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**ORIGINAL ARTICLE**

# Analysis of Intradermal Tranexamic Acid (Ta) vs Triple Combination (Hydroquinone 4%, Tretinoin 0.05%, Fluocinolone Acetonide 0.01%) Therapy for Melasma

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## ABSTRACT

**Objective:** Purpose of this study aims to compare the efficacy of intradermal tranexamic acid (Ta) therapy for the treatment of melasma with that of a fluocinolone-based triple combination therapy (Hydroquinone 4%, Tretinoin 0.05%, Fluocinolone Acetonide 0.01%).

**Study Design:** Comparative study

**Place and Duration:** Islamic Internatiomal Medical College Rawalpindi & Shahida Islam Medical Institute, Lodhran during the period from June ,2021 to December 2021.

**Methods:** There were 150 cases presented, including both sexes. All of the patients who were hospitalised for treatment had melasma. After obtaining agreement in writing, a thorough demographic profile was obtained. The patients were randomly split in half. Group A was treated with a fluocinolone-based triple combination (4% Hydroquinone, 0.05% Tretinoin, and 0.01% Fluocinolone Acetonide), while group B was treated with intradermal tranexamic acid (Ta). Effectiveness was measured by contrasting the two sets of results.

**Results:** We found that 80 (53.3%) patients were females and 70 (46.7%) patients were females. Among 150 cases, 75 (50%) had age 18-30 years, 50 (33.3%) patients had age 31-40 years and 25 (16.7%) patients had age > 40 years. Frequency of mixed melasma was higher among all cases followed by dermal and epidermal plasma. Frequency of malar-type melasma was significantly higher. We found that reduction in MASI score in group B was higher 1.9 from baseline 14.7 as compared to group A 6.1. Post-treatment we found side effects in group A and there was no any adverse outcomes observed in group B.

**Conclusion:** In this study, we found that intradermal tranexamic acid (TA) was an effective and safe technique for treating melasma, with no clinically relevant side effects and a substantial reduction in the MASI score.

**Keywords:** Melasma, MASI, Triple combination, Intradermal tranexamic acid

## INTRODUCTION

Melasma, named after the Greek word for "black," is a kind of restricted hypermelanosis that develops on sun-exposed skin.[1,2] It is an acquired hyperpigmentary condition that causes brown-black macules or patches to appear, most often, on the face.[3-6] Melasma can be symmetric or asymmetric.

The melanin content of melasma is evaluated with a Wood's lamp, and the following categories are established:[7]Epidermal type, in which colour is accentuated due to the excess of melanin in the basal or suprabasal areas. Increased staining is only evident in a small number of spots of mixed type, in which melanin is deposited in both the dermis and the epidermis. Some go so far as to describe a fourth kind, which only affects those with phototypes V and VI and hence is invisible in Wood's light. Centrofacial, malar, and mandibular describe its facial manifestations.

Current treatments include topical and systemic agents, light-based therapies, and lasers to remove and prevent recurrence of the lesions.[8] Other treatments include broad-spectrum sunscreens, retinoic acid (tretinoin), retinoids, ascorbic acid, tranexamic acid (TA), [9] and exfoliation (like salicylic acid and glycolic). The antifibrinolytic properties of TA stem from the protein's capacity to inhibit tissue plasminogen activator. Numerous surgical procedures, such as those involving the heart, the spinal, and joint replacement, have shown decreased blood loss and transfusion requirements (such as hip and knee replacements). To far, TA is the only medicine approved by the FDA for the treatment of heavy menstrual bleeding. It's not fair to compare the doses of TA used for antifibrinolytic purposes and the doses used to treat melasma. TA's bleaching effects are due to its capacity to block plasmin activity[10,11].

According to study results, intradermal TA was more effective than topical TA and a combination of 0.025 percent tretinoin, 2 percent hydroquinone, and 0.01% fluocinolone acetonide in reducing the severity of melasma. In a split-face randomised trial, TA intradermal injections once monthly reduced melanin content more than topical hydroquinone did in the first four weeks of treatment. Yet, even after 20 weeks, no significant changes had materialised .[12]

Both topical and intradermal administrations of ascorbic acid are effective treatments for melasma. Espinal-Perez et al. conducted a double-blind, randomised controlled research to compare the efficacy of ascorbic acid (5% concentration) and hydroquinone (4% concentration) in treating melasma. In this study, both treatments had positive results, and there were no noticeable differences in the colorimetric assessments. The percentage of patients reporting adverse effects was higher for those taking hydroquinone (68.7%) compared to those using ascorbic acid (6.2%). .[13]

Traditional methods of melasma prognosis, such as LASER and hydroquinone, have been shown to be more effective when combined with oral tranexamic acid[14], which has recently been used for the first time.[15] Due to the atrophogenic as well as other side effects of individual components of the combination therapy routine, concurrent the using verbal tranexamic chemical would assist in decreasing this same duration of active ingredient.

