

# Comparison of Efficacy, Safety, and Patient Satisfaction with Tranexamic Acid Mesotherapy versus Ascorbic Acid Mesotherapy in Melasma

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## ABSTRACT

**Objective:** To determine the efficacy, safety, and patient satisfaction with tranexamic acid mesotherapy versus ascorbic acid mesotherapy in melasma.

**Methodology:** It was a quasi-experimental study conducted in the Department of Dermatology, Sharif Medical & Dental College, Lahore, after taking approval from the Institutional ethical committee. Eighty patients of either gender with melasma of any type (epidermal, dermal, or mixed) with Fitzpatrick skin type IV & V were enrolled in the study by non-probability convenient sampling technique. Patients were divided into two groups A & B, each group included 40 patients. Group A had tranexamic acid in mesotherapy and in group B mesotherapy was done with 20% ascorbic acid. Melasma severity score was calculated before and after each session using melasma area and severity index (MASI) score. The procedure was performed every 6 weeks, with a total of 3 sessions. Patients were followed-up after 6 weeks of the last treatment session to see any change in MASI score. The efficacy of the products used was assessed by comparing pretreatment MASI scores with posttreatment scores. Safety was established by assessing the side effects and observing the degree of tolerability to the products used. Patient satisfaction was evaluated using the Likert scale.

**Results:** In group A, 32(80%) patients responded effectively (>50% reduction in MASI score) whereas in group B, ascorbic acid mesotherapy was effective in 24(60%) of the patients. The difference in responses was statistically significant ( $p < 0.05$ ). Overall, the MASI score of both groups also declined. In group A, only 6 patients had complaints of mild irritation and burning over the treated areas, which subsided in a few days. In group B, 4 patients had transient itching after the procedure that settled with the use of emollients. Patients in group A were more satisfied as compared to group B.

**Conclusion:** Tranexamic acid mesotherapy is more effective as compared to ascorbic acid mesotherapy in patients with melasma.

**Keywords:** *Melasma. Ascorbic acid. Mesotherapy. Tranexamic acid.*

## INTRODUCTION

Melasma is chronic hyperpigmentation affecting the face symmetrically.<sup>1</sup> It presents as dark brown hyperpigmented patches, which become more prominent after solar exposure. It has a prolonged and reverting course, frequently associated with low self-esteem, despair, and frustration in patients. Affected patients usually suffer from a significant psychological impact due to this discoloration.<sup>2</sup> Management of this chronic disorder is frequently pressing. It is of utmost significance to understand the chronic, resistant, and relapsing nature of the disease along with the provision of guidance to the patient about the importance of photoprotection, iron deficiency, hormonal disproportion, and other factors, before initiating any invasive therapy. This chronic cutaneous hyperpigmentation is frequently resistant to various therapies and management is challenging and frustrating both for the patient as well

as for treating physicians.<sup>3</sup> Melasma is classified into epidermal, dermal, and mixed types, based upon Wood's lamp examination. Melasma area and severity index (MASI) score is used to assess the severity of melasma. A variety of options are available for the management of this chronic relapsing disorder, which include topical therapies as well as oral and procedural options. Commonly used procedures include chemical peeling, microinjections, and lasers.<sup>4</sup> Mesotherapy has been introduced recently in the management of a variety of dermatological disorders. The technique involves a minimally invasive, non-surgical method of drug delivery intradermal.<sup>5</sup> Apart from melasma, it has shown promising results in skin rejuvenation, androgenetic alopecia, and body contouring.<sup>6</sup> Using mesogun and meso needles the drug is delivered intradermal to produce the desired effect. A variety of agents are being used with mesotherapy in the management of melasma with variable results.<sup>7</sup> Owing to variation in skin types and increased risk of post-inflammatory hyperpigmentation, in darker skin types, the results cannot be precisely applied in the local context. The two most common agents used in mesotherapy are tranexamic acid (TA) and ascorbic acid. Recently, tranexamic acid has been used as an innovative treatment for melasma.<sup>2</sup>

