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ORIGINAL ARTICLE

Efficacy of intradermal injected tranexamic acid vs intense pulse light in the treatment of melasma.

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ABSTRACT… Objective: To compare the efficacy of Intradermal Tranexamic acid and Intense Pulse Light (IPL) in the treatment of melasma. **Study Design:** Interventional study. **Setting:** Department of Dermatology, HIT Hospital. **Period:** Dec 2022 to May 2023. **Material & Methods:** 88 Female aged between 18 and 50 with melasma were included in this study. Participants who have used topical treatments for melasma, with any medical illness or bleeding disorder, history of photosensitivity were excluded. Participants of ITA group received intradermal tranexamic acid in a concentration of 4mg/ml monthly for four sessions. While the participants of IPL group were treated fortnightly for four sessions. mMASI was used to calculate the severity of melasma before and 2 weeks after last session. Patients perception of treatment efficacy and side effects were noted in each group. SPSS-28 was used. Paired t- test and independent t- test was applied to compare the effectiveness of both treatment modalities. A p-value ≤0.05 was considered as significant. Chi square was used to compare the side effects of both the groups. **Results:** Paired t-test indicated a highly significant p-value of less than 0.000 in both the groups. mMASI-II scores of both groups were compared using an independent t-test, p-value was found to be statistically insignificant at 0.512. Participants in ITA group experienced more side effects, comparison of side effects between both groups was done using chi-square test, and p-value was found to be statistically significant at 0.002. **Conclusion:** ITA and IPL have emerged as secure and efficacious therapeutic choices.

Key words: Intradermal Tranexamic acid (ITA), Intense Pulse Light (IPL), MASI Score (Melasma Area and Severity Index), Melasma.

INTRODUCTION

Melasma manifests as irregular patches of skin discoloration on face. Skin types III and IV exhibit a greater susceptibility to developing melasma when compared to type II, and females within the reproductive age group are more prone to this condition than males.[1] For women, especially in today's digital age, experiencing unnatural skin color variations can be distressing, leading to psychological implications. It becomes imperative, therefore, to address both the physical manifestations and the associated psychological impact of melasma.[2]

Melasma arises from a combination of factors, including exposure to sunlight, genetic influences, and hormonal changes. The pathogenesis of this skin condition is intricate and extends beyond the mere involvement of melanocytes. Histological studies have uncovered a diverse array of features, such as basement membrane disruption, mast cell participation, neovascularization, and modifications in keratinocytes.[2,3]

Melasma treatment presents challenges due to the incomplete understanding of its pathogenesis, prolonged course, and high likelihood of recurrence.[4] The management plan includes suppressing melanocyte activity to prevent melasma aggravation through UV protection and avoiding triggers.[5,6] Topical therapies like hydroquinone, retinoids, and vitamin C inhibit new pigment formation, while procedures like microdermabrasion and chemical

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peels aid in melanin pigment removal. Laser and light treatments effectively disperse melanin pigment, offering a groundbreaking approach to dermatological care, particularly for melasma. By utilizing specific wavelengths matching melanin's absorption spectrum, these treatments precisely target affected areas while preserving the surrounding normal skin.[7]

The utilization of tranexamic acid (TA) in treating melasma is a promising and innovative approach. However, the exact mechanism of its action remains not entirely understood. The anti-plasmin activity of TA is believed to be the main factor responsible for the hypopigmentation observed in the skin. This is thought to occur through the shrinkage of dermal vasculature and the reduction of melanin production, achieved by decreasing tyrosine kinase activity and altering the interaction between melanocytes and keratinocytes. TA can be administered both orally and topically, and numerous studies have been conducted to explore its effectiveness in this regard.[8]

Various studies have been conducted to compare the efficacy of intradermal tranexamic acid with topical creams. The results have consistently demonstrated a significant improvement in melasma with TA mesotherapy when compared to topical creams.[9,10] Similarly, the efficacy of IPL has been evaluated in comparison with topical therapy in some studies. These investigations have revealed substantial improvement in melasma with IPL treatment when compared to topical creams.[11,12]

The available scientific literature on the comparison between intradermal injection of tranexamic acid (TA) and Intense Pulsed Light (IPL) therapy for melasma treatment is limited. As a result, the primary aim of this study is to rigorously assess and compare the efficacy of intradermal tranexamic acid and IPL in the management of melasma.

