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Intralesional Tranexamic Acid vs Intralesional Autologous Platelet Rich Plasma in the Treatment of Resistant Melasma

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ABSTRACT

Objective: To compare intralesional tranexamic acid with intralesional autologous platelet rich plasma in the treatment of resistant melasma

Study Design: Quasi-experimental study

Place and Duration of Study: Departments of Dermatology, Pak Emirates Military Hospital and Combined Military Hospital Rawalpindi, Pakistan from Jun 2021 to May 2022.

Methodology: One hundred and forty diagnosed patients of melasma were randomized in 2 equal groups. Group-A was treated with Platelet rich plasma (PRP) mesotherapy while Group-B with intralesional Tranexamic acid. Melasma area treatment index (MASI) scores were calculated at baselines and at 16 weeks to monitor effectivity of both treatment modalities.

Results: Pretreatment MASI scores in Groups A and B were 21.08±6.08 and 21.44±6.36 (p=0.71). Post treatment MASI were significantly better at 16 weeks in Group-A at 7.79±1.86 as compared to Group-B at 9.15±4.69 (p=0.01). Difference in adverse effect profile between both groups was not significant.

Conclusion: Platelet Rich Plasma mesotherapy is a better treatment option for management of Melasma as compared to intradermal Tranexamic Acid.

Keywords: Melasma, Platelet Rich Plasma, Tranexamic Acid

How to Cite This Article: *Rehman M, Mashhood AA, Khan S, Hussain M, Hafeez J, Ghous I. Intralesional Tranexamic Acid vs Intralesional Autologous Platelet Rich Plasma in the Treatment of Resistant Melasma. Pak Armed Forces Med J 2025; 76(Suppl-1): S21-S24. DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-1.8989*

INTRODUCTION:

Melasma is a major cause of acquired facial melanosis, previously called chloasma.[1] It is a disease of adulthood more commonly affecting women, and despite in-depth studies its pathogenesis is still unclear.[2]

A wide range of predisposing factors are associated including family history, pregnancy, oral contraceptives, hormonal treatment, chronic solar exposure.[3] Despite the availability of a variety of treatment options like topical lightening agents, chemical peels, laser therapies and dermabrasion, its refractory and recurrent nature makes complete resolution difficult.[4]

Tranexamic acid is an antifibrinolytic agent, which was discovered as a cure for melasma incidentally, while being used for the control of chronic urticaria. The researcher noticed a significant improvement in melasma after 3 weeks.[5] Since then, various formulations of tranexamic acid including, topical, oral and intradermal have been studied as a therapeutic modality for melasma.[6]

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Received: 29 Jun 2022; revision received: 24 Jan 2023; accepted: 25 Jan 2023

Platelet Rich Plasma (PRP) is a form of regenerative medicine, generated by centrifugation of patients own blood.[7] Its ability to amplify natural growth factors has led to an ever-expanding use in various fields ranging from sports injuries to hair loss.[8] Platelets have an abundance of growth factors present in its alpha granules. Activated platelets release alpha granules containing more than thirty bioactive substances that lead to angiogenesis, collagen synthesis and decreased melanogenesis which has an overall 'rejuvenating effect'.[9]

Both these modalities are being used for management of melasma. The aim of this study was to compare these modalities and assess their adverse effects in local population of Pakistan.

METHODOLOGY

This Quasi-experimental study was conducted at the Departments of Dermatology of Pak Emirates Military Hospital Rawalpindi and Combined Military Hospital Rawalpindi, Pakistan from June 2021 to May 2022, after approval from the Institutional Ethical Review Committee (letter no. A/28/182 dated 29 Jun 2022).

Inclusion Criteria: Adult females aged 23-44 years, with a diagnosis of melasma based on clinical examination and woods lamp examination were

included.

Exclusion Criteria: Patients suffering from active facial infection or inflammation, photosensitivity, using oral contraceptives or hormone replacement therapy, pregnant, lactating females as well as those who were on active treatment for melasma or had any previous procedure such as PRP, Tranexamic Acid injection or Cryotherapy for melasma were excluded.

Sample size was calculated using OpenEpi Toolkit taking a mean difference of MASI scores pre and post procedure of 8.167±4.975 in PRP group, and 6.572 and 6.572±4.528 in Tranexamic acid group, which came to 140 individuals with 70 in each group.[10]

Patients presenting to Dermatology outpatient department in both these setups were included using non-probability consecutive sampling, after taking informed consent. A detailed medical history was taken, which was followed by dermatological examination of face. Skin type, type of melasma and severity of melasma were documented as per the MASI score.[11] Patients were requested to complete a questionnaire.

Patients were randomly distributed into two groups using balloting method, those in Group-A to be treated with intradermal PRP administered every 4 weeks for a total of 12 weeks (Figure-1). For the PRP group it was made sure that patients did not suffer from blood dyscrasias or bleeding abnormalities due to any underlying condition. Those in Group-B earmarked for TXA intradermal injections every 4 weeks for a total of 3 sessions.