## MATERIAL AND METHODS

This comparative study was conducted at Islamic Internatiomal Medical College Rawalpindi & Shahida Islam Medical Institute, Lodhran during the period from June ,2021 to December 2021 and comprised of 150 patients. Following the collection of written consent, a thorough collection of demographic data was made. Patients who did not provide written consent, were known to have a history of coagulation disorder, were allergic to any of the study medicines, were pregnant or nursing, or had a history of bleeding disorders were not eligible to participate.

Patients' ages ranged from 18 to 50. There were a total of 150 patients, which were evenly split between two groups (A and B), each containing 75 people. Melasma lesions in Group A were treated topically with a fluocinolone-based triple combination (4%

hydroquinone, 0.05% tretinoin, and 0.01% fluocinolone acetonide) every night for three nights. All patients were instructed to take sun safety precautions, including applying sunscreen four times a day (at least 30 minutes before going outside), and carrying an umbrella or scarf with them at all times. After applying topical anaesthetic with lidocaine and prilocaine, patients in Group B received 0.05 mL of TA (concentration 4 mg/mL) intradermally into each 1 cm2 area of melasma every 15 days with an insulin syringe and 30-gauge needle. Patients in both groups were monitored every two weeks for a total of four evaluations to determine whether or not the treatment was effective. Every patient was carefully watched for any negative reactions during their therapy. Melasma improvement was measured using the melasma area maximum intensity (MASI) at each follow-up appointment. The MASI score was calculated by assigning weights to different parts of the face based on the subjective evaluation of their area (A), shadows (D), and uniformity (H). The middle of the head (d e), right malar area (rm), left malar area (lm), as well as chin (c) made up 30%, 30%, 30%, as well as 10% of the total face, respectively. Data was analysed using SPSS 22.0, and the final MASI score was computed as follows: Forehead = 0.3 (D+H) A + right malar = 0.3 (D+H) A + left malar = 0.3 (D+H) A + chin = 0.1 (D+H) A. The frequency and percentage breakdown of categorical variables were used for analysis.

## RESULTS

We found that 80 (53.3%) patients were females and 70 (46.7%) patients were females. Among 150 cases, 75 (50%) had age 18-30 years, 50 (33.3%) patients had age 31-40 years and 25 (16.7%) patients had age > 40 years.(table 1)

Table-1: Demographics of enrolled cases

| Variables | Frequency | Percentage |
|---|---|---|
| Gender | | |
| Female | 80 | 53.3 |
| Male | 70 | 46.7 |
| Age (years) | | |
| 18-30 | 75 | 50 |
| 31-40 | 50 | 33.3 |
| >40 | 25 | 16.7 |

Frequency of mixed melasma was higher among all cases followed by dermal and epidermal plasma.(figure 1)

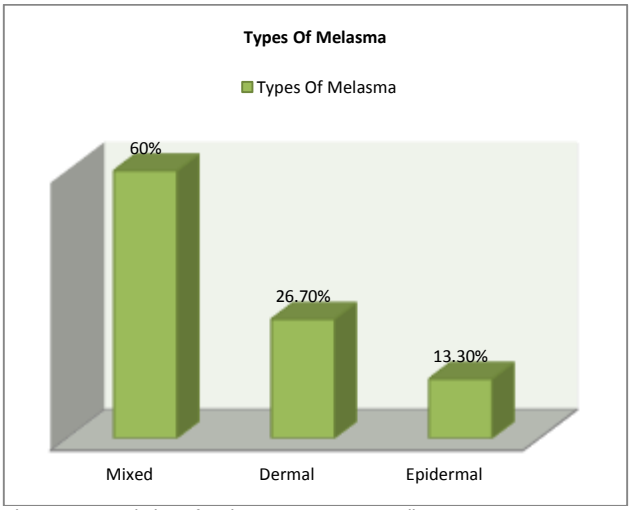


Figure-1: Association of melasma types among all cases

Frequency of malar-type melasma was significantly higher found in 92 (61.3%), centrofacial in 35 (23.3%) and mandibular in 23 (15.3%) cases.(figure 2)

