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Original Research Article

A study of intradermal tranexamic acid for treatment in melasma patients

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ABSTRACT

Background: Melasma is a common acquired pigmentary dermatosis due to a disorder in the melanogenesis process. Although several treatments are currently used, it remains a great challenge. It was recently reported that intradermal tranexamic acid (TA- plasmin inhibitor) is an effective treatment for melasma. Aims of the study were to assess the efficacy and side-effects of localized microinjection of TA for the treatment of melasma.
Methods: A total of 30 patients with melasma, who did not respond to topical therapy were included in the study, after taking informed consent. The severity and extent of pigmentation was assessed by modified melasma area severity index (MASI). Patients were then administered localized microinjections (10 mg/ml) of TA weekly for 6 weeks. The response to treatment was assessed by MASI and clinical photographs at each session and after 3 months of stopping treatment.
Results: Among 30 patients significant decrease in the MASI from baseline was observed. 36.6% patients showed >75% improvement, 43.3% showed 50-75% improvement, 6.8% showed 30-49% improvement, and 13.3% showed <30% improvement at the end of 6 weeks. Side effects were minimal, and all the patients tolerated the treatment well. At 12 weeks 32% of patients developed mild recurrences and the rest of the patients maintained the same MASI.
Conclusion: Based on our results, intradermal TA (10 mg/ml) can be used as potentially new, effective and safe treatment for melasma.

Keywords: Intralesional, Melasma, Tranexamic acid

INTRODUCTION

Melasma, also known as chloasma, is the most common cause of benign acquired facial melanosis, due to a disorder in melanogenesis functional process.[1] Melasma is manifested by hyperpigmented macules or patches, commonly occurs in females with dark skin types living in areas of intense ultraviolet (UV) light exposure.[2] Several factors like UV radiation, pregnancy, hormonal activity, thyroid abnormalities, and medications trigger the synthesis of melanosomes and increased melanosomes transfer to keratinocytes.[3] Treatment of melasma poses a great challenge due to recurrence and refractory nature. Various treatment modalities are available, these include sunscreens, hypo pigmenting agents, dermabrasion, chemical peels, and laser therapy.[1,4]

Tranexamic acid (TA), a newer treatment modality for melasma is a hemostatic agent, has hypo pigmentary effect and also prevents ultraviolet-induced pigmentation.[5,6] In addition to its hemostatic effects, it also exhibits anti-allergic and anti-inflammatory effects in angioedema like conditions.[7] Its anti-inflammatory property appears to be related to its inhibitory effect on melanogenesis.[5,7] In 1979,

Nijor used TA to treat chronic urticarial patients, this was accidental discovery and reported the action of tranexamic acid in melasma.[8] Tranexamic acid when administered in its oral and topical forms or injected locally reported to improve melasma. The aim of the study is to study the efficacy and side effects of intradermal TA (10 mg/ml) in melasma.

METHODS

The study was conducted for a period of 1 year from August 2018 to August 2019 in Department of Dermatology at Dr. PSIMS & RF, Chinnoutapally. The sample size was 30.

Inclusion criteria

Inclusion criteria was as follows: all the patients with melasma who have not responded to conventional topical therapy (kligmans regimen) patients who have developed recurrences after stopping kligmans.

Exclusion criteria

Pregnancy and lactating women were excluded from the study.

Methodology

Participants who met the fixed criteria were included in the study. After explaining about the study, informed consent was taken from the participants and detailed history was taken regarding the duration of melasma and previous treatment used. The lesions were examined under woods lamp and dermoscope. Modified melasma area and severity index (MASI) scoring system (Figure 1) was used to assess the severity of melasma and to compare the response in each patient with their initial score to find the improvement.[1] Patients were administered intradermal injections of tranexamic acid. 4 U (10 mg/ml) of tranexamic acid was drawn in a 40 U/ml 30 gauge insulin syringe and diluted with normal saline up to 1 ml (remaining 36 U out of total 40 U). Intradermal injections were given at the site of melasma, after application of topical anesthetic, keeping a distance of around 1 cm from each injection. Six such sessions at a week interval were carried out. Various measures for strict photoprotection were explained to each patient, for better and sustained improvement. All patients were given the same sunscreen (of sun protection factor 50) for the entire 3 months. To assess the response, clinical photographs were taken at each visit; modified MASI scores were calculated at the beginning and end of each session. Final response was evaluated according to the MASI scores and clinical photographs. Any complications and side effects were noted during each visit and the patients were examined at monthly intervals to look for any relapse or side effects for another 3 months.

