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Efficacy of Oral Tranexamic Acid in the Treatment of Melasma: A Pilot Study

Shafia N Kakru[1], Md Raihan[2*], Mirza Aumir Beg[3], Basit Kakroo[4]

[1]Lecturer;[2]Associate Professor, Department of Dermatology, Venerology and Leprosy, Hamdard Institute of Medical Sciences and research, Delhi, India.[3]Assisant professor, Department of Pedodontics, Suda Rustagi College of Dental Sciences & Research, Faridabad, Haryana.[4]Basit Kakroo, Medical student at the University Of East Anglia, Norwich Medical school.

ABSTRACT

Background: *Melasma a common skin pigmentary disorder poses a great challenge to clinicians due to unsatisfactory results and high recurrence rate. Many treatment modalities have been tried by clinicians without significant improvement in the lesion.* ***Methods:*** *This cross sectional study was done on 90 patients including both male and female and were diagnosed with moderate to severe melasma. TA 250 mg (thyrodin) bid for six months was prescribed along with topical sunscreen. Digital photography was performed at the first visit and at subsequent visits. The effects of treatment were evaluated by two dermatologists independently. Results were assed clinically and photographically.*

Result: *90 patients with moderate to severe melasma were enrolled in the study. The average age was 36 years. 44patients (48.8%) had good improvement, 25 patients (27.7%) had excellent improvement and 17 patients (18.8%) had fair improvement and 4 patients (4.4%) had no improvement.*

Three patients complained about gastric upset. None of the patients had serious systemic side effects, only few had oligomenorrhoea, palpitation. Patient's satisfaction was similarly noted. ***Conclusion:*** *oral administration of TA is effective and safe treatment for melasma.*

Key Words*: Melasma, oral tranexamic acid*

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***Address for Correspondence**
Dr. Md Raihan,
Associate Professor, Department of Dermatology, Venerology and Leprosy, Hamdard Institute of Medical Sciences and research, Delhi, India.

INTRODUCTION

Melasma an acquired hypermelanosis characterized by slowly enlarging tan to brown macules on the skin of face and arms, usually on the cheeks, forehead, nose, and upper lip.[1] Melasma is a common acquired disorder of pigmentation and is known to occur in all skin types, all ethnic groups and both sexes but It is relatively more common in darker skin type (Fitzpatrick skin type III and IV) and more in women of child bearing age than men. Exact etiology of melasma is unknown, but genetic factors and exposure to UV irradiation are considered as main causes in addition to endocrine factors (e.g. pregnancy, hormonal therapy and ovarian dysfunction), drugs (e.g. phenytoin, phototoxic drugs), cosmetics, vascular and systemic diseases like thyroid dysfunction and anemia of multifactorial origin. These factors cause an increase in synthesis of melanosomes in melanocytes and their transfer to keratinocytes. Melasma lesions typically fade in winter and aggravate in summer. Chloasma (melasma related to pregnancy) usually diminishes within few months of delivery but melasma lesions due to oral contraceptives are usually persistent.[2,3,4]

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There are three clinical patterns of melasma, malar (most common), centrofacial and mandibular.[5] On the basis of visible light, wood's light and lesional histology, melasma has been classified as epidermal, which has increased melanin predominantly in basal and suprabasal layers of epidermis with pigment accentuation on Wood's lamp. The dermal type has perivascular melanin laden macrophages in superficial and deep dermis and does not accentuate with Wood's lamp. The mixed variety has elements of both and appears as deep brown colors with Wood's lamp accentuation of only the epidermal component.[4] The current treatments includes sun avoidance, sunscreens, topical use of depigmenting agents such as hydroquinone, azelaic acid and kojic acid[6] alone or in combination with other topical therapies such as tretinoin[7], topical corticosteroids, chemical peels and dermabrasion. Also different kinds of lasers that help in removing selective pigment have become increasingly popular.[8] Despite the multiplicity of all these therapies, their efficacy and safety remain controversial.[9] In the treatment of melasma the introduction of tranexamic acid (TA) is relatively a new concept. TA, a synthetic derivative of amino acid lysine widely used as antifibrinolytic agent inhibits plasminogen-keratinocyte interaction which decreases tyrosinase activity leading to decreased melanin synthesis by melanocytes.[10,11]

