged 20 to 30 years (50%), followed by those aged 30 to 40 years (35%). Most cases (93%) exhibited a gradual onset, with centrofacial (52.5%) and malar (37.5%) patterns being predominant. Mixed pattern (67.5%) was common. Pre-treatment mean MASI scores for tranexamic acid and PRP sides were 7.54 and 6.92, respectively, with post-treatment scores of 4.6 and 2.83, respectively.
Conclusions: Intradermal PRP demonstrated significantly superior efficacy over intradermal tranexamic acid in managing melasma, particularly in the longer term. Thus, PRP, coupled with good compliance, may substantially reduce the disease burden compared to conventional tranexamic acid treatment.

Keywords: Melasma, Tranexamic acid, PRP, MASI

INTRODUCTION

Melasma is derived from a Greek word “melas” meaning “black”. Melasma is a acquired more or less symmetrical hypermelanosis of sun-exposed skin.[1,2] A common presentation to dermatology outpatient clinics is melasma, a chronic disorder marked by grey-brown patches and macules with clearly defined geographic borders that affect sun-exposed areas of the face like the bridge of the nose, cheek, upper lip, forehead, and mandibular area. Based on a wood's lamp inspection, melasma is divided into epidermal, dermal, and mixed types. It typically begins after pregnancy and is most frequently observed in women in the reproductive age range. In about 10% of all cases, men are the ones that are impacted. Melasma can be aggravated and precipitated by a number of causes, including sex hormones, oral contraceptives, phototoxic medications,

hereditary susceptibility, and sun exposure.[3] Melasma is more common in Asians and middle east countries.[4] Uncertainty surrounds the fundamental pathophysiology. Unbalanced hormones, particularly oestrogen in females, are regarded to be a significant predictor. The hormonal aetiology is also supported by the greater occurrence of instances involving oral contraceptive pills (OCPs). Additionally, thyroid issues, ovarian irregularities, and the photosensitization impact of several medications are thought to be connected to this appearance.[5,6]

Ultraviolet (UV) radiations in the sunlight is one of the commonest agreed factors known for production of alpha melanocyte stimulating hormone and corticotropin, as well as interleukin 1 and endothelin 1, all of which contribute to increased melanin production by intra-epidermal melanocytes.[7] The diagnosis is usually clinical and on examination. There is hyperpigmentation that is usually tan or bluish and strong history of OCPs use or pregnancy is usually suggestive. Various treatment options such as topical depigmenting agents, chemical peels, dermabrasion, laser therapies, platelet rich plasma have been utilized in different studies.[8-10] Intralesional Tranexamic acid (Tranexamic acid) is a plasmin inhibitor which decreases abnormal fibrinolysis to reduce blood loss.[11] Tranexamic acid also inhibits UV induced plasmin activity in keratinocytes by inhibiting the binding of plasminogen to keratinocytes leading to less quantity of free arachidonic acid and reduced ability to produce prostaglandins, thereby reducing melanogenesis.[12] Tranexamic acid also has a role in inhibiting keratinocyte activating melanocytes pathway.

Tranexamic acid also reduces hyperpigmentation by blocking generation of single chain urokinase PA by keratinocytes which increases melanocytic activity.[13] The platelet rich plasma (PRP) is a plasma suspension obtained after centrifugation of whole blood, containing higher platelet, complement factors and a range of growth factor, chemokines-cytokine and various plasma protein concentration.[14,15] These platelet derived growth factors lead to increased synthesis of hyaluronic acid, which is responsible for maintaining skin tone and volume, hence reducing the skin pigmentation. The aim of this study was to compare and evaluate the efficacy and safety of intradermal injection of Tranexamic acid and PRP in the treatment of different types of melasma.

