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Original Article

Efficacy of 5% tranexamic acid in melasma

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Abstract

Objective To determine the efficacy of topical 5% tranexamic acid cream in patients of melasma.

Methods Total 100 patients of either gender with clinical diagnosis of melasma were enrolled in the study after taking informed written consent. The demographic data was collected on a pre-designed proforma. Baseline modified MASI score was calculated and pictures were taken of all patients at baseline. The patients were advised to apply 5% topical tranexamic acid cream at night along with sunscreen during day time for 12 weeks daily. All patients were evaluated for improvement of melasma using percentage reduction in MASI score at the end of 12 weeks and pictures were also taken again.

Results The patients' average age was 29.23 6.58 years. With a male to female ratio of 0.2:1, there were 100 patients, 81 of whom were female, and 19 who were male. At the conclusion of 12 weeks, the modified MASI score had decreased by a mean of 41.4314.56. After 12 weeks, the modified MASI score was reduced by less than 50% in 63% of patients whereas it was reduced by more than 50% in 37% of patients. In our study, 37 (37%) patients experienced efficacy.

Conclusion This study concluded that the topical 5% tranexamic acid cream was effective in 37% of melasma patients in our study population (>50% reduction in baseline Modified MASI score) after 12 weeks.

Key words
Tranexamic acid; Melasma.

Introduction

Melasma is a typical acquired hypermelanosis of sun-exposed skin, commonly observed in people with darker skin types, and it significantly impairs one's appearance.[1] Females are more commonly affected than males.[2] It presents as hyper pigmented irregularly shaped macules and patches Most frequently involved locations are cheeks, chin, nose-bridge, forehead and above the upper lip.[3]

Exact pathogenesis of melasma is not known, but different factors like pregnancy, ultraviolet light exposure and use of oral contraceptives are considered for causing hypermelanosis. Prolonged sun exposure causes exacerbation of melasma and sun avoidance generally fades it.[4]

Treatment of melasma is generally difficult. Many treatment modalities have been used including topical treatments such as hydroquinone alone or in combination with retinoids and steroids, azelaic acid, topical salicylic and glycolic acid.[3,5] Other therapeutic options include chemical peels, and laser, but none of them showed significant results.[5] Due to this recalcitrant nature of melasma, more clinical trials of newer therapeutic options are needed.[1]

Tranexamic acid has arisen as an efficacious treatment for intractable melasma. Chemical

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name of tranexamic acid is trans-4-cyclohexanecarboxylic acid. It has hypopigmentary effects in melasma and reduces chances of sun light induced hyperpigmentation.[6,7] It inhibits melanin production through plasminogen activator-plasmin system. Tranexamic acid decreases melanogenesis in epidermal melanocytes and provides rapid and sustained lightening.[10,11] Tranexamic acid has been found to be effective both if given orally as well as topically. One side effect of oral tranexamic acid is risk of clotting and thus screening is mandatory. However, there are limited large-scale studies on its use and safety outcomes.[5]

Oral tranexamic acid has shown high percentage of improvement i.e. up to 89.7% in different clinical trials, which is significant knowing the fact that the disease is often non responsive to different therapies.[8] The effectiveness of topical tranexamic acid has also been demonstrated in a research where topical tranexamic acid resulted in a 67.3% decrease in the melasma area and severity index (MASI) score.9 With oral tranexamic acid, the MASI score was reduced by 49%, according to another study.[10] In an Indian study, topical tranexamic acid caused a 27% reduction in MASI score.[11]

Objective of this study is to determine the efficacy of topical 5%tranexamic acid cream in patients of melasma by calculating percentage reduction in MASI score, since controversial data is present in literature regarding its efficacy in melasma.

Methods

This study was conducted over a period of six months in Jinnah hospital Lahore, from 5-8-2020 to 5-2-2021.

Total 100 patients of melasma with modified MASI score>5, in age group of 16-60, and of either gender were enrolled in this study. Pregnant patients and patients on any oral or topical anti-melasma therapy within last 2 months were excluded from the study. After taking written informed consent and briefly explaining the procedure all enrolled patients were advised to apply topical 5%tranexamic acid cream at night and sunscreen during daytime throughout study period of 12 weeks. No other topical or oral treatment was advised in this time. For assessment of efficacy of treatment modified MASI scoring and colored photographs were done at baseline and then at the end of 12 weeks. Percentage reduction in modified MASI score was calculated at the end of 12 weeks.

Results

A total of 100 patients were enrolled in this trial. The patients' ages ranged from 16 to 45 years, with a mean age of 29.23 6.58 years **(Table 1)**. Of the 100 patients, 19 (or 19%) were men and 81 (or 81%) were women. The patients' male to female ratio was 0.2:1.

Cheeks were the most frequently affected site in the majority of patients, or 35 (35%).Forehead was the next commonly involved area in 30(30%) patients, followed by nose in 15(15%), central face in 10(10%), chin in 7(7%) and lips in 3(3%) patients. The mean duration of disease was 38.84±34.07 months with minimum and maximum duration of 2 and 144 months respectively **(Table 1)**.

The patients' mean modified MASI score at the beginning of treatment was 10.654.81, and after 12 weeks it was 6.173.24 **(Table 2)**. The improved MASI score's mean percentage decrease was 41.43, with the minimum and greatest percentage reductions being 0 and 86.69, respectively **(Table 2)**.

Table 1 Baseline characteristics of study population (n = 100).

	Mean	*Standard deviation*	*Minimum*	*Maximum*
Age (years)	29.23	6.58	16	45
Duration	38.84months	34.07	2months	144months
Baseline modified MASI score	10.65	4.81	2	24

Table 2 Percentage reduction in modified MASI score after 12 weeks (n = 100).