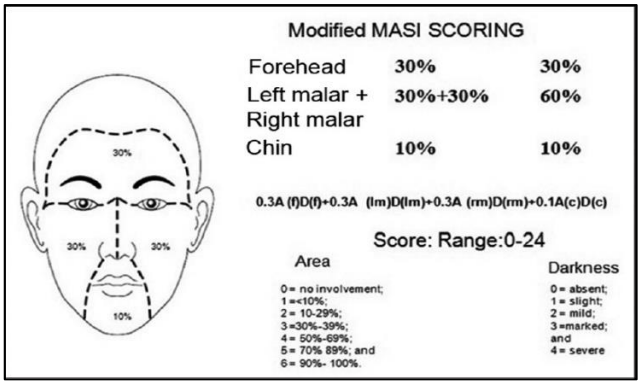

Figure 1: Modified melasma area and severity index scoring.

RESULTS

All the 30 patients belonged to the age group of 25-40 years. The number of women was more (21) compared to men (9). All the patients had skin type 4 or 5. 17 (56.66%) patients had mixed pattern of melasma, 9 (30%) had epidermal and 4 (13.33%) had dermal (Table 1). The distribution of melasma was either centrofacial or malar (Table 1). None of the patients were on any drugs.

Table 1: Distribution of subjects according to age group, pattern of melasma and types of melasma.

Variables	Number of subjects (%)
Age group (in years)	
25-30	7 (23.33)
30-35	10 (33.33)
35-40	13 (43.33)
Pattern of melasma	
Centrofacial	12 (40)
Malar	18 (60)
Type of melasma	
Epidermal	9 (30)
Dermal	4 (13.33)
Mixed	17 (56.66)

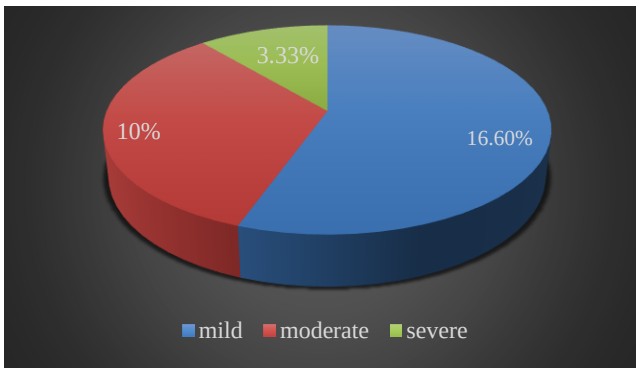

Figure 2: Response percentage.

Table 2: Mean melasma area and severity index score of the patients at the beginning and end of the study with percentage improvement is shown below.

	Mean pre MASI	Mean post MASI	Percentage of improvement	P value between pre and post MASI
Intralesional TA	7.766	2.686	63.01%	<0.0001

Table 3: Mean melasma area and severity index score of the patients at the end of the study and 3-months after follow-up is shown below.

	Mean post MASI	Mean MASI after 3 months follow up	P value between post MASI and follow up MASI
Intralesional TA	2.686	3.276	>0.1

Out of 30 patients, 36.6% showed greater than 75% improvement, 43.3% showed 50-75% improvement, 6.8% showed 30-49% improvement, 13.3% showed <30% improvement (Figure 2).

Mean melasma area and severity index score of the patients at the beginning and end of the study with percentage improvement is shown in Table 2. Mean decrease in melasma area and severity index score before and after treatment was seen. The percentage of improvement was 63.01% with p<0.0001.

After 3 months of follow-up

Only 31% showed re-pigmentation after 3 months. we classified re-pigmentation in to mild, moderate and severe. 1-2% increase of MASI from post treatment MASI is considered as mild re-pigmentation, 2-3% increase from post treatment MASI as moderate re-pigmentation. >3% increase from post treatment MASI as sever re-pigmentation. Only 10% showed severe re-pigmentation in our study (Figure 3).

Mean melasma area and severity index score of the patients at the end of the study and after 3 months follow-up shown in Table 3. There is no significant increase between post treatment MASI and 3 months follow up MASI, with p>0.1.

Adverse effects

All the patients experienced injection site pain. Blebs are formed at injection site, lasted for 3-4 hours after treatment.

DISCUSSION

Tranexamic acid (trans 4 amino methyl cyclohexane carboxylic acid) is a plasmin inhibitor used to prevent abnormal fibrinolysis to reduce blood loss. TA leads to the inhibition of the plasminogen activator from transforming plasminogen in to plasmin. Plasminogen is also found in the basal layer of the human epidermis.[9] The main mechanism of the hypo-pigment effects of TA is due to its antiplasmin activity.[10]

In addition, TA is similar to tyrosine in a portion of its structure, which can inhibit tyrosinase competitively.[11] Also, plasmin transforms the vascular endothelial growth factor (VEGF) into a diffusing form, and histological examination showed that TA plays an important role in the reduction of erythema and vascularity and the number of mast cell in the dermis.[12,13]

The usual effective oral dose of tranexamic acid for melasma is 250-500 mg, 2-3 times daily. Commonly reported side effects include nausea, diarrhoea, orthostatic reactions, disturbances in colour vision, occasionally anaphylactic shock and acute renal cortical necrosis.