METHODS

This split-face prospective study, which involved 40 patients with melasma, was carried out from June to December 2022 at the outpatient department of dermatology, Sri. Lakshmi Narayana institute of medical sciences, Puducherry. The inclusion criteria comprised of cases of either gender with age range of 20 to 50 years suffering from melasma. The diagnosis of melasma was made clinically on the basis of hyperpigmentation at sun-exposed areas and Wood's lamp examination. An informed consent was taken from each subject to include in this study and explained about the potential side effects of the drug/therapies, and ensured the confidentiality of the data. The detailed demographic and clinical data were recorded regarding age, gender, duration of melasma and severity of melasma labelled on the basis of standard MASI score.[16] Exclusion criteria included pregnancy, patients with known platelet dysfunction, patients with local inflammatory skin disorder and those with prior history of allergy to tranexamic acid. After explaining all the procedures to the subjects, the face was washed thoroughly. Topical anaesthetic cream Prilox (25 mg lidocaine 25 mg Prilocaine) was applied on the face for 45 minutes and then wiped off to obtain completely dry skin. Assessment of disease severity Digital photographs were taken for the lesions before and after the end of treatment by using Apple iPhone 13 Pro Max- camera 12 MP. Wood's lamp (Lumio®UV 3Gen- dermlite) and dermoscopic (by DermLite DL4 dermatoscope) examinations were conducted on all patients before the treatment to determine the type of melasma (epidermal, dermal, and mixed) as well as the vascular and pigmentation components of melasma.

The patients were administered intradermal injections of tranexamic acid. About 2U of tranexamic acid was drawn in a 40U/ml 30-gauge insulin syringe and diluted with normal saline up to 1 ml (remaining 38 U out of total 40 U) to get a concentration of approximately 4 mg/ml of tranexamic acid. Intradermal injections were given at the site of melasma, after application of topical aesthetic, keeping a distance of around 1 cm from each injection. Four sessions at intervals of 21 days were carried out. Various measures for strict photoprotection were explained to each patient. All patients were given the same sunscreen (of sun protection factor 50) for the entire 18 months. The left side of the face was treated with intralesional injection of PRP using 40U/ml insulin syringe.

Approximately 1 ml of PRP was injected intradermally for the lesions. To assess the clinical response, clinical photographs were taken at the beginning of the therapy and then serially after 21 days. mMASI scoring was performed at 21 days intervals and any adverse events and complications were recorded. The response to treatment in each patient was graded at the end of the study as: No response (no improvement), mild response (<50% improvement), good response (50% to 75% improvement). Each case was followed up for 6 months to look for further improvement/relapse.

The data was entered and analysed with the help of SPSS version 24.0 Frequencies and percentages were calculated for categorical data and mean and standard deviation for numerical data. Independent sample t-test was used for numerical data and Chi-square and Fisher's Exact t-test for categorical data and post stratification. A p value of 0.05 or less was considered significant. Institutional ethical committee clearance was obtained before the start

of the study and written informed consent was obtained from each participant before enrolling them in the study.

RESULTS

In our study, a total of 47 patients were included out of which 7 were excluded as per the exclusion criteria, a total of 40 patients were included in the study. Among the study participants, the majority were females (80%) and were in the age group of 20 to 30 years (50 %) followed by 30-40 years (35%).

Table 1: Socio demographic profile of the study participants.

Variables	N	%
Age (years)		
20-30	20	50
30-40	14	35
40-50	6	15
Gender		
Male	8	20
Female	32	80
Onset		
Gradual	37	92.5
Sudden	3	7.5
Type of melasma		
Centrofacial	21	52.5
Malar	15	37.5
Mandibular	4	10
Pattern of melasma		
Epidural	8	20
Dermal	5	12.5
Mixed	27	67.5
Total	40	100

Around 93% of the study participants had gradual onset of the disease while the rest 7 % had sudden onset. Majority of the melasma were Centro facial (52.5 %) followed by malar (37.5%) and mandibular (10%), mixed was the common type of pattern (67.5%) found in the side (Table 1).

Table 2: Comparison of mean MASI score.

MASI score	Before treatment (n=20)	After treatment (n=20)	P value
Tranexamic acid side	7.54±4.67	4.6±3.41	0.02
PRP side	6.92±5.0	2.83±2.91	0.003

*Independent t test was applied

In our study, the mean MASI score of the Tranexamic acid and PRP side before treatment was 7.54 and 6.92 respectively and post treatment MASI Score was 4.6 and 2.83 respectively (Table 2). When asked about the satisfaction of the treatment 53% of the patients in the Tranexamic acid side were very satisfied while 40 % of the patients in the PRP side were very satisfied (Table 3).

Table 3: Patient satisfaction between the sides.

