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Original Article

Efficacy of oral tranexamic acid in patients with melasma

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Abstract

Background Tranexamic acid has emerged as a promising treatment for melasma; however, few controlled studies exist. Oral tranexamic acid has been reported to be effective for treating melasma however, the effect of topical tranxemic acid remains controversial. The purposed mechanism is that it reduces the synthesis of melanin by its inhibitory effect on plasminogen-keratinocyte interaction which in turn decreases tyrosinase levels.

Objective To determine the efficacy of oral tranexamic acid for management of patients presenting with melasma.

Methods A total of 80 patients of moderate to severe melasma, 15 to 50 years of age were included. Patients were given 250 mg tranexamic acid twice daily alongwith sunscreen creams for the duration of 3 months. The patients were followed up every month. Efficacy was assessed by decrease in mMASI score from the baseline.

Results Eighty patients with age range from 15 to 50 years were included in the study. Mean age was 31.94±6.29 years. There were 23 (28.75%) males and 57 (71.25%) females with male to female ratio 1:2.5. Mean duration of disease was 10.19 ± 2.09 months. Mean baseline modified melasma area severity index (mMASI) score was 23.04±5.14. Efficacy of oral tranexamic acid in patients with melasma was found in 32 (40.0%) patients.

Conclusion Oral tranexamic acid is efficacious, safe and well tolerated treatment option for patients with moderate to severe melasma.

Key words
Melasma; Oral tranexamic acid; Efficacy.

Introduction

Melasma is an acquired disorder of facial pigmentation with highest prevalence in the Asian population.[1] It is more prevalent in darker skin types which include Fitzpatrick skin types III-V.[2,3] The pathogenicity is not yet not clear but it is known to be triggered by , pregnancy, oral contraceptive pills, exposure to ultraviolet light, use of steroidal agents, and photosensitizing drugs. More than 40% of patients have their first degree relatives affected with the disease which shows genetic predisposition.[4] Melasma can affect the upper lip, the malar region, forehead and chin and is usually bilateral and symmetrical. It can present in malar (most common), centrofacial and mandibular distribution.[5] Despite advancements in dermatological therapies, treatment of melasma is challenging.[3] Most of the time, melasma is treated with avoidance of triggering

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factors, photoprotection and various combinations of topical depigmenting agents.[2] Different topical treatment modalities include; topical depigmenting agents like hydroquinone, tretinoin, azelaic acid, kojic acid, corticosteroids and their various combinations. Laser therapy, dermabrasion and chemical peels with varying degrees of success are also in use.[2]

In recent years, off-label Tranxemic acid (TA) has emerged as potential treatment for melasma. The purposed mechanism is that it reduces the synthesis of melanin by its inhibitory effect on plasminogen-keratinocyte interaction which in turn decreases tyrosinase levels.[3,5] It may also reverse the abnormal dermal changes like increased vasculature in melasma. Oral TA has emerged as a promising treatment for melasma; however, few controlled studies exist.[6] Sharma *et al*. reported that oral TA is effective in 64.1% patients in resolution of melasma[7] while another study reported 27.7% efficacy.[5] Though the literature supports the fact that TA can be used in melasma but most of the studies suggested that further trial are required to confirm the role of this modality in treating melasma. Moreover, there is limited local literature available regarding the use of oral TA in melasma. We have conducted this research so that we may know how efficacious the oral TA is in our set of population and in future we will be able to implement the results of this study locally in our population.

Methods

Study is a descriptive case series conducted in the Department of Dermatology, Shalamar Teaching Hospital, Lahore. Total of 80 patients of both genders, aged between 16-50 years who had moderate to severe melasma were included in the study with non-probability, consecutive sampling technique. Patients taking any oral or topical treatment for melasma within last 3 months, patients hypersensitive to trial drug and with abnormal bleeding time, clotting time and platelet count were excluded. Females, who were pregnant, nursing, had history of >2 spontaneous abortions or taking oral contraceptives or other blood thinning drugs were also excluded. Patients who gave history of diabetes (BSR>200mg/dl) or hypertension (BP≥140/90mmHg), ischemic heart disease, deep venous thrombosis and stroke were also excluded