MATERIAL & METHODS

This interventional study was done in the Dermatology Department of HIT Hospital, Taxila from December 22 to May 23. After Ethical approval (letter no HITEC IRB 32-2023) 88 Female participants between the ages of 18 and 50 with melasma were enrolled through purposive sampling technique. History of photosensitivity, herpes simplex, pregnant and lactating mothers, individuals who have used topical treatments for melasma in the past two months, those with any medical illness or bleeding disorder, and individuals on anticoagulant therapy are excluded from the study.

Sample size was calculated to be 88 (44 females in each group) by using the hypothesis tests for two population proportions (one sided test). Intradermal Tranexamic acid in group A (P1= 31%)[13], IPL in group 2

B (P2= 49.5%).[11] Taking level of significance 5% and Power of test 80%, using the following formula

$$n=\{Z1-\alpha\ 2P(1-P)+Z1-\beta\ P1(1-P1)\ +\ P2(1\ -\ P2)\}^{2}\ \div\ (P1\ -\ P2)^{2}$$

After formal written consent comprehensive medical history and physical examination were conducted by a Dermatologist and documented on a structured proforma. mMASI score (Melasma Area and Severity Index) was used to assess the severity of melasma. Its range is 0-24, <8 is considered Mild, 8-16 is Moderate and >16 is Severe.[14]

For random allocation of patients in two groups, lottery method was used. 44 participants in group ITA received intradermal TA injection. Inj Tranexamic acid (TA) is available in 5ml ampoule having 500mg of transaxamic acid. In order to prepare a concentration of 4mg/ml, 4 IU of TA /96 IU of distilled water in insulin syringe was used for mesotherapy. Face was cleaned with alcohol swab then local anesthetic; Lignocaine cream was applied for 35-45 minutes. Injection TA was injected intradermal 1cm apart in the patch of melasma. Side effects were noted at each visit. We repeated the session after 4 weeks (i.e 0,4,8 and 12). Total duration of treatment in ITA group was 16 weeks while the participants of IPL group were treatmented fortnightly for four sessions using filters of 510nm for skin type III and 560 nm for skin type IV. Both groups used broad

spectrum sunblock of SPF 60. Total duration of treatment in IPL group was 8 weeks, with follow up after every 2 weeks (0,2,4,6). mMASI was again calculated 2 weeks after last session. Side effects were recorded and patient's perception of treatment efficacy was noted at the end of study as, Minimal= 0-25%, Moderate = 25-50%, Substantial=50-75%, Remarkable =75-100%.

Statistical analysis was done using SPSS-28. Means and standard deviation was calculated for age, duration of illness and MASI score. Qualitative variables like efficacy (minimal, moderate, substantial and remarkable response; implying a <25%, 25-50%, 50-75% and >75% reduction in MASI score from baseline respectively), marital status and sunscreen were presented in the form of frequencies and percentages. Difference in mean mMASI score in both the groups was assessed using paired t- test. Independent t- test was applied to compare the effectiveness of the two treatment modalities. A p-value ≤0.05 (5%) was considered as significant. Chi square was used to compare the side effects of both the treatment modalities.

RESULTS

This study comprised 88 female participants, with 44 individuals allocated to each group. The age range of participants spanned from 18 to 50 years, with a mean age of 34.48 ± 5.96 years in the IPL group and 31.95 ± 5.2 years in the ITA group. The mean duration of melasma was 3.94 ± 2.37 years in the IPL group and 3.81 ± 3.32 years in the ITA group, as illustrated in Table-I.

