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ORIGINAL ARTICLE

Comparing the Effectiveness of Oral Formulation of Tranexamic Acid in Treating Melasma versus Topical Treatmentlike Kojic Acid

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ABSTRACT

Aim: To compare the efficacy and safety of oral tranexamic acid with topical kojic acid in treatment of melasma.
Method: This study was an interventional, randomized control trial done in Department of Dermatology Akhtar Saeed Trust Hospital Lahore from January 2020 till June 2020. 40 patients with moderate to severe melasma were enrolled for this study. These were divided into two groups A and B. In group A 20 patients were given oral tranexamic acid along with topical treatment and in group B, 20 patients were treated only with topical treatment. Oral tranexamic acid was given in dosage of 250 mg twice a day for 3 months and then follow-up was done at 8th and 12th wks. The evaluation of effectiveness of treatment was done with MASI(Melasma Area Severity Index). Comparison was done in the mean of the MASI scores obtained in both groups.
Result: In both groups female patients were more in number. The mean age of patients in group A was 29.75 years & in group B it was 32.55 years. MASI scoring was done in both groups at baseline and at 8th& 12th wks. There was a significant decrease in this score in group A patients with oral tranexamic acid (12.08±2.8 vs 9.1±2.2 at 8th wk. andvs 8.2±2.0 at 12thwk.; P <0.05for both). Whereas in group B patients the decrease in mean MASI score was significant at 8thwk.& insignificant at 12th wk. (12.6±2.9 vs 10.9±2.4at 8th wk. and vs 10.3±2.4at 12th wk.; p<0.05 for former but p>0.05 for later).
Conclusion: Oral tranexamic acid is a safe and effective treatment modality for treating moderate to severe melasma.
Keywords: Melasma, oral tranexamic acid

INTRODUCTION

Melasma (chloasma) is a common acquired pigmentary dermatosis,It presents as ill-defined light to dark brownish macules and patches, in symmetrical distribution on face.[1,2]. Its prevalence ranges from 8.8% to 40% based on ethnicity.[3] No racial differentiation is present in its occurrence, but its prevalence is more in dark complexioned people & in female gender.[4]Its etiology is multifactorial like UV radiation, pregnancy, hormonal activity, thyroid disorders, and certain drugs.[5] All these factors trigger the increased synthesis of melanosomes and cause increased transfer of melanosomes to keratinocytes.Regarding the treatment, it is relatively difficult to treat and can have an adverse psychological impact on many patients.[6]

The existing treatments for melasma up till now do not provide a sustained result. Topical hydroquinone is thought to be a good treatment for it.[7] Other treatment modalities include azelic acid, kojic acid, ascorbic acid, arbutin, corticosteroids and retinoids.[3] Combination therapies like corticosteroid, hydroquinone and retinoid are mostly used. Further some physical therapies like chemical peels and lasers are also used for treating melasma.[8]All these therapies have their own side-effects too.

Recently, the concept of inclusion of different formulations of tranexamic acid in treating this benign pigmentary disorder has been introduced. Normally tranexamic acid (trans- 4 (Aminomethyl) cyclohexane-carboxylic acid, TA), a plasmin inhibitor (hemostatic agent)

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to treat abnormal fibrinolysis to prevent excessive bleeding. It is a synthetic derivative of the amino acid(lysine), exerting its effectthrough reversible interactions with lysine binding sites and thusinhibitingPA from converting plasminogen to plasmin.[9] Plasminogen is also found in basal layer of epidermis in humans. TA is similar in a portion of its structure to tyrosine; it can competitively inhibit tyrosinase.[10]The hypopigmentation effect of TA is mainly due to its antiplasmin activity.[11]It has been used as topical formation, intradermal injections, and oral form to treat skin hyperpigmentation.[12]

This study has been done to see the efficacy and safety of oral tranexamic acid in patients of melasma.