Satisfaction	Tranexamic acid side (%)	PRP side (%)
Very satisfied	21 (52.5)	16 (40)
Moderately satisfied	16 (40)	18 (45)
Poorly satisfied	3 (7.5)	6 (15)

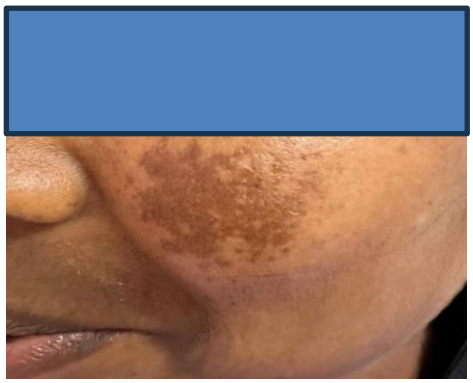

Figure 1: Before intradermal PRP injection.

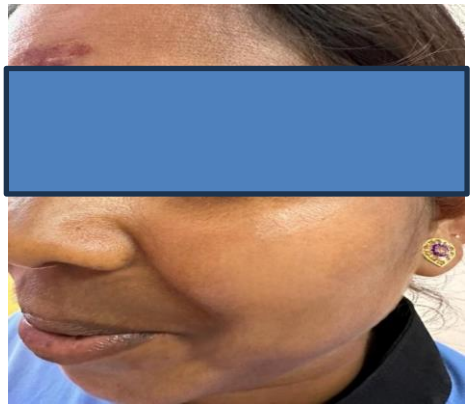

Figure 2: After intradermal PRP injection (4 sessions).

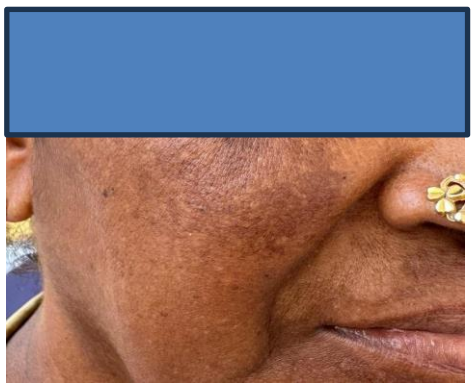

Figure 3: Before intradermal tranexamic acid.

Figure 4: After intradermal tranexamic acid (4 sessions).

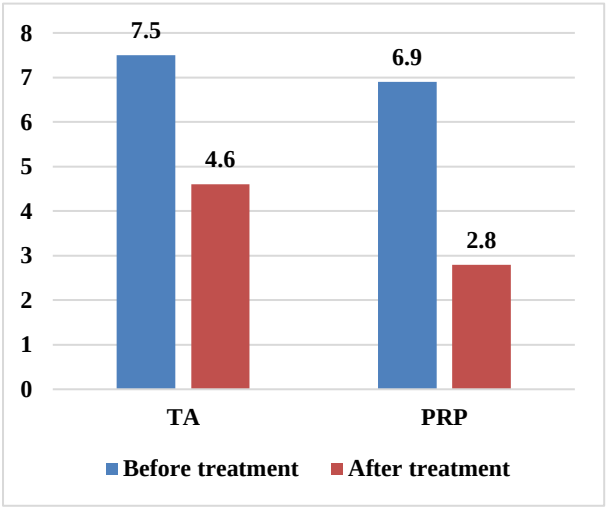

Figure 5: Distribution of study sides based on mean MASI score (n=40).

DISCUSSION

Melasma is a distressful condition for patients as it affects the face and has a negative impact on quality of the life of patients, affecting their psychological and emotional well-being. Although the exact mechanism of action of Tranexamic acid in treating melasma is unknown, it is generally accepted that it inhibits UV-induced plasmin activity in keratinocytes. First, Tranexamic acid prevents plasminogen and keratinocyte contact. This reduces the production of prostaglandins and free arachidonic acid, which in turn increases tyrosinase activity. Due to its ability to increase diffusible forms of vascular endothelial growth factor, plasmin is also involved in angiogenesis. Thus, by blocking plasmin, Tranexamic acid causes a decrease in angiogenesis. The urokinase-type plasminogen activator secreted by human keratinocytes is what drives melanocyte activity in vitro. Patients with melasma experience less hyperpigmentation because of Tranexamic acid's inhibition of this mechanism.[17] This split-face study included 40 cases with melasma, in which the right side of the face received intradermal tranexamic acid injection, while the left side received intradermal PRP injection. In the current study, Among the study participants, the majority were females (80%) and were in the age group of 20 to 30 years (50%) followed by 30-40 years (35%). Likewise In the study by Elraouf et al there were 39 females among the included cases who represented 97.5% of the cases.[18] This was in agreement with Ewaiss et al's study, which showed that all the included cases in their study were females and the studies by Serra et al and Jin et al.[19-21]