Patients fulfilling the inclusion and exclusion criteria were recruited in study from outpatient department of Dermatology, Shalamar Hospital Lahore. Written informed consent was taken. Demographic data (name, age, gender, site of melasma, duration of symptoms) was also recorded. Examination under wood's lamp was performed and the patients were advised to do platelet count, bleeding time and clotting time on first visit. Patients with normal platelet count, bleeding time and clotting time were given 250 mg tranexamic acid twice daily along with sunscreen creams. At baseline, mMASI score was noted and picture of patches was obtained. Patients were followed up every month for total of 3 months for resolution of melasma. mMASI score was calculated at the end of 3 months and photographs of patches were taken. Efficacy was labelled if there was decrease in mMASI score from baseline. Data was processed by using Statistical Package for Social Sciences, version 21.

Results

Eighty patients who had moderate to severe melasma were included in the study. The mean age of the study sample was 31.94±6.29 years. Fifty eight patients (72.50%) were between 15 to 35 years of age as shown in **Table 1**. There were 23 (28.75%) male and 57 (71.25%) female patients with male to female ratio 1:2.5. Mean

Table 1 Distribution of patients according to site and type of melasma

	No. of patients (n=80)	*% age*
Site of melasma		
Malar	24	30
Centrofacial	42	52.50
Mandibular	14	17.50
Type of melasma		
Epidermal	42	52.50
Dermal	21	26.25
Mixed	17	21.25

duration of disease in our study was 10.19±2.09 months. Distribution of patients according to site and type of malesma is shown in **Table 1**. Mean baseline mMASI score was 23.04±5.14. In our study, efficacy of oral tranexamic acid for management of patients presenting with melasma was found in 32 (40.0%) patients **(Figure 1-3)**. Stratification of efficacy with respect to age groups, gender, duration, site and type of melasma and baseline mMASI are shown in **Table 2.**

Table 2 Stratification of efficacy with respect to age groups, gender, duration, site and type of melasma and baseline mMASI.

	n= 80	*Efficacy*		*p-value*
		Yes	*No*	
Age				
15-35	58	30	28	0.0001*
36-50	22	02	20	
Gender				
Male	23	07	16	0.167
Female	57	25	32	
Duration of melasma(months)				
≤ 12 months	66	27	39	0.719
> 12 months	14	05	09	
Site of melasma				
Malar	24	08	16	0.005*
Centrofacial	42	13	29	
Mandibular	14	11	03	
Type of melasma				
Epidermal	42	22	20	0.001*
Dermal	21	01	20	
Mixed	17	09	08	
Baseline mMASI				
≤ 25	59	22	37	0.407
> 25	21	10	11	

Discussion

Melasma is an acquired disorder of hyperpigmentation which involves photo exposed areas of skin. It negatively affects the life both psychologically and socially.[8] Exact mechanisms remain somewhat unclear but ultraviolet exposure and female sex hormones play a role in a person with genetic predisposition.[9]

Melasma has been treated with topical triple combination therapy and sun protection traditionally. Recently, tranexamic acid (TA) has been studied in the treatment of melasma. Oral, intradermal and topical preparations of TA has been evaluated for the purpose.[10] TA is a fibrinolytic agent with antiplasmin properties, so it can inhibit the release of paracrine melanogenic factors which stimulate the melanocytes.[10] Various studies have reported TA to be effective and safe in melasma. Consensus has yet to be built on the use of TA for melasma.[2]

This study concludes that oral TA in a dose of 250 mg twice a day for three months in a patient with melasma seems efficacious. The mean age of patients in my study was 31.94±6.29 years which is very much comparable with Ejaz A *et al.*[11] who had a mean age of 32 years but higher than Bari AU *et al.*[12] and Ethawi AMD *et al.*[13] who had a mean age of 23 years. On the other hand, Lee HS *et al.* had found higher mean age

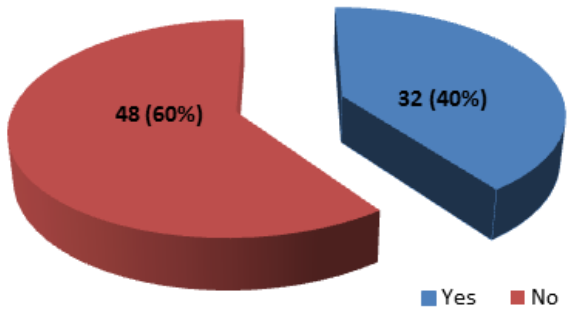

Figure 1 Efficacy of oral Tranexamic acid in patients with melasma.