Following this face was washed with water and soap to get rid of dirt or makeup. Lidocaine/Prilocaine (EMLA) 5% topical cream was applied for 30-45 mins and then wiped off to get dry skin.

PRP Preparation: In Group-A, phlebotomy was done and 20ml blood was drawn and mixed with sodium citrate anticoagulant. Platelets were concentrated in two step procedure using centrifuge machine. In first step centrifuge was spinned at 1500 RPM for 10 minutes in order to separate Red Blood Cells from plasma with platelets. In second step Plasma was spinned at 4000 RPM for 10 minutes, which created two layers, upper two third containing platelet poor plasma and lower third containing platelet rich plasma or PRP. Upper two-third platelet poor plasma was discarded. Insulin syringe was used to collect PRP and mixed with 0.1ml of calcium chloride per ml of PRP with aim to activate platelets. Finally, each squared centimeter of affected skin was injected intradermally with activated PRP using 30G insulin syringe.

Tranexamic Acid Preparation: In Group-B, Tranexamic acid preparation was used. It was prepared by taking 0.04ml of 100mg per ml (or 4mg) in an insulin syringe and filling rest with normal saline to make a 1ml solution. Each squared centimeter of affected skin area was injected intradermally using insulin syringe with this solution.

For both the groups, 3 treatments sessions were done at 4, 8 and 12 weeks. MASI score was recorded at baseline, [4, 8, 12] and 16 weeks. Feedback was also taken from patients regarding any adverse effect observed that included local bruising, edema, irritation, erythema and pain as per numerical rating scale.[1-10]

Data was analyzed using Microsoft Excel 365. Categorical data was expressed as frequencies with percentages, while quantitative data was expressed as Mean±SD. Both samples were compared using independent t-test for quantitative data and chi square test was ued for categorical data while considering *p*-value of 0.05 or less as significant.

RESULTS

A total of 140 cases were included in this study over a period of 9 months with 70 patients in each group. All included patients were females. Mean age of Group-A was 33.69±6.21 years and Group-B was 33.11±5.53 years (p=0.51). Duration of symptoms in Group-A and B were 35.49±18.44 and 36.28±17.86 respectively (p=0.77). Rest of Demographic features are summarized in Table-I.

Patients underwent treatment and were followed up at 16 weeks. Mean pretreatment MASI at start of treatment was 21.08±6.08 in Group-A and 21.44±6.36 in Group-B (p=0.72). MASI score was better at all further treatment cycles at 4, 8 and 12 weeks in Group-A as compared to Group-B (summarized in Table-II) however it was only significantly better (p<0.05) at week 12 (Figure-1).

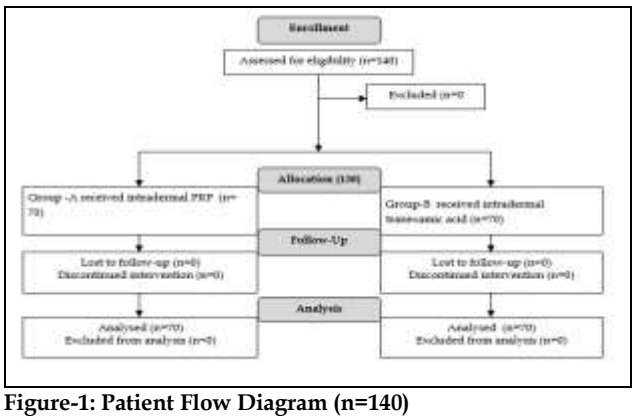

Figure-1: Patient Flow Diagram (n=140)

Table-I: Demographic Differences across Group (n=140)

		Group-A	Group-B	*p*-value
Pretreatment MASI (mean ± SD)		21.08±6.08	21.44±6.36	0.71
Post-treatment MASI	4 weeks (mean ± SD)	20.12±5.82	20.55±5.87	0.63
	8 weeks (mean ± SD)	15.25±4.25	16.35±5.10	0.13
	12 weeks (mean ± SD)	11.19±2.98	12.47±4.72	0.036
	16 weeks (mean ± SD)	7.79±1.86	9.15±4.69	0.014
Treatment Response (Percent improvement)		61.19%	56.36%	0.02
Adverse Effects	Bruising, n (%)	9(10.59%)	5(5.88%)	0.27
	Edema, n (%)	8(9.41%)	6(7.06%)	0.58
	Erythema, n (%)	58(68.24%)	69(81.18%)	0.06
	Irritation, n (%)	5(5.88%)	9(10.59%)	0.27
	Pain (mean ± SD) (Pain Scale 1-10)	3.45 ± 0.84	2.72 ± 0.83	<0.001

Post treatment MASI were significantly better at 16 weeks in Group-A at 7.79±1.86 as compared to Group-B at 9.15±4.69 (p=0.01).

