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IP Indian Journal of Clinical and Experimental Dermatology

Journal homepage: www.ijced.org/

Original Research Article

Comparison of oral versus topical tranexamic acid for treatment of melasma

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ARTICLE INFO

Article history:
Received 21-04-2023
Accepted 08-05-2023
Available online 03-07-2023

Keywords:
Melasma
oral tranexamic acid
topical tranexamic acid
tranexemic acid
TA

ABSTRACT

Background: Melasma is one of the most common causes of hyperpigmentation and is a prevalent cosmetic concern for patients. Tranexemic acid is an effective mode of treatment available in both oral and topical forms.

Aim: To evaluate and compare the therapeutic effectiveness of topical and oral tranexamic acid for the treatment of melasma.

Materials and Methods: A total of 84 patients who presented to dermatology OPD with melasma were divided into two groups, namely A and B. Group A patients were treated with oral tranexamic acid 250 mg twice daily, and patients in Group B were treated with topical 5% tranexamic acid with follow-up every 4 weeks until 3 months.

Results: Among the oral treatment and topical patient groups, a statistically significant difference in the mean percentage of reduction in MASI score from baseline was observed at 12 weeks (61.31±9.48 for oral vs 52.64±8.03 for topical) with $p<0.05$. Systemic side effects like abdominal pain, nausea, and oligomenorrhea were observed with oral tranexemic acid, while topical side effects like erythema, skin irritation, and xerosis were observed with topical tranexemic acid treatment.

Conclusion: Oral tranexamic acid gave a more promising result when compared to topical tranexamic acid. Despite having GI disturbances with oral tranexamic acid, it had more patient compliance and could be a promising therapeutic approach for melasma.

1. Introduction

Pigmentary disorders are reported as the main cause of demand for dermatological care by 23.6% of men and 29.9% of women.[1] Melasma is an acquired pigmentary condition, characterised by irregular brown macules and patches symmetrically distributed on sun-exposed areas of the body. 20–30% of indian women between 20 and 40 years old are affected by melisma.[2] It primarily affects women and shows up symmetrically on body regions that are exposed to the sun.[3] Melasma is generally a clinical diagnosis consisting of three predominant facial patterns: centrofacial, malar, and mandibular. The major clinical pattern in 50–80% of cases is the centrofacial pattern, which affects the forehead, nose, and upper lip, excluding the philtrum, cheeks, and chin.[4,5] The malar pattern is restricted to the malar cheeks on the face, while mandibular melasma is present on the jawline and chin. Extra-facial melasma can occur on non-facial body parts, including the neck, sternum, forearms, and upper extremities.[4] It is most commonly seen in middle-aged women. Melasma can be divided on the basis of morphology – epidermal, dermal, and mixed. Epidermal: characterised by dark brown patches with a well-defined border. Mixed - most common type is characterised

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https://doi.org/10.18231/j.ijced.2023.015

by a combination of light and dark brown patches and bluish discoloration. Dermal characterization is characterised by light brown and bluish patches with an ill-defined border.

Causes of melasma include a genetic component, as >30% have a family history of melasma, elevated levels of oestrogen and progesterone during pregnancy, contraceptive pill, hormone replacement therapy, thyroid disease, drugs including dilantin, an anti-malarial drug, tetracycline, minocycline, use of cosmetic products, malnutrition, liver dysfunction, B12 deficiency and UVA, UVB, and visible light exposure causing peroxidation of lipids in cellular membranes, leading to generation of free radicals, which stimulate melanogenesis.

Pregnant women are more prone to alterations to their skin and its appendages during pregnancy due to immunologic, endocrine, metabolic, and vascular changes.[6] Scientists now think of melasma as the stress mask since anxiety features and psychotropics have recently been found to be intimately related to the onset of the condition.[7] The basic histological abnormalities identified in melasma, melanogenesis, and melanocytosis, are thought to grow as a result of all the variables.[8] As such, no investigation is necessary, but the wood's lamp examination can be used to identify the depth of melanin pigmentation and determine the type of melasma – epidermal, dermal, or mixed. The severity of facial melasma can be estimated by using colorimetry, mexametry, and the MASI score (Melasma Area and Severity Index). (lutein/zeaxanthin). Tranexemic acid is a fibrinolytic agent that has a role in the inhibition of paracrine melanogenic factors that normally stimulate melanogenesis.[9] Therefore, it has been evaluated for the treatment of melasma in topical and oral formulations with varying efficacy and safety, which requires further large-scale randomised controlled trials.[10] No thromboembolic adverse events have been reported even though low doses of oral TA, an anti-fibrinolytic with potential side effects including deep vein thrombosis, significant pulmonary embolism, and acute myocardial infarction, have been used to treat melisma.[11]