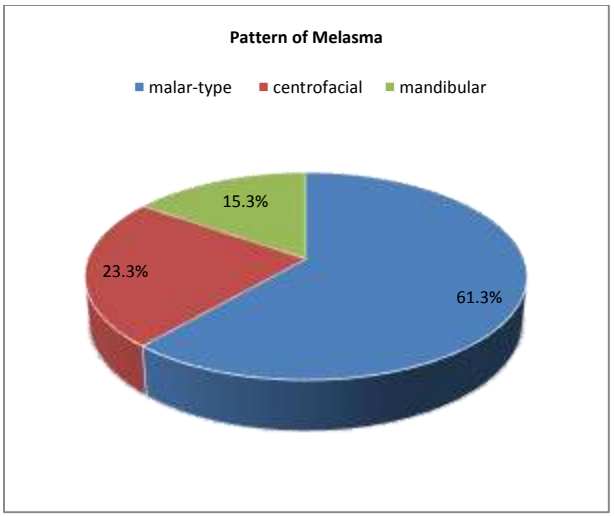


Figure-2: Pattern of plasma among all cases

We found that reduction in MASI score in group B was higher 1.9 from baseline 14.7 as compared to group A 6.1.(table 2)

Table-2: Outcomes of MASI in between two groups

| Variables | Group A | Group B |
|---|---|---|
| MASI Score | | |
| At start | 14.7 | 14.7 |
| Post-treatment | 6.1 | 1.9 |

Post-treatment we found side effects in group A 8 (10.7%) and there was no any adverse outcomes observed in group B.(table 3)

Table-3: Comparison of side effects among both groups

| Variables | Group A (75) | Group B (75) |
|---|---|---|
| Side effects | | |
| Yes | 8 (10.7%) | 0 |
| No | 67 (89.3%) | 75 (100%) |

## DISCUSSION

Melasma has long been a difficult treatment problem for dermatologists. There are a number of therapy options, each with its own set of potential adverse effects but shared goal of decreasing melanin synthesis. To add insult to injury, none of them are particularly helpful in triggering a long-term remission.

In cases of menorrhagia and major surgical procedures, tranexamic acid, also called as trans-4-aminomethyl cyclohexanecarb oxylic acid, is a helpful drug due to its plasmin inhibiting activity. It has been hypothesised that tranexamic acid, a plasmin inhibitor, can shield keratinocytes against UV radiation-induced melanogenesis[17]. In particular, plasmin raises levels of eicosanoids and melanocyte-stimulating hormone, both of which promote melanogenesis (- MSH). [18,19].

In our study 150 patients were presented. Among 150 cases, 75 (50%) had age 18-30 years, 50 (33.3%) patients had age 31-40 years and 25 (16.7%) patients had age > 40 years. Majority were females in our study. Findings were comparable to the previous studies.[20,21] Frequency of mixed melasma was higher among all cases followed by dermal and epidermal plasma. Frequency of malar-type melasma was significantly higher. In both our study and the study of Nicolaidou et al. [22], the mixed form of melasma was more prevalent. Epidermal melasma was determined to be the most common kind using the Wood's lamp examination, as reported by Achar and Rathi[23]. Environment or regional differences may be at the root of this shift in results. Our findings corroborate the findings of Singaporean and South Indian researchers Thappa[24] and Goh and Dlova[25].

We found that reduction in MASI score in group B was higher 1.9 from baseline 14.7 as compared to group A 6.1. 3% TA was used to suspend Ebrahimi &Naeini[26] from the skin on one side of the face, while 3% hydroquinone, 2% vitamin C, and 0.01% dexamethasone were used to do the same on the other side. Significant improvements were seen in MASI scores for both groups, with little to differentiate them. Our investigation led us to this conclusion. To evaluate how well weekly TA micro-injections work in treating melasma, researchers Lee et al.[27] have begun an open-label study with prospective participants. In a statistical sense, the MASI score went down from 12 to 8 after 12 weeks. To treat melasma, Shin et al.[28] studied the clinical safety and efficacy of oral TA in combination with 1064-nm quality-switched ferromagnetic materials yttrium aluminum alloy garnet (QSNY) laser.[29] Kato et al. used 750 mg of verbal tranexamic acid for four weeks in patients who received Q-switched Ruby laser.[29]

## CONCLUSION

In this study, we found that intradermal tranexamic acid (TA) was an effective and safe technique for treating melasma, with no clinically relevant side effects and a substantial reduction in the MASI score.

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