In our study, the mean MASI Score of the tranexamic acid and PRP side before treatment was 7.54 and 6.92 respectively and post treatment MASI Score was 4.6 and 2.83 respectively. A study by Elraouf et al the mean MASI score after treatment did not reveal a difference between the two sides that is statistically significant (2.49±1.58 and 2.17±1.41 in the Tranexamic acid side and PRP side, respectively).[18] However, the percentage of score reduction was higher in the PRP side (53.66±11.27) as compared with the Tranexamic acid side (45.67±8.10) (p=0.014). Our results agreed with those of Mumtaz et al who showed that Intradermal PRP was significantly better than intradermal tranexamic acid in the management of melisma. The mean mMASI score at baseline was 29.84±5.14 vs. 29.56±4.39 in the intradermal platelet-rich plasma side and tranexamic acid side, respectively, with no statistically significant difference between the two sides (p=0.21). mMASI was significantly better in the PRP side at 4 weeks in which p=0.01. Mean mMASI was 12.81±1.78 vs. 18.38±3.50, p=00,001 at 12 weeks and 8.72±3.40 vs. 14.97±4.33, p=0.02 at 24 weeks in the PRP side and tranexamic acid side, respectively.[7] Our results were in line with those of Gharieb et al who showed that there was a statistically significant difference, as evidenced by the mean difference in mMASI scores between the two sides (p=0.017). Patients who were treated with PRP saw more improvement.

This was in accordance with the results of Hofny et al who reported that the use of PRP is linked to a considerable to outstanding improvement in melasma patients, as demonstrated by the significant decline in the baseline MASI and mMASI scores, and in accordance with the levels of patients' satisfaction. Only two patients (8.7%) were unsatisfied with their improvement, whereas 39.1% of patients were very satisfied, 39.1% were satisfied, 13.1% were slightly satisfied, and 39.1% were satisfied overall.[23]

In the study by Gamea et al who compared the efficacy of topical tranexamic acid 5% in liposome base alone versus its combination with intradermal platelet-rich plasma for melasma treatment, patients of the combined Tranexamic acid+PRP side were more satisfied with the treatment outcome than those of the Tranexamic acid side and the difference was statistically significant.[24] In a study by Zhang et al., who investigated the effect of platelet-rich

plasma combined with tranexamic acid (Tranexamic acid) in the treatment of melasma and its effect on the serum levels of vascular endothelial growth factor (VEGF), endothelin-1 (ET-1), and melanin-stimulating hormone (MSH), they reported that PRP combined with Tranexamic acid can improve the treatment outcome, maintaining normal levels of VEGF, ET-1 and MSH, and reducing the recurrence rate.[25] Due of its autologous nature, PRP therapy has a higher safety profile. A further benefit is the abundance of growth factors which facilitate a number of mechanisms that result in facial rejuvenation.

Limitations

Limitations of this study include its single-center design, which may restrict the generalizability of findings to broader patient populations. The relatively small sample size and predominance of female participants within a specific age range further limit the applicability of results across diverse demographics. Additionally, the lack of randomization in treatment allocation introduces the potential for bias, affecting the interpretation of treatment outcomes.

The duration of follow-up may not have been adequate to assess the long-term efficacy and safety of the evaluated treatments. While the modified Melasma Area Severity Index (mMASI) scores were utilized, additional objective measures and patient-reported outcomes could provide a more comprehensive assessment of treatment efficacy and patient satisfaction. Factors such as concurrent medication use, hormonal fluctuations, and sun exposure, which can influence melasma progression and treatment response, were not fully controlled for. Furthermore, absence of a control group or alternative treatment arm limits direct comparison of the efficacy of intradermal Tranexamic acid and platelet-rich plasma with standard care or placebo. Future research endeavors should address these limitations to provide clearer insights into optimal melasma management strategies and patient outcomes.

CONCLUSION

Intradermal platelet-rich plasma demonstrates notable superiority over intradermal tranexamic acid in effectively managing melasma, particularly over extended durations. Integrating intradermal PRP into melasma treatment protocols promises accelerated results and improved outcomes, thereby enhancing patients' quality of life. Consequently, the utilization of PRP alongside adherence to treatment regimens presents a compelling strategy for significantly mitigating melasma compared to traditional approaches.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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