2. Materials and Methods

84 Patients with melasma were selected for the study after a thorough clinical examination. Patients were evaluated clinically and randomly categorised into two groups, namely A and B. Group A patients were administered oral tranexamic acid 250 mg twice daily, and patients in group B applied topical 5% tranexamic acid to designated sites on their faces twice daily, along with sunscreen three times daily in both groups.

MASI scoring was performed every four weeks. Clinical evaluation of melasma severity was performed at baseline at 4, 8, and 12 weeks. The area of the face is divided into 4 parts according to MASI: 30% forehead, 30% right malar, 30% left malar, and 10% chin.

Melasma severity is assessed by three variables:

1. A-percentage of total area involved on a scale of 0 (no involvement) to 6 (90–100% involvement).
2. D-darkness on a scale of 0 (absent) to 4 (maximum)
3. H-homogeneity hyperpigmentation on a scale of 0 (minimal) to 4 (maximum) now.
4. MASI is then calculated by the equation: (DF+HF) AF + 0.3 (DMR+HMR) AMR + 0.1 (DC+HC) AC.

2.1. Inclusion criteria

Patients with clinical features suggestive of melasma

2.2. Exclusion criteria

1. Pregnant females.
2. Women taking contraceptive pills during studies.
3. Patients taking drugs like tetracycline, non-steroidal anti-inflammatory drugs, phenytoin, and spironolactone.
4. Patients on anticoagulants or having any bleeding disorders.
5. Patients have impaired renal function test.

3. Results

Table 1: Characteristics of participants

Patients characteristics	Frequency
Age (Years)	≤ 30 =28 31-40 = 35 41-50 = 17 > 50 = 4
Duration of melasmsa	≤ 6 Months = 36 > 6 Months = 48
Sex	Female = 68 Male = 16
Fitzpatrick skin type	Type III = 11 Type IV = 46 Type V = 27
Family history	Present = 55 Absent = 29
History of endocrine disease	Present = 15 Absent = 69
Clinical type	Centrofacial = 59 Malar = 25 Mandibular = 00
Morphological type	Epidermal = 17 Dermal = 12 Mixed = 55

84 cases were included in this study, of which 28 patients were younger than or equal to 30 and 35 patients were in the age group 31–40. 36 patients had a history of melasma of less than 6 months, and 48 patients had a history of more than 6 months. Of the 84 cases, 16 were male and 48 were female. The patients were categorised into two

Table 2: I: The mean MASI score of the baseline and all reassessment visits after treatment with oral TXA VS Topical TXA

	Oral TXA	Topical TXA	P value
Pre MASI score	20.50	19.90	0.437
MASI at 4 Weeks	14.55	16.19	0.014
MASI At 8 Weeks	10.98	13	0.001
MASI at 12 Weeks	7.93	9.45	0.005
P value	0.00	0.00	

Table 3: The amount of changes in the mean MASI score of each group

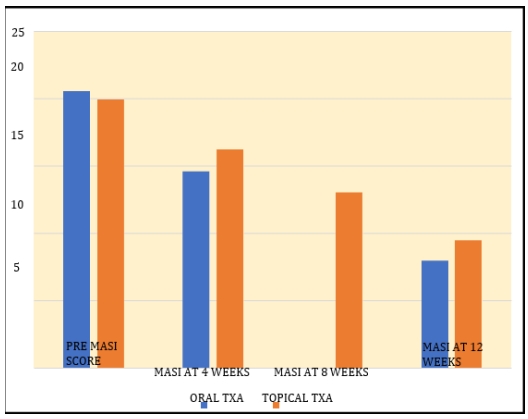
The amount of changes in the mean masiscore of each group				
Groups	**Baseline-week 4**	**Week 4 –week 8**	**Week s-week 12**	**P value**
Groupa (oral TXA)	5.95	3.57	3.05	0.00
Groupb (topical TXA)	3.17	3.19	3.55	0.00

Table 4: The frequency (Percentage) of side effects in two groups

Groups	**Yes**	**No**
Oral TXA	6 (14.2 %)	36 (85. 7 %)
Topical TXA	5 (11.1 %)	37 (11. 9 %)