Graphical representation of week by week drop in MASI score is given as in Figure-2.

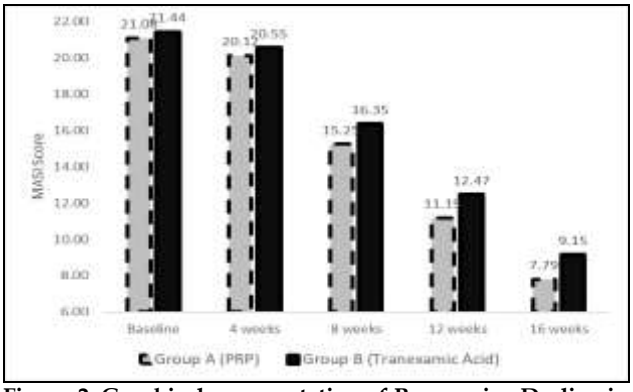

Figure-2: Graphical representation of Progressive Decline in MASI Score across Groups

Treatment response calculated as average percentage improvement on a case-by-case basis also had a significant difference between two groups with Group-A at 61.19%±10.13% and Group-B at 56.36%±16.59% (p=0.02).

Patients reported more pain during procedure in Group-A as compared to Group-B with mean Pain scale reading of 3.45 ±0.84 vs 2.72±0.83 (p<0.0001). The rest of side-effects profile (summarized in Table-II) had insignificant difference between two groups.

DISCUSSION

Melasma is a frequent presentation in the dermatology outpatient department. Although a benign condition the resulting cosmetic disfigurement is a cause of major concern and studies have shown that this has a significant impact on the quality of life.[12] Young females with a naturally brown skin (Fitzpatrick skin type III and IV) are more commonly affected.[13] The overall prevalence in Pakistan is still unknown but local studies reported that among pregnancy induced skin changes, frequency of melasma was 63.5% which is the reason it is also called 'the mask of pregnancy.[14,15] Its chronic nature makes treatment especially challenging and despite the availability of a variety of treatment options there is still no single long term effective modality.

Table-II: Comparative Results and Adverse Effects (n=140)

	Group-A		Group-B
Age (Years) (Mean ± SD)	33.69±6.21		33.11±5.53
Disease Duration (Months) (Meann ± SD)	35.49±18.44		36.28±17.86
Family History	25(29.41%)		27(31.76%)
Occupation	Employed, n (%)	24(28.24%)	23(27.06%)
	Housewife, n (%)	61(71.76%)	62(72.94%)
Previous Treatments, n (%)	71 (83.53%)		64(75.29%)
Skin Type	3, n (%)	41(48.24%)	39(45.88%)
	4, n (%)	43(50.59%)	43(50.59%)
	5, n (%)	1(1.18%)	3(3.53%)
Melasma Type	Epidermal	54(63.53%)	56(65.88%)
	Dermal, n (%)	31(36.47%)	29(34.12%)

In our study both tranexamic acid and PRP injections showed significant improvement in melasma. However intradermal PRP showed a statistically significant better response than TXA injections.

One study did a comparison between topical tranexamic acid alone and its combination with autologous PRP. Both the groups showed a statistically significant improvement in the mMASI score, however those treated with topical tranexamic acid plus PRP had statistically significant better improvement (p=0.024).[16] This shows that as compared to topical tranexamic acid, PRP has a significant response in melasma treatment. Our study has gone one step ahead and compared intradermal tranexamic acid with melasma.

Another study compared the efficacy of PRP vs intradermal tranexamic acid for melasma improvement. Like our study, both groups showed significant improvement however, the group that received intradermal PRP demonstrated significantly better improvement at week 4, 12 and 24.[17]

A recent study comparing intralesional PRP vs tranexamic acid took clinical images at every visit and calculated both MASI and mMASI scores. Both tranexamic acid and PRP were found to be safe and effective therapeutic options and although PRP mesotherapy was found to be slightly better than intradermal TXA the results were not statistically significant.[18]

Sirithanabadeekul et al. did the first randomized placebo-controlled trial study assessing the response of PRP in melasma. It was a split face study in which PRP was injected intradermally on one side of face and normal saline on the other. Evaluation at 6 weeks showed significant reduction in MASI score from 4.92±0.96 to 3.5±0.67, an improvement of 28.9% vs only 9% on the control side.[19]

LIMITATION OF STUDY

As we did not follow up patients for a longer duration of time, we cannot comment based on our results regarding lasting effectivity, recurrence, and long-term side effects of both treatment options. Our study also did not include male subjects due to lack of males consenting for procedures for management of melasma.

CONCLUSION

PRP mesotherapy is significantly better than intradermal TXA as a treatment option for melasma. Both the procedures are safe and effective with no long-term side effects.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MR & AAM: Data acquisition, data analysis, critical review, approval of the final version to be published.

SK & MH: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

JH & IG: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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