Tranexamic acid employs anti-pigmentary effects via

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its inhibiting UV light-induced plasminogen activator and plasmin activity. Following UV radiation, the synthesis of plasminogen activator by keratinocytes is induced, resulting in the amplified conversion of plasminogen to plasmin. Plasminogen activator itself leads to increased melanin synthesis by inducing tyrosinase activity.<sup>8</sup> The conversion of plasmin consequences in melanogenesis and neovascularization due to augmented production of both arachidonic acid and fibroblast growth factor by plasmin.<sup>3</sup> By inhibiting plasminogen activation, tranexamic acid lessens UV melanogenesis and neovascularization produced by exposure to ultraviolet light.<sup>2</sup> Ascorbic acid exerts its anti-pigmentary effects via its antioxidant effects and on its effect on tyrosinase inhibition.<sup>9</sup> It has shown its efficacy when given intravenously in a variety of ailments like recurring infections, malignancies, ischemic heart disease, rheumatologic, and metabolic disorders. It promotes healing in fractures, wounds, ulcers, and pressure sores as well.<sup>10</sup> Anti-pigmentary effects of ascorbic acid are due to its ability to chelate copper ions, resulting in inhibition of intracellular enzymatic steps obligatory for pigmentation. Owing to its hydrophilic and unstable molecule, it possesses poor penetration into the skin due to the hydrophobic stratum corneum. Additionally, the negatively charged structure of ascorbic acid limits its penetration.

In the local context, TA mesotherapy has been studied, but the data pertaining to efficacy & safety of ascorbic acid, its comparison with TA, and evaluation of patient's satisfaction is limited. To the best of our knowledge, it's the first study, comparing the two newer agents. Results of this comparison may provide a better understanding and insight for the selection of agents in mesotherapy based upon duration and type of melasma.

### METHODOLOGY

The study was conducted in the Department of Dermatology, Sharif Medical & Dental College, Lahore after taking approval from the Institutional ethical committee (No: SMDC/SMRC/179-21, 26-03-2021). The study was conducted from April to September 2021. It was a quasi-experimental study. A total of 80 patients were included in the study, using the non-probability convenient sampling technique. Patients were divided into two groups A & B, each group included 40 patients. Group A had TA in mesotherapy and group B mesotherapy was done with 20% ascorbic acid. The sample size was calculated by using the WHO calculator for groups for the difference in the proportion of 20% between the groups giving the significance of 0.05 and power of 80%. Patients with

Fitzpatrick skin type IV & V on physical examination, between ages 18-40 years, having melasma (epidermal, dermal, or mixed type under Wood's Lamp examination), and who had not responded to at least one of the topical treatments for melasma in past 6 months were included. Patients on oral contraceptive pills, pregnant and lactating females, those with active acne, herpes simplex infections, keloid or hypertrophic scars at the site of melasma were excluded from the study, due to the possibility of worsening of the disease after the procedure. Patients on systemic steroids from the last 6 months, vitiligo, history of photosensitivity, and patients with a history of bleeding disorder were also excluded. A written and informed consent was taken from the patients after explaining the procedure in detail. A detailed personal, medical, and family history was taken. Melasma severity score was calculated before and after each session using melasma area and severity index (MASI) score. This was used to quantify the severity of melasma and changes observed during therapy.

After gentle cleaning, topical anesthetic 10.56% lidocaine cream (LeedFrost)<sup>R</sup> was applied over the area to be treated for about 30-40 minutes, to produce an adequate numbing effect. Photographs were taken before and after treatment, with the patient's consent. In group A, injection Transamine of 500 mg/5 ml ampoule was used. It was diluted in an insulin syringe of 100 IU with normal saline to give strength of 4 IU (4 mg) of TA and 96 IU of normal saline.<sup>2</sup> Pure L-ascorbic acid 20% (locally dispensed in pharmacy) was used all over the affected area in patients of group B. In both groups, multiple microinjections were given on patches of melasma. The patients were advised to follow protecting measures against sunlight and use sunscreens with sun protection factor SPF 50+ even at home. The procedure was performed every 6 weeks, with a total of 3 sessions. Patients were followed-up after 6 weeks of the last treatment session to see any change in MASI score. Since the treatment protocol for mesotherapy is still under debate, we performed every 6 weeks, with a total of 3 sessions to allow for full recovery in between the sessions. Patients were evaluated for any complications such as infection, irritation, peeling, and redness. The efficacy of the products used was assessed by comparing pretreatment MASI scores with posttreatment scores. Fifty percent or greater reduction in MASI score after 3 treatment sessions were considered to be effective. Safety was established by assessing the side effects and observing the degree of tolerability of the products used. Patient satisfaction was evaluated using a Likert scale of 1-5, (1=extremely satisfied, 2=satisfied, 3=moderately

satisfied, 4=dissatisfied, 5=extremely dissatisfied). Percentages of the respondents in grade 1 & 2 were combined to be categorized as extremely satisfied, grade 3 was taken as moderately satisfied and respondents in grade 4 & 5 were combined in the category of extremely dissatisfied.