The mean MASI-I score in the IPL group before treatment was 14.04 ± 5.46. Following the treatment sessions, the MASI-II score decreased to 7.65 ± 3.89, and a paired t-test indicated a highly significant p-value of less than 0.000. Similarly, in patients treated with ITA group, the mean MASI-I score was 13.23 ± 6.19, which reduced to 7.03 ± 4.79 after treatment. The paired t-test yielded a statistically significant p-value of less than 0.000. When comparing the MASI-II scores of both groups using an independent t-test, the resulting p-value was found to be statistically insignificant at 0.512, as shown in Table-II.

Subjects in ITA group experienced more side effects as compare to IPL group, comparison of the side effects between both groups was done using the chi-square test, the p-value was found to be statistically significant at 0.002, as presented in Table-III.

In both groups, patient perceptions of treatment efficacy were noted, with the IPL group showing a greater level of perceived effectiveness in comparison to the ITA group, as shown in Figure-1

	IPL Group (N=44)		ITA Group (N=44)	
	Mean ± SD	**Percentage %**	**Mean ± SD**	**Percentage %**
Age (Years)	34.48± 5.96		31.95± 5.2	
Duration (Years)	3.94 ±2.37		3.81± 3.32	
Percentage Improvement	46.17±15.92		48.5± 22.11	
Marital status Married Unmarried		 95.45% (42) 4.54% (2)		 97.72% (43) 2.27% (1)
Use of Sunscreen Positive Negative		 50% (22) 50% (22)		 36.36% (16) 63.66% (28)
Skin type III IV		 72.72% (32) 27.27% (12)		 45.45% (20) 54.45% (24)

Table-I. Demographic data of participants

IPL Group			ITA Group			
Mean MASI-I	Mean MASI-II	*p-value	Mean MASI-I	Mean MASI-II	**p- value	***p-value between MASI II of both groups
14.04 5.46	7.65 3.89	0.000	13.23 ± 6.19	7.03± 4.79	0.000	0.512

Table-II. Comparison of treatment efficacy in both groups

*p- value in IPL group, **p- value in TA group, ***p- value between mean MASI II of both groups

	Side Effects	TA Group (N=44)	IPL Group (N=44)	Total (N=88)	P-Value
1	Nil	11 (25%)	26 (59%)	37 (42%)	0.002
2	Blebs	3 (6.8%)	0 (0%)	3 (3.4%)	
3	Erythema	16 (36.63%)	9 (20.45%)	25 (28.4%)	
4	Pain	11 (25%)	4 (9%)	15 (17%)	
5	Erythema and bleb	3 (6.8%)	1 ((2.27%)	4 (4.5%)	
6	Erythema and pain	0 (0%)	4 (9%)	4 (4.5%)	

Table-III. Comparison of side effects in both groups

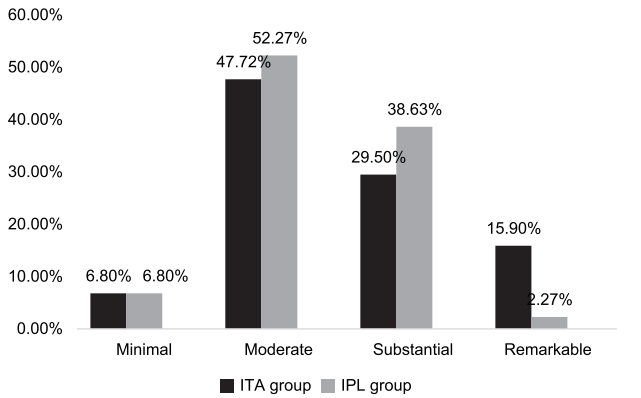

Figure-1. Patient perception of treatment efficacy in both groups (N=44 in each group)

DISCUSSION

The results of our study provide imperative insights into the effectiveness of ITA and IPL therapy in treating melasma. Findings of our study highlight the considerable efficacy of both intradermal tranexamic acid and IPL therapy in reducing melasma severity.