METHODS

This pilot study was conducted at Outpatient Department of Dermatology, Hamdard institute of Medical Sciences and Research New Delhi. The study enrolled 90 patients of age group 20 years and above of either gender with moderate to severe melasma fulfilling the inclusion criteria. The study was done between April 2017 to October 2017. Informed written consent was taken from all patients. A detailed history was taken from all patients regarding the etiological factors (sun exposure, cosmetic use, oral contraceptive use or phototoxic drug, past pregnancies, menstrual history, and thyroid dysfunction) and also family history was taken into account. All patients were checked for bleeding time, clotting time and platelet count before the start of the study. Based on Wood's lamp examination diagnosis of melasma (epidermal, dermal or mixed) was made. Inclusion criteria included patients with moderate to severe melasma and absence of any significant inflammatory signs. The exclusion criteria ruled out women with a pregnancy or a breastfeeding, a history of thrombosis, abnormal bleeding profile, over expectation for the treatment, any other treatment therapies within 6 months, refusal to allow photographs and those who were unable to follow-up for a duration of six months. The proper record of the size and severity of each melasma lesion was made. Photographs were taken in the beginning and also at each visit under the same exposure condition. All patients were asked to return to OPD every 4 weeks for analysis of the changes in the lesion. They also were instructed to apply broad-spectrum sunscreens. A tablet of Tranexamic acid (Tyrodin) was prescribed orally at the dosage of 250mg twice daily for a period of 6 months. No other medication either topical or oral was taken by the patients. Results were assessed by clinical improvement and also photographic assessment was made. The results were rated as excellent if improvement was >90 %, good if >60%, fair if >30% and no improvement If <30%. Patient's satisfaction was also taken into record at each visit.

RESULTS

In the beginning 100 patients were enrolled in this study but 10 patients were dropped out due to their failure to complete the study. Ninety patients were finally taken. Amongst ninety patients 13 (14.4%) were male and 77 (85.5%) were females with 60 patients (66.6%) having moderate melasma and 30 patients (33.3%) having severe melasma. Mean age of patients was 36 years. The youngest age of patient was 19 years and 52 years being the oldest. All patients were with Fitzpatrick's skin type III and IV skin. The duration of melasma ranged from 4 years to 15 years. 46 patients (51.1%) had malar pattern, 25 (27.7%) had centrofacial pattern, 18 patients (20%) had mixed and only 1 patient (1.1%) had mandibular pattern. The malar pattern being the most common followed by centrofacial and then mixed. On the basis of woodslamp examination 55 patients (61.1%) had epidermal, 20 patients (22.2%) had mixed and 15 patients (16.6%) had dermal type of melasma. Epidermal type of melasma being the most common type. Baseline characteristics of the melasma patients are given in Table 1.

Table 1: Distribution of Patients

Variables	N	Percentage %
Males	13	14.4
Females	77	85.5

Table 2: Age-wise distribution of patients

AGE	N	Percentage %
≤20	2	2.2
21-40	60	55.5
>41	28	36.6

Table 3: Distribution of patients on the basis of duration.