**STATISTICAL ANALYSIS**

Data entry and analysis was done using Statistical Package for the Social Sciences (SPSS) version 23. Categorical data was presented by using mean and SD. Frequencies and percentages of efficacy, safety, and patient satisfaction to treatment in both groups were reported. Data was stratified for duration of disease in both groups and then compared using the Chi-square test. Improvement in MASI score was compared by independent t-test. A p-value of ≤0.05 was taken as significant.

**RESULTS**

The demographic details of patients in both groups are mentioned in Table 1. In group A, 32(80%) patients responded effectively (>50% reduction in MASI score) whereas in 8(20%) patients TA mesotherapy was not effective. In group B, ascorbic acid mesotherapy

was effective in 24(60%) of the patients while in 16(40%) patients treatment was not effective. The difference in responses was statistically significant (p <0.05). Overall, the MASI score of both groups also declined 6 weeks after the last session. Pretreatment scores declined from 18.78±10.32 to 5.44±2.11 in group A, and from 19.44±12.41 to 7.44±5.21 in group B (Table 2). A statistically significant difference was found in both groups, when pretreatment MASI score was compared to posttreatment score after 6 weeks (p-value=0.0001).

The data was stratified based upon the duration of disease. The patients with a longer duration of disease (>2 years) had significantly less response compared to opposites in both the groups (Table 3).

Safety was established by evaluation of side effects. In group A, only 6 patients had complaints of mild irritation and burning over the treated areas, which subsided in a few days. In group B, 4 patients had transient itching after the procedure that settled with the use of emollients. At the end of 3 sessions, the patient's satisfaction was calculated.

In group A, 28(70%) patients were extremely satisfied, 10(25%) were moderately satisfied, and 2(5%) were dissatisfied. In group B, 20(50%) patients were

**Table 1: Demographic Details of Study Groups**

Study Variables		Group A	Group B
Gender	Male	12	14
	Female	28	26
Mean Age (Years)		22.07±4.003	29.27±3.071
Mean Duration of Disease (Years)		11.43±1.340	10.87±1.320

**Table 2: Comparison of Pretreatment and Posttreatment MASI Scores in Group A & B**

Study Groups	Pretreatment	Posttreatment	p-value
A	18.78±10.32	5.44±2.11	0.0001*
B	19.44±12.41	7.44±5.21	

\*Significant p-value

**Table 3: Stratification of Data on the basis of Duration of Melasma**

Group	Duration of Disease (Years)	Number of Patients	Effective n(%)	Not Effective n(%)	p-value
A	<2	31	29(72.5%)	2(5%)	<0.05
	>2	9	3(7.5%)	6(15%)	
B	<2	28	22(55%)	6(15%)	
	>2	12	2(5%)	10(25%)	

extremely satisfied, 15(37.5%) were moderately satisfied, and 5(12.5%) were dissatisfied respondents (Figure 1).

## DISCUSSION

Melasma is a chronic disorder of hyperpigmentation. It generally has a chronic and relapsing course and affected individuals are frequently depressed and stressed.<sup>1</sup> A variety of management options are available for this condition but the results are highly variable. Various topical and invasive treatment modalities are available across the globe with variable results.<sup>2</sup> Various agents have been used in mesotherapy for the management of melasma. Literature review reveals that tranexamic acid and ascorbic acid have been used either alone or in combination with peeling agents in patients with melasma, with variable results. In this study, we compared tranexamic acid mesotherapy with 20% ascorbic acid in mesotherapy in patients with melasma. This study showed that the duration of melasma ranged from 1 to 10 years. According to results, 80% of the patients treated with tranexamic acid mesotherapy had an effective response, while those with ascorbic acid mesotherapy had a 60% success rate in terms of decline in MASI score.