Figure 2 Before (above) and after (below) the treatment.

Figure 3 Before (above) and after (below) the treatment.

i.e. 41 years, in his study compared to our study.[14] The variability in age might be due to different study cohorts belonging to different geographical areas and diverse ethnic groups.

In this study, out of 80 patients, 23 (28.75%) were male and 57 (71.25%) were females with male to female ratio 1:2.5. Many previous studies have also shown female predominance as observed in our study.[11,13,14] In our study, majority of patients were presented between 15-35 years age. Similar findings were also observed by Al-Hamdi KI *et al*.[15]

Fifty two percent of the patients in our study have epidermal type of melasma and same percentage of the patents presented with centrofacial type of melasma. Colferai MMT *et al*. also reported that most patients i.e., 70% in his study group were having centrofacial type of melasma.[10]

In our study, based on mMASI, 40% of patients presenting with melasma were improved.

Various other studies used patients' ratings and decrease in MASI score and concluded oral TA to be efficacious in melasma.[9,16]

Tan AWM *et al*. reported 69% efficacy with oral TA using MASI but his 72% of the patients relapsed in two months after stopping oral TA despite the fact that they were using various combinations of topical lightening agents.[16] Two other studies conducted with oral TA in melasma reported 49% and 50% improvement as compared to 18% and 5.9% in placebo group when treatment was given for 3 months.[6,10]

Wu *et al*. studied the effect of oral TA in melasma for 6 months and reported that 10.8% patients showed 90% reduction, 54% of patients showed 60% reduction and 31% of patients showed 30% reduction after 6 months of treatment.[17]

Li *et al*. gave 500mg of oral TA for 4 months in melasma and he followed up his patients at 0, 4th, 8th, 12th and 16th week and accessed colour

and size of the lesions. He used Skin Tone Colour Scale and a 5-point scoring system for the purpose and reported improvement in 85% of his patients in 4th week, 97% of the patients in 8th and 12th weeks, and in 100% of the patients at 16 week.[18]

Another study observed the results with different doses of oral TA in melasma: 500 mg, 750 mg, 1000 mg, or 1500 mg daily doses were used. Treatment was given for 8 weeks in first stage and later up till 2 years in the second stage; patients were free to stop the drug themselves during second stage. By using MASI score and melanin index, it was reported that all 4 doses were effective, and the efficacy correlated with the dosage and duration of treatment.[19]

Relationship between efficacy of TA and age of the patients came out to be statistically significant with p value of 0.0001. Out of 58 patients whose ages were from 15-35 years, 30 patients showed improvement in terms of improvement of mMASI. Out of 22 patients whose ages were from 36-50 years, only 2 patients showed improvement.

Statistical correlation between site of melasma and efficacy of TA also turned out to be significant with p value of 0.005. Eight patients out of 24 of malar type, 13 patients out of 42 of centrofacial type and 11 patents out of 14 of mandibular type showed improvement.

The relationship between type of melasma and efficacy was sought which came out to be significant with p value of 0.001. Out of 42 patients with epidermal melasma, 22 patients showed improvement; one patients of dermal melasma out of 21 and 9 patients of mixed melasma out of 17 showed improvement. Kurana *et al.* conducted a study on oral and intralesional TA in melasma. His results in intralesional group showed mean fall in MASI of 3.12(±4.99) in epidermal melasma and 1.01(±4.81) in mixed type.[20]

Many studies reported a relapse of melasma following stoppage of oral TA. Future research should be directed to devise the methodology to have sustained effects with oral TA. However it was well tolerated drug with only minimal gastric side effects.[10,17] No such side effect was reported in our study.

Conclusion

This study concluded that oral TA was efficacious in 40% of our patients when accessed according to mMASI score. Long duration follow-up studies with greater number of patients and may be with higher doses is the need of the hour to further explore the efficacy of TA in melasma in terms of sustained results.

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