METHOD

This interventional, randomized controlled clinical trial was carried out on 40 patients in Department of Dermatology, Akhtar Saeed Trust Hospital Lahore from January 2020 toJune 2020. After taking permission from the ethical committee of the institute, informed written consent was taken from the patients. Inclusion criteria included both female and male patients with moderate to severe melasma having age above 18 years.Those having age <18 years, pregnancy, lactation, bleeding, diathesis, heart disease, hypertension, patients having menstrual irregularities, on anticoagulants or oral contraceptive pills and who had some form oftreatment for melasmainlast 1 month were excluded from this study. 40 patients were divided into 2 groups, group A and B. All the patients that were enrolled for the study their detailed history was taken,

instruments like woods lamp &dermatoscopewere used to grade (epidermal, mixed, dermal) type of melasma. All the patients in group A had their tests done like platelet count, bleeding, and clotting time. If there was any issue in these, then they were excluded from the study. First, group A was treated with oral tranexamic acid along with broad-spectrum sunscreen and topical formulation of kojic acid whereas the patients in group B were given treatment only with Kojic acid and broad-spectrum sunscreen. Capsule tranexamic acid was prescribed to group A patients in a dose of 250 mg twice a day for 3 months and cases were followed up at base line, $8^{th,}$ and 12^{th} weeks. Patient's response to treatment was evaluated with the help of Melasma Assessment Severity Index (MASI) score. This score was calculated at the start of therapy and at 8^{th} and 12^{th} weeks, respectively. The scoring for MASI shows 48 as the highest & 0 as the lowest. Statistical analysis was done using SPSS. Comparison of the mean MASI scoring achieved in both groups was done using the student's T test along-with the comparison of the statistical significance was obtained.Patient's response to treatment was assessed using the Likert scale(excellent, good, fair, and poor) the four-point scale. If any adverse effects encountered in patients, they were also noted down.

RESULTS

Out of the forty patientsincluded in this interventional study, group A hadtwenty patients(with oral TA) and twenty patients were in Group B (only topical treatment- Kojic acid). The mean age of patients in group A was 29.75 and in group B was 32.55. The characteristics of patients in both groups are shown in Table 1

In group A, males were 7 and females were 13 and in group B males were 6 and females were 14. The duration of disease in both groups ranged from 1 year to 12 years. MASI scoring was done in both groups at start i.e., baseline, then at 8^{th} and 12^{th} weeks. There was a significant decrease in MASI score among group A patients with oral tranexamic acid, in comparison to the score at zero, at 8^{th} and then at 12^{th} weeks(12.08± 2.8 – 9.1 ± 2.2) at 8^{th} week and 8.2 ± 2.0 at 12^{th} week $P<0.05$ for both. Whereas in group B patients i.e., patients without oral tranexamic acid, the MASI score reduced from 12.6 ±24 to 10.9 ± 2.4 at 8^{th} week and then 10.3 ± 2.9 at 12^{th} weeks. In this group, the decrease in MASI score was significant at 8^{th} week $P<0.05$ and was insignificant at 12^{th} weeks $P> 0.05$. As shown in Table 3.

Table 1: Characteristics of patients in both groups.

	Group A	Group B
Gender		
Male	7	6
Female	13	14
Type of melasma		
Epidermal	13	13
Dermal	5	3
Mixed	2	4
Distribution		
Malar	7	7
Mixed	10	11
Centrofacial	2	2
Mandibular	1	0

In group A patients, few side effects were found like abdominal cramps in 2 patients (10%) and oligomenorrhea in 1 patient (5%). Others had no side effects. In group B patients, erythema was found in 2 patients (10%) and dryness in 1 patient (5%). Patient satisfaction in group A showed excellent response in 10 (50%), good in 8 (40%) and fair in 2 (10%) patients, whereas in group B excellent response was in 3 (15%), good in 7 (35%), fair in 9 (45%) and poor in 1(5%) of patients. As shown in Table 2.

Fig. 1 and 2 show the pictures of patient showing improvement in group A.

Table 2: Frequency of improvement after 12^{th} week in both groups

	Group A	Group B
Gender		
Male	7	6
Female	13	14
Type of melasma		
Epidermal	13	13
Dermal	5	3
Mixed	2	4
Distribution		
Malar	7	7
Mixed	10	11
Centrofacial	2	2
Mandibular	1	0

Table 3: Comparison of MASI in both groups at baseline (0 weeks), 8^{th} and 12^{th} week

Improvement	Number	Percentage
Group A		
Excellent	10	50%
Good	8	40%
Fair	2	10%
Poor	0	0
Group B		
Excellent	4	20%
Good	7	35%
Fair	8	40%
Poor	1	5%

Table 4:

	0 weeks	8^{th} week	12^{th} week
Group A	12.08	9.1	8.2
Group B	12.6	10.9	10.3

Fig. 1& 2 depicts the improvement in melasma achieved in group A patients

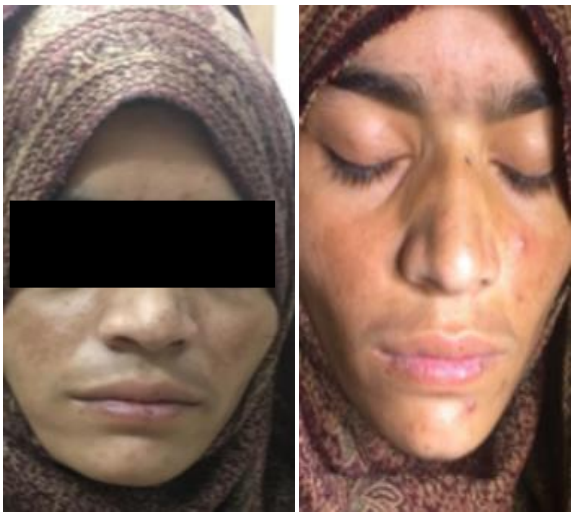
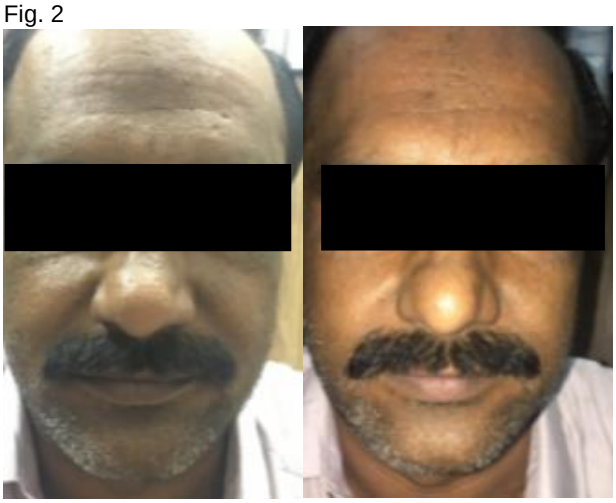


Fig. 2



DISCUSSION

Melasma (chloasma) a benign pigmentary dermatosis, consisting of hyperpigmented macules and patches, common on face in symmetrical distribution.[1]

Different topical therapies are being used for treating melasma like bleaching agents, retinoids, ascorbic and kojic acid. Combination therapy like steroid, bleaching agent and retinoids are also used.[3] Laser therapy is also a good treatment, but recurrence is troublesome.[9,16]

Treating melasma is difficult though different studies have depicted that various treatment modalities show some effectiveness in treatment of epidermalmelasma,but this is not seen in dermal & mixed types.[13,14]

All this has led dermatologists towards safer treatment options and use of tranexamic acid is one of them. In articles by Perperet al[17] and Kim et al[18] TAis thetreatment of melasma. Tranexamic acid is a plasmin inhibitor and is a lysine analogue and it exerts its effect by reversibly blocking lysine binding sites on plasminogen molecules, which leads to suppression of melanocyte activity.[10]

In this study the mean age of patients in group A was 29.75 years and in group B patients was 32.55. In a study done by Qaziet al[19]the commonest age group was between 30-39 years which is comparable with current study.[20]

In our study in both groups female patients were more as compared to male patients, which is in accordance with some other studies like study [redacted]ther study like the one we conducte[redacted]ical tranexamic acid gel.[22] The resu[redacted]e in pigmentation was not that significant in comparison to control group. But in our study the group with oral tranexamic acid had a significant decrease in MASI score at week 12 as compared to group on topical treatment, in this group the decrease in MASI score was insignificant at 12 weeks. Another study was conducted in Chinese population with same dosage of tranexamic acid as in our study and results showed tranexamic acid to be a safe, rapid, and effective treatment for melasma.[23]

The contraindications of TA include defective colour vision, intravascular clotting conditions&hypersensitivity to it. The commonest side effects of tranexamic acid aregastrointestinal complaints (nausea, diarrhea, and abdomen pain).[15]

In our study in group A patients, only 2 had abdomen cramps and 1 patient had oligomenorrhoea like another study done by Safoora et al which showed almost similar results.[24]

So, our results corresponded with other studies in showing that effective lightening was seen following oral tranexamic administration in patients of melasma.

The short duration of treatment with TA, follow up & use of MASI score along with the few number of patients in each group were the limitations of this study . So further studies needed with higher number of participants and longer follow-up to assess the dosage and efficacy of tranexamic acid in treating melasma.

CONCLUSION

We concluded from our study that adding oral tranexamic acid to our routine treatment measures for melasma provides a swift and effective improvement in it. So oral tranexamic acid is a safe recommendation for treating melasma.

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