The findings of our study are consistent with the other studies. In a split-face clinical trial conducted in Iran by Tehranchinia et al in 2018, included 55 patients. This study compared the efficacy of tranexamic acid and hydroquinone (TA+HQ) or hydroquinone alone (HQ) treatment. By week 16, the TA+HQ group demonstrated significantly better therapeutic outcomes when compared to the HQ group ($p = 0.001$).[10] Another study conducted in Pakistan by Komal et al compared the efficacy of intradermal tranexamic acid (ITA) with topical azelaic acid (TAA). The study included 116 patients. The mean MASI score in ITA group before and after 6 weeks of treatment drop significantly. The difference in efficacy between the two groups was found to be statistically significant ($p = 0.001$).[13]

Another study done in Egypt by Fawzy et al, sixty females received weekly sessions of intradermal tranexamic acid treatment. The decrease in mMASI score after treatment was found to be statistically significant (p value < 0.001*).[15] In a quasi-experimental study by Muneeb et al, 170 patients were enrolled. These patients received monthly four sessions of intralesional injections of tranexamic acid and showed statistically significant differences ($p < 0.05$). The study concludes that intralesional microinjection of TA appears to be a promising and novel therapeutic tool for melasma treatment.[16]

The outcomes of our study align with those of previous research. A study in Egypt conducted by Arwa et al in 2018 compared the efficacy of IPL with PDL (Pulsed Dye Laser) in 28 female patients with melasma. Both treatments resulted in a significant reduction in the hemifacial mMASI score, with the IPL group showing better outcomes for epidermal melasma and lesions with a vascular component.[17] Another Egyptian study by Ilgen et al in 2019 included 101 patients of melasma stated that the number of IPL sessions allied with a decrease in the mean MASI score, supporting IPL's effectiveness in treating melasma. There

was a statistically significant correlation between the number of IPL sessions and MASI scores (p = .035).[18]

A meta-analysis done by Jiarong Yi in 2020 reviewed 8 studies involving 215 patients from various databases to assess the combined therapy of intense pulsed light (IPL) for melasma treatment. The results demonstrated a substantial reduction in MASI score (SMD = 0.61, CI [0.42, 0.80], P < 0.0001 for a fixed-effects model), while patient self-assessment using a four-point scoring scale revealed a significant improvement (RR = 1.44, CI [1.17, 1.76], P = 0.0004 for a fixed-effects model).[19] A study by Shakeeb et al in 2018 included three groups. There were compelling findings suggest that combining the triple combination cream with IPL treatment can yield superior outcomes in managing melasma compared to using either treatment alone.[20]

Furthermore, the patient perceptions of treatment efficacy were assessed, with a considerable number of individuals reporting moderate to substantial improvements in both the ITA and IPL groups. Additionally, we examined the occurrence of side effects, and the results indicated a statistically significant difference between the two groups (p = 0.002). Our study's findings are in accordance with the results of other research studies by Tehranchinia and Ilgen et al.[10,18]

In summary, while our study contributes valuable insights into the comparative efficacy of ITA and IPL therapy for melasma treatment, several limitations warrant consideration. The relatively small sample size and short duration of the study might not fully capture the potential long-term effects of the interventions. Future research with larger, more diverse samples and rigorous control measures is needed to further elucidate the potential of these therapies and address these limitations.

CONCLUSION

In summary, the findings of this study highlight the promising efficacy and tolerability of ITA and IPL therapy for melasma management. Importantly, it was observed that ITA was linked to a higher occurrence of side effects compared to IPL. Additionally, patient preferences leaned towards recognizing IPL treatment as more effective than ITA.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Tehseen Naveed	Data analysis, Interpretation.	
3	Javeria Hafeez	Discussion.	
4	Memoona Aslam	Revision, Write up.	
5	Sobia Awan	Drafting the manuscript, Revision.