Duration (years)	N	Percentage %
< 1	7	7.7
1-5	50	55.5
>5	33	36.6

Table 4: Distribution of patients

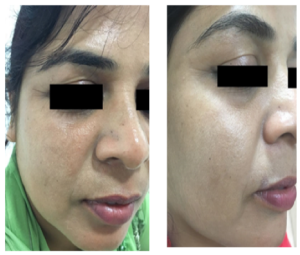
Type	N	Percentage %
Epidermal	55	61.1
Mixed	20	22.2
Dermal	15	16.6

The analysis of the results demonstrated 44 patients (48.8%) excellent improvement, 25 patients (27.7%) good improvement, and 17 patients (18.8%) fair improvement and

Table 5: Distribution of patients

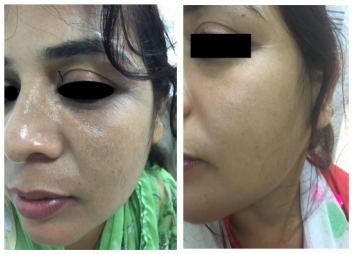
Pattern	N	Percentage%
Malar	46	51.1
Centrofacial	25	27.7
Mandibular	1	1.1
Mixed	18	20

no improvement was seen in 4 patients (4.4%). After a 6 month follow-up period, with completion of treatment 75 (83.3%) patients had no recurrence while 15 patients (16.6%) had recurrence. Our study showed that TA in low dose does not cause any serious side effects and is relatively safe. Three patients (3.3%) in our study showed gastric upset (nausea), four patients (4.4%) showed oligomenorrhoea and one patient (1.1%) reported palpitation. No serious side effect was reported in our study.



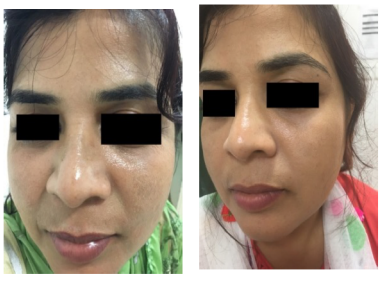
Before After

Fig 1. Before and after treatment with tranexamic acid.



Before After

Fig 2. Before and after treatment with tranexamic acid.



Before After

Fig 3. : Before and after treatment with tranexamic acid.

DISCUSSION

Melasma is a common skin pigmentary disorder of Asian and Latin American, predominantly affecting women, causes are still unknown .Genetic predisposition, ultraviolet (UV) exposure and hormonal factors and some drugs (e.g. phenytoin) play role in its pathogenesis.[12] Melasma not only causes cosmetic problem but also can cause psychological distress. Hydroquinone has been considered a gold standard treatment[13] but this treatment is neither a satisfactory nor a safe method due to its severe adverse reactions including erythema, stinging, colloid milium, irritant and allergic contact dermatitis, nail discoloration, and paradoxical post-inflammatory hypermelanosis.[14] Laser therapy has shown good effect but it has downtime and has a side effect of post-inflammatory hyperpigmentation.[15] The most effective and safe treatment for melasma is yet to be explored. TA has been routinely used through oral administration, and it also could be used with intradermal microinjection.[16]

TA has been previously used as haemostatic agent due to its anti-fibrinolytic effect and in 1979 was first introduced by Nijor.[17] Role of TA in melasma study done by Sufan and Hangyan et al showed oral administration of TA is a very effective and safe therapy.[18]

Dunn and Goa et al[13] studied the role of TA in melasma and showed TA acts by inhibition of tyrosinase activity which is vital in melanin synthesis in epidermal melanocytes. A study done by Safoora and Riffat on effect of TA in melasma showed oral tranexamic acid is a safe and effective treatment.[20] Similar studies as ours, effect of TA in melasma in Nepali population[20] and also in Chinese population[21] and it was concluded by the authors that TA is an effective and safe treatment for melasma. The dose of TA given in melasma is very less as compared to the dosage given for its haemostatic effect that makes the fatal side effects like thromboembolism, myocardial infarction, cerebrovascular accident rare. The results of our study are comparable with other studies done on effect of oral TA in melsama. We have noted encouraging results with TA in melasma and in our study we didn't come across any serious side effects.

CONCLUSION

It's concluded that TA is an effective and relatively safe therapy in melasma. Our study was non-invasive, caused no irritation of the skin, no risk of post-inflammatory hyperpigmentation and no downtime was required and was affordable by the patients. Further research on long term administration TA and reduction of recurrence rate is also needed.

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