Kaleem et al. reported a significant reduction in MASI score with tranexamic acid mesotherapy. They reported a significant decline in the mean score ( $p < 0.05$ ). They also reported minimal side effects from this agent and declared it to be a safe and cost-effective therapy for the management of this chronic disorder.<sup>2</sup> The results of this study were in accordance with the current study, as it was found that average MASI scores in the TA group was  $18.78 \pm 10.32$  prior to the treatment sessions and

dropped down to  $5.44 \pm 2.11$  after 3 mesotherapy sessions, representing a drop by  $14.22(68.11\%)$  in the MASI scores of this group.

Ascorbic acid formulations have been introduced in the recent past and are extensively utilized in mesotherapy; however, data pertaining to its safety and efficacy in the management of melasma is limited.<sup>11</sup>

Literature review reveals that most of the studies are limited to the role of a topical form of ascorbic acid in the treatment of melasma. Irajji et al. compared a cocktail of TA, ascorbic acid, and glutathione with TA and ascorbic acid cocktail, in a split-face, double-blinded randomized controlled trial. Improvement was more in the triple agent-treated group, however, the colorimetric comparison was similar in both the groups.<sup>5</sup> McKesey et al. conducted a systematic literature review of all the treatment options available for melasma. He reported that oral tranexamic acid may be a safe, systemic adjunctive treatment for melasma and suggested more studies to establish its efficacy.<sup>12</sup> Lueangarun and colleagues reported significant efficacy of TA mesotherapy in patients with melasma, however, at 48 weeks follow-up majority of the patients developed recurrence.<sup>13</sup> Balevi et al. used salicylic acid peel and compared it with salicylic acid peeling combined with ascorbic acid mesotherapy in patients with mixed types of melasma. He reported a significantly better outcome in terms of improvement of MASI score in the ascorbic acid treated group.<sup>14</sup> Our study found an effective response by the intradermal application of ascorbic acid. Karrabi et al. compared topical cysteamine 5% cream with TA mesotherapy in patients with melasma and reported significantly better results in the group treated with TA.<sup>15</sup>

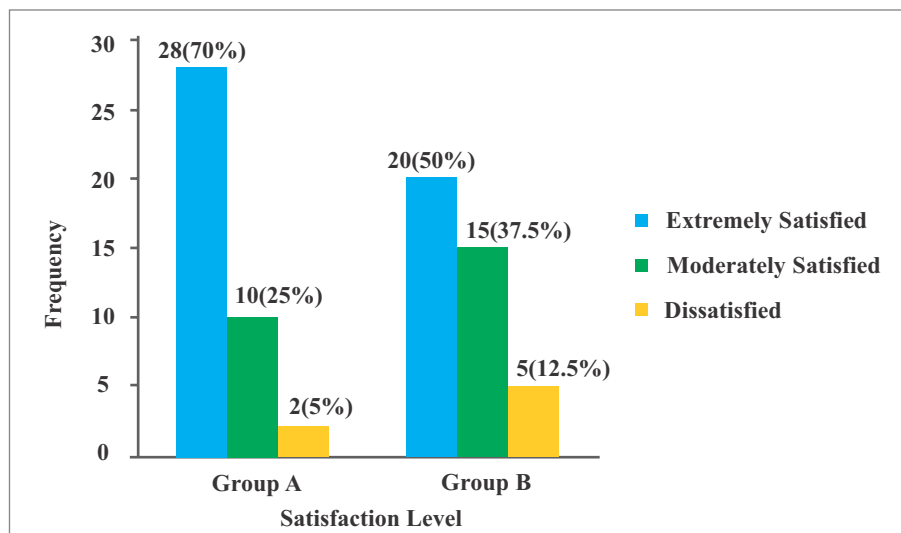


Figure 1: Patients' Satisfaction with therapy



## CONCLUSION

Both tranexamic acid and ascorbic acid mesotherapy are safe and effective management options for the treatment of melasma. Tranexamic acid, however, is significantly better in terms of reduction in MASI scores.

## LIMITATIONS & RECOMMENDATIONS

The study needs to be seen in the context of its limitations. The study included a small sample size and was conducted at a single center with a short-term follow-up. However, the accordance of the results with those from across the globe suggests the generalizability of the results. Further research to evaluate the efficacy of other treatment modalities like lasers or other agents combined with TA or ascorbic acid mesotherapy is recommended.

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