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Original Research Article

Comparative study of localised intradermal microinjection of tranexamic acid and oral tranexamic acid for the treatment of melasma

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ABSTRACT

Background: Melasma is an acquired hypermelanosis affecting the sun- exposed areas of the skin, most commonly the face and neck. Different treatment modalities have been utilized in different studies with varying, not so satisfactory outcomes. The aim of the study was to compare the efficacy of localized intradermal microinjection of tranexamic acid with oral tranexamic acid in melasma patients.
Methods: It is a prospective comparative study. All patients enrolled in the study were divided into 2 groups - twenty in each treatment group. In group A, patients were given intradermal injections of tranexamic acid (4 mg/ml) once at three week intervals (0, 3, 6, 9, 12 weeks) for 12 weeks. Group B patients were given oral tranexamic acid 250 mg twice a day for 12 weeks. Following parameters were evaluated before and after 12 weeks of treatment: a) digital photographs b) MASI score c) patient subjective assessment d) dermoscopic photographs. Software (SPSS, version 16.0 statistical packages) was used.
Results: Clinical efficacy of the treatment in 2 different groups showed higher efficacy with intradermal microinjection (35.6%) compare to oral tranexamic acid (21.7%). Patient's subjective assessment showed good improvement in 63.15% of cases in group A, whereas in group B 27.8% of cases showed good improvement.
Conclusions: Intralesional localized microinjection of tranexamic acid is a promising new therapeutic modality for the treatment of resistant melasma.

Keywords: Melasma, Tranexamic acid, Microinjection

INTRODUCTION

Melasma is an acquired, symmetrical hypermelanosis of the face and is particularly seen in women with skin types IV to VI living in areas with intense UV radiation. The exact etiopathogenesis is unknown. However, various etiological factors proposed in the literatureinclude sun exposure, pregnancy, hormonal therapy, genetic factors and vascular factors.[1]

Various treatment modalities such as topical depigmenting agents, chemical peels, dermabrasion and laser therapies have been utilised with varying, not so satisfactory outcomes.[2-5]

Tranexamic acid, (TXA) a plasmin inhibitor, is now gaining popularity as a depigmenting agent. TXA prevents the binding of plasminogen to the keratinocytes, which ultimately results in less free arachidonic acids and thus inhibits UV- induced plasmin activity in keratinocytes.[6] Oral TXA also produces significant decrease in the mMASI in melasma patients.[7] TXA administered intradermally is effective for dermal and mixed variants of melasma. TXA is a safe and well

tolerated drug at the usual dosage.[8] The contraindications of the drug include acquired defective colour vision, active intravascular clotting conditions and drug hypersensitivity.[7] In the present study; we are comparing the efficacy of localised intradermal microinjection of tranexamic acid with oral tranexamic acid in melasma patients.

METHODS

This prospective, comparative study was conducted at AJ Institute of Medical Sciences, Mangalore, Karnataka from October 2017 to March 2018. In this study, sample size was 40, with twenty in each treatment group. Adult males and females between 18 and 50 years of age with skin phototypes II to V according to Fitzpatrick's classification and clinical diagnosis of melisma were included in this study. Informed written consent was taken from all the subjects. The study was approved by Ethical Committee of the Institutional Review Board.

Exclusion criteria were clotting disorders, use of anticoagulant, history of hypersensitivity to the vehicle or active substance, history of hormonal therapy, pregnant or lactating females and history of any other depigmenting treatment in the past 1 month.

Complete history taking and detailed cutaneous examination with regard to melasma was performed in all subjects. Wood's lamp examination was done to determine the type of melasma. A modified MASI (melasma area and severity index) scoring system was used to assess the severity of melasma. Following parameters were evaluated before and after 12 weeks of treatment: a) digital photographs examined by an independent investigator (classified as unchanged, presence or absence of improvement), b) MASI score c) patient subjective assessment (rating the improvement as good, bad and no change) d) dermoscopic photographs.

All patients enrolled in the study were divided into 2 groups, twenty in each treatment group. In group A. patients were given intradermal injections of tranexamic acid 0.05 ml (4 mg/ml) in each cm of melasma, after application of topical anaesthesia with lidocaine hydrochloride 2%, once at three week intervals (0, 3, 6, 9, 12 weeks) for 12 weeks. Group B patients were given oral tranexamic acid 250 mg twice a day for 12 weeks. Laboratory tests including complete blood count and coagulation tests were performed on all patients to assess the safety parameters. Patients were instructed to apply only sunscreen SPF 30 every 4 hours during the day while on treatment

Efficacy of the treatment was calculated using the formula (mMASI score before-mMASI score after)/mMASI score before×100 (Table 3).