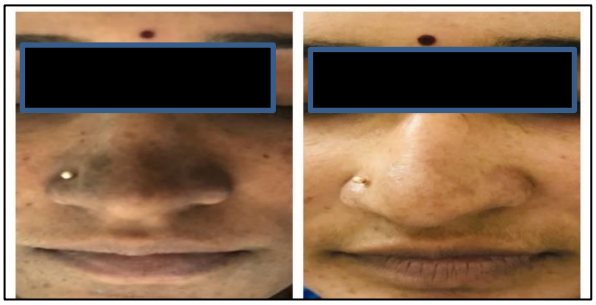

Figure 4: Before and after treatment response.

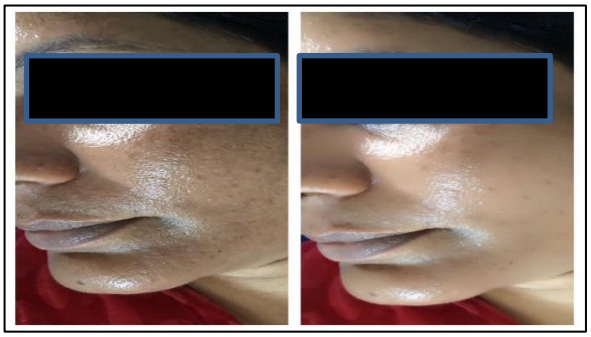

Figure 5: Before and treatment response.

Localized microinjection, also known as mesotherapy, is a widely used technique in medicine. It aims at directly applying an adequate amount of medication at the given site thus avoiding oral medications. This allows lower

dosage of drugs to be used and minimizes side effects caused by oral TA.

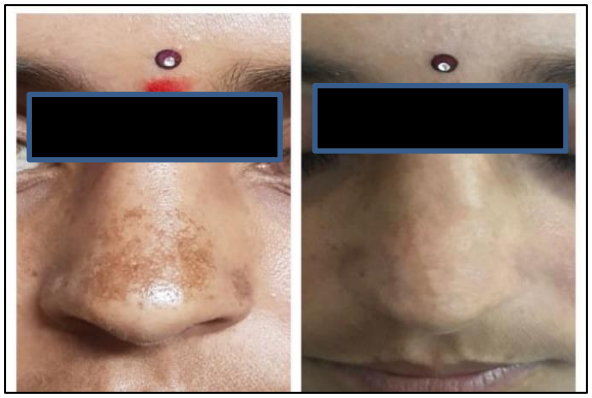

Figure 6: Before and after treatment response.

In prospective comparative study in 2018, Shetty et al concluded intradermal tranexamic acid has a higher clinical improvement compared to oral TA.[14]

Sharma et al during a study in 2016, concluded that there is no significant difference in MASI reduction score between oral TA and intradermal TA.[15]

In a comparative study, 2019 by Khurana et al done on 64 patients concluded that oral group showed better results compared to microinjections.[1] They conclude that Increasing the frequency and dose of intralesional injections to once a week rather than a month would increase the efficacy. Saki et al used 20 mg/ml TA injection monthly 3 months, concluded that monthly TA injection was better than daily HQ.[16] The Table 4 shows comparison of different studies with our study. Pazyar et al in his study using TA 4mg/ml once in three weeks in group A got 61.1% reduction in mean MASI, and only 30% reduction in mean MASI was observed using 10 mg/ml TA once in 3 weeks in group B, whereas in our study by using 10 mg/ml TA once in every week we got 63.01% reduction in mean MASI.[17] Differences in response between the studies may be due to many factors such as genetics, severity, duration and type of melasma, study design, etc.

Table 4: Comparison of our study with different studies

Studies done by different authors	TA concentration (mg/ml)	Percentage of Mean MASI reduction (%)
Shetty et al[8]	4	35.6
Sharma et al[9]	4	79.00
Khurana et al[1]	4	43.55
Pazyar et al[11]	Group A (4) Group B (10) (once in 3 weeks)	61.1 30
Our study	10 (weekly)	63.01

CONCLUSION

On the basis of the above findings, tranexamic acid can be used as a safe and effective therapeutic agent for the treatment of melasma. We conclude that increase in the dose (10 mg/ml) and frequency of intralesional TA injections to once a week rather than a month showed good results without significant side effects.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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