	Mean	*Standard deviation*	*Minimum*	*Maximum*
Modified MASI score at baseline	10.65	4.81	2	24
Modified MASI score at 12 weeks	6.17	3.24	2	14
Percentage reduction in modified MASI score	41.43%	15.56%	0	86.96%

Table 3 Stratification according to severity of disease.

		Efficacy		*Total*	*p-value*
		Yes	*No*		
Severity according to MASI at baseline	≤ 15	33 (40.2%)	49(59.8%)	82 (100.0%)	
	>15	4 (22.2%)	14 (77.8%)	18 (100.0%)	0.152
	Total	37 (37.0%)	63 (63.0%)	100 (100.0%)	

Out of 100 patients, 37 (or 37%) showed a modified MASI score drop of more than 50%.

There was no statistically significant difference between the subgroups when the data were stratified by age, sex, place of involvement, length of disease, and severity of disease **(Table 3**).

Discussion

Melasma is a very common dermatological problem especially in females of child bearing age,[12] and it also results in considerable psychosocial impact.

Strict sun protection and withdrawal of triggering factors are required for reversal of pigmentation. Hydroquinone has been considered as the gold standard in treating melasma for over five decades now. Its efficacy has been unquestionable, but its adverse effects profile makes it undesirable. Tranexamic acid is a well-known ant fibrinolytic agent used in menorrhagia. An incidental improvement in melasma was noticed with tranexamic acid in 1979 by Sadako.[13,14]

The present study was undertaken to determine the efficacy of 5% tranexamic acid cream in treatment of melasma. Promising results has been shown with oral, intradermal as well as topical Tranexamic acid. Limited data is present in literature regarding efficacy of topical tranexamic acid in reducing severity of melasma.

In the present study mean age of patients was 29.23±6.58 years ranging from 16 to 45 years. In 2019 study was done by Janney *et al*;[11] in it mean age of patients was 35.86±7.51 years ranging from 20 to 50 years which is comparable with current study. In another study on melasma, done by Singh *et al*;[15] the mean age of melasma patients was 28.6±5.01 years which is also comparable with our study.

In our study 81% of patients were females while males were 19% with male to female ratio of 0.2:1. In a study done by Khuraiya *et al.*[9] in 2019, 76% of patients were females and 24% were male with male to female ratio of 0.3:1. Zhang *et al.*[16] conducted a study on melasma in 2018,in which 16% patients were male and 84% were female with male to female ratio of 0.19:1 which is again comparable to our study.

The mean duration of disease in our patients was

38.84±34.07 months with minimum and maximum duration of 2 and 144 months respectively which is comparable to study done by Sarvjot V *et al*;[17] where the duration of disease ranged from 24 to 96 months with a mean age of 48.80±24 months.

Cheeks were the most commonly involved site in our study in majority of patients i.e. 35(35%) and forehead was the 2nd most commonly involved area in 30 (30%) patients, followed by nose in 15 (15%). Central face, chin and lips were involved in 10 (10%), 7% and 3% respectively. However Centrofacial area was most commonly involved (74.3%) in a study done by Qazi *et al*;[18] which was followed by cheeks and chin pattern seen equally in 20% patients and nose involvement was seen in just 5.7% patients. This may be due to difference in the age groups and duration of disease of study populations.

In the present study, more than 50% reduction in modified MASI score was achieved in 37% patients (37 out of 100patients). 41.43±14.56 was mean percentage reduction of modified MASI score in enrolled patients. We compared our results with various other studies using tranexamic acid in various forms i.e. oral, intradermal and topical.

In meta-analysis done by Lei Zhang *et al.*[16] tranexamic acid proved to be a promising therapeutic approach for melasma, as it reduced MASI and Melanin index. No significant difference in Erythema Index was observed with tranexamic acid treatment.

An 89.7% improvement in melasma was obtained with oral tranexamic acid in retrospective analysis done by Lake *et al.*[8] in 2019, which is very high. Considering the increased risk of clotting, screening was made mandatory before initiation.

In a study conducted by Zohreh Tehranchinia *et al*; the addition of tranexamic acid injections to standard hydroquinone therapy demonstrated an improvement in the efficacy of topical treatment.[19] Numerous studies[20-22] have shown that oral tranexamic acid is effective in treating melasma. Oral tranexamic acid has been associated with a variety of systemic adverse effects, including menstruation irregularities, digestive issues, and orthostatic imbalances.[23,24]

In order to examine the effectiveness of intradermal tranexamic acid injection, 50% glycolic acid peeling, and topical silymarin cream in treating melasma, Elfar *et al*. conducted a clinical trial in 2015. Patients were followed up with three months after their treatment. Transexamic acid intradermal microinjection significantly reduced the MASI score, although its response rate was lower than that of glycolic acid peeling and silymarin cream.[25]

Janney *et al*. conducted a comparison of the effectiveness of topical 5% tranexamic acid and hydroquinone in 2019.[11] Although the patient satisfaction score was considerably higher in the tranexamic acid group (p value= 0.03), there was no significant difference between the two groups in terms of lowering MASI (p> 0.05).

In another study done by Khuraiya *et al.*[9] in year 2019 there was 67.3% reduction in MASI score with topical tranexamic acid which was considerably higher than our study. This may be due to difference in ethnicity of study populations.

The limitations of our study are that number of participants is relatively small as compared to prevalence of disease in the population. The trial was neither blinded nor placebo controlled, and there was no follow up after completion of study.

Conclusion

In the present study, efficacy of topical 5% tranexamic acid cream in treatment of melasma was determined using percentage reduction in modified MASI score from baseline after 12 weeks. Topical tranexamic acid was found to be effective, inexpensive and easily available therapy for a condition that is usually long standing and difficult to treat.

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