Table 5: Comparison of results with other studies

	Study lPooja J. Sahu et al[3]	**Study 2Vinod K. Khorana et al[4]**	**Study 3Bahareh Ebrahimi et al[5]**	**Our study**
Total patients	60	64	50	84
Age	Age group -18 -50 years	Age group -20 to 50 years	Age group = more than 18 years	Age group -20 - 60 years
Sex	Female- 55;Male -5	Female -54 ; Male -10	Female -50	Female -68 ;Male -16
Clinical type	Centrofacial -20 Malar -39 Mandibular -1	Centrofacial -27 Malar -37 Mandibula r -0	All malar patients were included.	Centrofacial -59 Malar -25 Mandibular -0
Morphological type	Comparison not done	Epidermal - 17 Dermal - 3 Mixed -24	All Epidermal melasma were chosen.	Epidermal - 17 Dermal -12 Mixed -55
Treatment received	20 patients - oral tranexamic acid 250 mg twice daily. 20 patients -topical Tranexamic acid . 20 patients - Modified Kligman's regimen	32 patients - oral tranexamic acid 250 mg twice daily. 20 patients -localized microinjections (4mg/ml) of tranexamic acid monthly.	Group A - topical 3% tranexamic acid Group B -3% hydroquinone and 0.01% dexamethasone.	42 patients - oral tranexamic acid 250 mg twice daily. 42 patients - topical 5 O/o Tranexamic acid.
Pre MASI Score	Oral TXA-13.35 Topical TXA -14.39	Oral TXA -7.48± 3.73	Topical TXA- 31.68 ±10.32	Oral TXA -20.50 Topical TXA-19.90
MASI at 4 weeks	Oral TXA-13.28 Pvalue - 0.040 Topical TXA - 14.33P value -0.131	Comparison at 4th weeknot done	Topical TXA -22.60 ± 10.37 P value -0.31	Oral TXA-14.55 Pvalue - 0.000 Topical TXA -16.19P value -0.000
MASI at 8 weeks	Oral TXA - 10.81 P value -0.0001 Topical TXA-13.93 P value -0.001	Comparison at 8th week not done	Topical TXA-15.84± 12.01 P value -0.38	Oral TXA-10.98 P value -0.000 Topical TXA -13 P value -0.000
MASI at 12 weeks	Comparison not done	Oral TXA -3.18 ± 1.93 P value -<0.01	Topical TXA-10.76 ± 9.43 P value -0.91	Oral TXA -7.93 P value -0.000 Topical TXA -9.45 P value -0.000



Graph 1: The mean MASI score of the baseline and all reassessment visits after treatment with oral TXA VS topical TXA

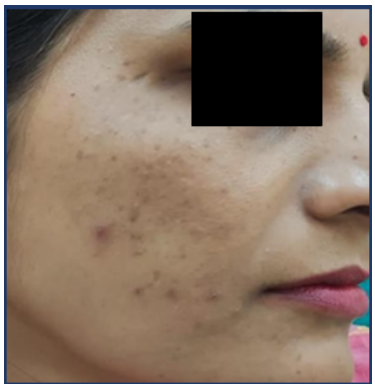
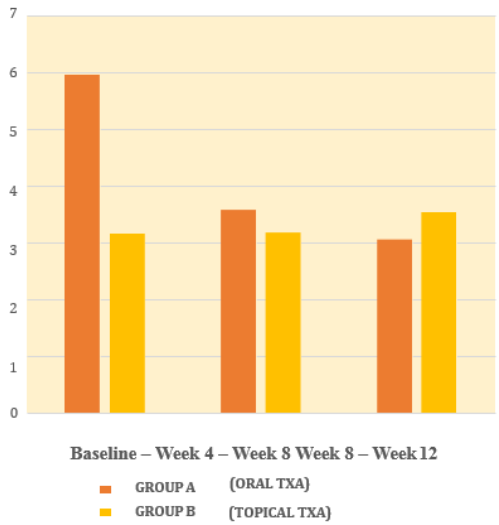