Clinical efficacy was categorized into excellent response: if more than 75% fall in mMASI score. Very good response: if 50-75% fall in mMASI score. Good response: if 25-50% fall in mMASI score. Poor response: if less than 25% fall in mMASI score (Table 4).

Statistical analysis

Software (SPSS, version 16.0 statistical package) was used throughout. Mean and standard deviation was used for continuous variables. P value of less than 0.05 was considered significant.

RESULTS

Out of forty patients, 37 patients completed the study, 19 in group A and 18 in group B. There was no significant difference among the two groups regarding the demographic data such as age of patients and duration of disease (Table 1). The most common detected Fitzpatrick skin phototype was type 4. When we correlated the efficacies of treatment with the demographic factors, we found that treatment efficacy was higher in female patients and in patients with Fitzpatrick skin phototypes of II and III. Younger patients showed faster improvement than the older patients.

Table 1: Age and duration of disease.

		Group A (n=19)	Group B (n=18)
Patient's age (in years)	Range	21-48	19-49
	Mean±SD	34.0±6.40	32.6±5.90
Duration of disease (in years)	Range	2-8	1-11
	Mean±SD	5.32±2.16	6.48±3.19

The most common type of melasma was malar pattern. Under wood's lamp examination, epidermal type was most common (Table 2).

In group A patients, mMASI score was 11.83±1.72 at the baseline and it reduced to 7.62±1.64 after 12 weeks. In group B, mMASI score reduced from baseline value of 10.61±1.59 to 8.30±1.92 after 12 weeks. Higher clinical efficacy was observed with intradermal microinjection (35.6%) compare to oral tranexamic acid (21.7%) with p value <0.05 (statistically significant) (Table 3).

Patient's global assessment showed good improvement in 63.2% of cases in group A, whereas in group B 27.8% of cases showed good improvement (Table 4).

Regarding the side effects of the treatment

In group A, there was erythema and wheal at the site of injection in all patients which lasted for 4-6 hours. In group B, no side effects were reported.

Table 2: Type of Melasma among the study group.

		Group A		Group B	
		(no. of patients)	(% of patients)	(no. of patients)	(% of patients)
Types of melasma	Malar	15	78.9	11	61.1
	Centrofacial	4	21.1	7	38.9
	Mandibular	0	0	0	0
Pattern of melasma	Epidermal	10	52.6	9	50
	Dermal	3	15.8	3	16.7
	Mixed	6	31.6	6	33.3
Total		19		18	

Table 3: mMASI score for group A and B, before and after 12 weeks of treatment.

mMASI	Group A (n=19)	Group B (n=18)
Before treatment	11.83±1.72	10.61±1.59
After treatment	7.62±1.64	8.3±1.92
Percentage of improvement (%)	35.6	21.7
P value	<0.001	<0.05

Figure 1: Intradermal tranexamic acid. (A) Before treatment; (B) after 2nd session; (C) after 3rd session; (D) after 4th session; (E) after 5th session.

Table 4: Shows the response to treatment in study group.

Response to treatment	Group A		Group B	
	(no. of patients)	(% of patients)	(no. of patients)	(% of patients)
Good	12	63.2	5	27.8
Poor	5	26.3	10	55.6
No response	2	10.5	3	16.7
Total	19		18	