Fig. 2: Post-treatment with oral tranexemic acid



Graph 2: The amount of changes in the mean MASI score of each group

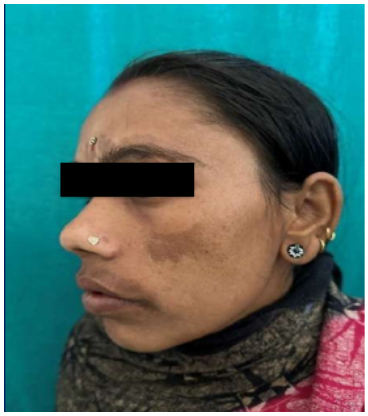


Fig. 3: Pre-treatment

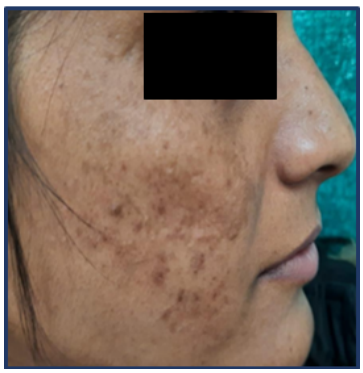


Fig. 1: Pre-treatment

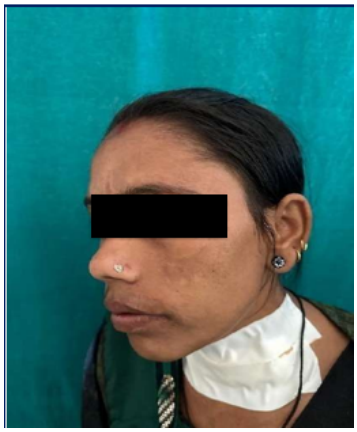


Fig. 4: Post-treatment with oral tranexemic acid

groups. Group A – oral tranexamic acid 250 mg twice daily, whereas Group B – topical 5% tranexamic acid for 12 weeks. The mean MASI score at baseline with oral TXA and topical TXA was 20.50 and 19.90, respectively, which by the end of the 12th week reached 7.93 and 9.45 (p value = 0.005) (Table 1). The changes in the MASI scores of both groups were statistically significant during the study period. The amount of change in the mean MASI score of both groups was statistically significant in all reassessment visits (p value 0.00) (Table 2) (Table 3) (Graph 1) (Graph 2). More systemic side effects were observed (abdominal pain, nausea, and oligomenorrhea), and some topical side effects were observed (erythema, skin irritation, and xerosis).

4. Discussion

Melasma is a common acquired dermatosis characterised by the presence of light-to-dark brown macules and patches involving the sun-exposed areas of the face and neck. Traditionally, the mainstays of treatment for melasma have been topical bleaching agents and strict photoprotection. Additional adjuvant treatment modalities include chemical peels, dermabrasion, and laser treatments, all of which have demonstrated limited efficacy.[12,13] Recently, there has been an interest in studying the effects of tranexamic acid (TA) on melasma. TA has been evaluated for the treatment of melasma in various formulations, including topical, intradermal, and oral.[12] TA is a fibrinolytic agent that has antiplasmin properties. It has been hypothesised that TA can inhibit the release of paracrine melanogenic factors that normally stimulate melanocytes. In our study of 84 patients, the mean MASI score at 12 weeks after starting treatment in patients who received oral tranexamic acid was 7.93 and in patients receiving topical tranexamic acid was 9.45. Both groups had a reduction in MASI score, and the p value in both groups is 0.000, which is highly significant. In study 1 by Vinod K. Khurana et al, the mean MASI score at the 12th week with oral tranexamic acid was 3.18±1.93, and the p value was highly significant.[14] In the study by Bahareh Ebrahimi et al mean MASI score at the 12th week in patients receiving topical TXA is 10.76±9.43 which means that with the use of topical TXA, a reduction in MASI score was observed.[15]

5. Conclusion

Melasma is a pigmentary disorder affecting mainly the face. Various treatment modalities are available, such as topicals, superficial chemical peels, and lasers, but none has yet given promising results, the quest for the best treatment modality is on. According to the above study, both modalities of treatment of melasma with topical TA and oral TA are effective, but a comparative analysis suggested that results were better with oral tranexamic acid than topical tranexamic acid. Patient compliance was higher with oral tranexamic acid. It was also observed that there were more gastro-intestinal side effects with oral TA, like abdominal pain, nausea, and oligomenorrhea, and some topical side effects were observed with topical 5% tranexamic acid, like erythema, skin irritation, and xerosis.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Cite this article: Agrawal M, Varma K, Kumar U, Bhargava S, Mahadik A, Agrawal V. Comparison of oral versus topical tranexamic acid for treatment of melasma. *IP Indian J Clin Exp Dermatol* 2023;9(2):84-89.