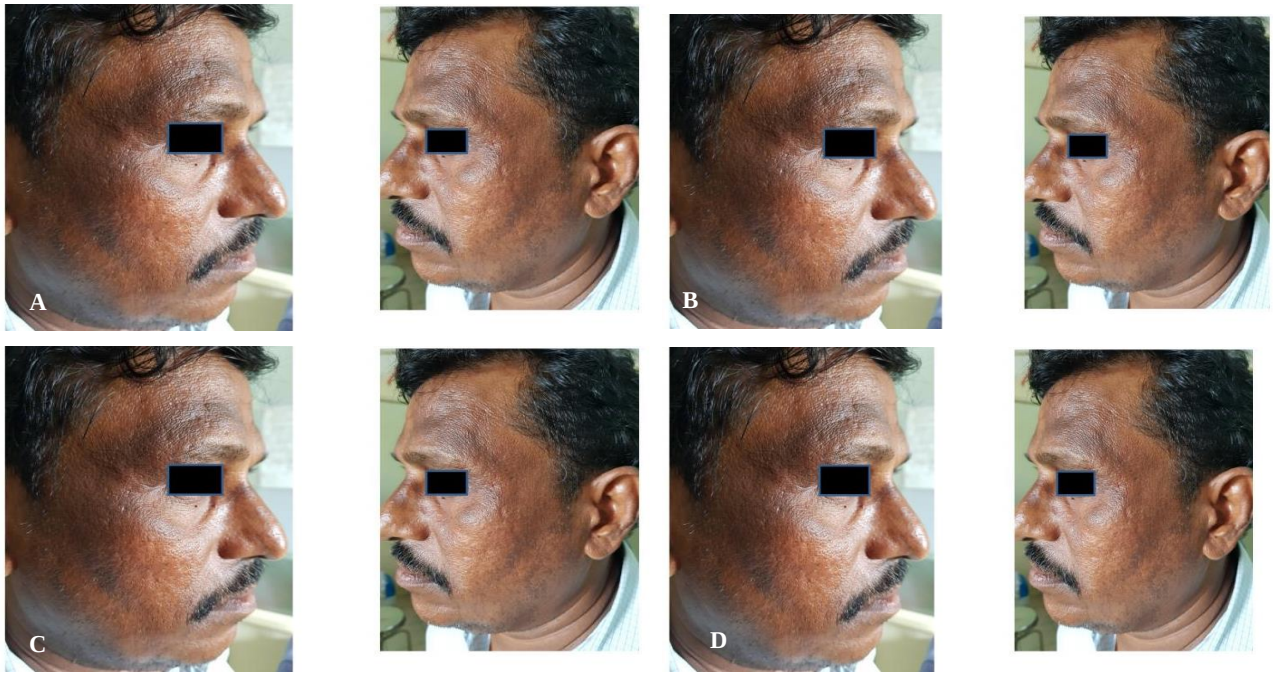

Figure 2: Oral tranexamic acid. (A) Before treatment, (B) after six weeks; (C) after nine weeks; (D) after twelve weeks.

DISCUSSION

Tranexamic acid was reported to be useful in the treatment of melasma in 1979 by Nijor in Japan.[9,10] Tranexamic acid blocks the conversion of plasminogen (present in the epidermal basal cells) into plasmin by inhibiting plasminogen activator.[11,12] The dose of oral TXA used in melasma is far less than that prescribed for its hemostatic action. In randomized controlled trial study conducted by Karn et al in Nepal, oral TXA was administered to melasma patients in a dose of 250 mg twice daily for 3 months. The authors concluded that it provides a rapid and sustained improvement in the treatment of melasma.[7] Li et al studied TXA intradermally on guinea pigs and found that at the basal layer of exposed epidermis, the number of melanocytes remained the same, but the melanin content was significantly lowered. This highlights the fact that TXA has no effect on the number of melanocytes but affects melanin expression.[13,14]

In group A, patients were given intradermal injection of tranexamic acid. This mode of drug delivery showed 35.6% of efficacy with good clinical response. Patient's subjective assessment showed good improvement in 63.15% of cases by photographic evaluation. In another study conducted in Korea on melasma patients, TXA was directly administered intradermally (4 mg/ml) weekly for a period of 12 weeks. More than 75% patients experienced a statistically significant improvement.[11]

In group B, patients were given oral tranexamic acid. After 12 weeks of treatment, mMASI score showed significant decrease from the baseline with the clinical efficacy of 21.7%. Patient's subjective assessment showed good improvement in 27.8% of cases by photographic evaluation.

Nausea and diarrhoea are the most common side effect.[8] Other systemic side effects observed with low dose administration include oligomenorrhea, gastric upset and palpitations.[15] Though it is used in low doses for a short duration as a systemic depigmenting agent, it is always vital to rule out underlying coagulation defects to prevent untoward adverse events. Wu et al observed a differential response of TXA on melasma patients having coexisting freckles and senile lentigo. They noted that the treatment

was unresponsive to freckles and senile lentigo, whereas the melasma responded well.[16]

CONCLUSION

Tranexamic acid is safe and well tolerated drug for the treatment of melasma. Both intradermal and oral modes of administration are effective for melasma. Intralesional localized microinjection of tranexamic acid is a promising new therapeutic modality for the treatment of resistant melasma.

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Ethical approval: The study was approved by the institutional ethics committee

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