

# Topical tranexamic acid versus hydroquinone for patients presenting with melasma

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## Abstract

**Objective** To compare the outcome with topical tranexamic acid versus hydroquinone for management of patients presenting with melasma.

**Methods** The present study was conducted in the outpatient department of dermatology unit 1. 354 patients fulfilling selection criteria were enrolled and divided in two groups. In group A, patients were prescribed topical cream of 5% TA and in group B, patients were prescribed topical cream of 2% hydroquinone. MASI score was assessed at presentation and at 4 weeks of follow up.

**Results** In this study the mean age of cases in Tranexamic acid group was  $35.42 \pm 10.68$  years and in Hydroquinone group was  $36.25 \pm 10.42$  years. In Tranexamic acid there were 13(7.3%) male and 164(92.7%) female cases and in Hydroquinone group there were 26(14.7%) male and 151(85.3%) female cases. Mean duration of pigmentation in Tranexamic acid group was  $6.45 \pm 3.10$  months and in Hydroquinone group was  $6.50 \pm 3.02$  months. The mean MASI score at baseline in Tranexamic acid group was  $36.14 \pm 6.85$  and in Hydroquinone group was  $36.61 \pm 6.81$ . The mean MASI score at last follow up in Tranexamic acid group was  $23.68 \pm 7.96$  and in Hydroquinone group was  $19.32 \pm 8.33$ . The mean MASI score was statistically less in Hydroquinone group as compared to Tranexamic acid group, p-value < 0.01. In Tranexamic acid group 39(22%) cases had side effects and in Hydroquinone group 83(46.9%) cases had side effects.

**Conclusion** This study concludes that MASI score was significantly reduced in hydroquinone group but cases in topical tranexamic acid group developed less side effects. So, further studies are required to establish the use of topical tranexamic acid.

## Key words

Melasma, MASI, topical tranexamic acid, hydroquinone.

## Introduction

Melasma is a highly prevalent, chronic pigmentary disorder.<sup>1</sup> Melasma is characterized by irregular light to grey brown macules and patches on sun-exposed skin commonly affecting the cheeks, forehead, upper lip, nose, chin and occasionally forearms.<sup>1</sup> It is a common acquired disorder of pigmentation, and is known to occur in all skin types, ethnic groups and both

genders. It is relatively more common in darker skin types (III and IV) and women of child bearing age than men.<sup>2</sup>

Even though melasma is a widely recognized cause of significant cosmetic disfigurement worldwide, there is a lack of systematic and clinically usable treatment algorithms and guidelines for melasma management.<sup>3</sup> Melasma can be difficult to treat. The pigment of melasma develops gradually and resolution is also slow. Resistant cases or recurrences of melasma occur often and are certain if strict avoidance of sunlight is not rigidly heeded.<sup>4</sup> The mainstay of treatment for melasma remains topical

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depigmenting agents. Hydroquinone is a classic and still commonly used first-line agent, either alone or in combination with other agents, although there are concerns regarding adverse effects with long-term use. It is a hydroxyphenolic chemical that inhibits tyrosinase, an enzyme that converts L-tyrosine to L-DOPA and the rate-limiting step in the pathway of melanin synthesis. But the major adverse effect of hydroquinone is mild skin irritation, especially when the more effective, higher concentrations are used.<sup>4</sup>

In an attempt to search for a new treatment for melasma, Wu *et al* studied administration of tranexamic acid (TA) in Chinese patients. At follow-up, more than half of patients (54%) showed good results. This treatment may be effective for some patients, but further study is needed.<sup>5</sup> Other reports have also described successful treatment with TA.<sup>6,7</sup>

One randomized trial showed that with TA, mean MASI score was  $22.60 \pm 10.37$  while with hydroquinone, mean MASI score was  $19.48 \pm 10.93$ . Although the difference was insignificant ( $p=0.31$ ). But in terms of side effects, 23.1% patients of TA group while 51.3% patients of hydroquinone group showed side effects (erythema, skin irritation, dryness of skin or hypertrichosis). Significant side effects were noted for hydroquinone compared with TA ( $P = 0.01$ ). Authors concluded that the topical TA is as effective as hydroquinone but more safe medication for the treatment of melasma.<sup>8</sup>

The rationale of this study is to compare the outcome with topical TA versus hydroquinone for management of patients presenting with melasma. Through literature it has been observed that TA can be a good replacement for hydroquinone. As the effectiveness of TA in reducing MASI score was equivalent as reported by hydroquinone, but side effects are

significantly less as compared to hydroquinone. But no local evidence has been available in this regard. Through this study, we want to get local evidence so that we may be able to implement the results of this study. Moreover, the previous studies were conducted on small sample size. We conducted this study on large sample size to get more authentic and reliable results, which would be able to be implemented in future. This can help to improve our practice and in future we might be able to implement a better management regimen for management of melasma with least side effects.

## Methods

The present study was conducted at outpatient department dermatology unit 1, Mayo hospital, Lahore. 354 patients fulfilling selection criteria were enrolled in the study. Patients of age 16-60 years of either gender presenting with melasma, with baseline MASI score of  $>25$  for  $>3$  months were included, while pregnant or lactating females, patients taking contraceptive pills, taking any photosensitizing drugs like NSAIDs, tetracyclines, spironolactone, phenytoin, carbamazepine, patients having any bleeding disorders ( $PT > 15$  sec,  $aPTT > 20$  sec) or taking any kind of anticoagulants, and patients taking treatment for melasma within the last 3 months (phototherapy or corticosteroid agents) were excluded.

Informed consent was obtained and demographic history including name, age, gender, duration of melasma was noted. Then patients were randomly divided in two groups by using lottery method. In group A, patients was prescribed topical cream of 5% TA and in group B, patients was prescribed topical cream of 2% hydroquinone. At first presentation, MASI score was assessed by researcher herself. Then patients were followed-up for 4 weeks in OPD. Patients were advised to apply cream to

completely cover the affected area. After 4 weeks, patients were assessed again for MASI score after treatment (as per operational definition). Side effects in terms of erythema, skin irritation, dryness of the skin, xerosis, hypertrichosis, inflammation and scaling were also measured. All this information was recorded through proforma. The data were entered and analyzed in SPSS version 20. Mean & standard deviation was calculated for variables like age, duration of melasma, baseline MASI and after treatment MASI score. Frequency and percentage was calculated for gender and side effects (yes/no). Both groups were compared for mean MASI score by using independent sample t-test and for side effects by using chi-square test. P-value  $\leq 0.05$  was taken as significant. Data were stratified for age, gender, baseline M. ASI score and duration of melasma to deal with effect modifiers. Post-stratification, respective test of significance was applied with p-value  $\leq 0.05$  taken as significant.

## Results

The mean MASI score at baseline in Tranexamic acid group was  $36.14 \pm 6.85$  and in Hydroquinone group was  $36.61 \pm 6.81$ . The mean MASI score at last follow up after 4 weeks in Tranexamic acid group was  $23.68 \pm 7.96$  and in Hydroquinone group was  $19.32 \pm 8.33$ . The mean MASI score was statistically less in Hydroquinone group as compared to Tranexamic acid group, p-value  $< 0.01$  (**Table 1**).

In Tranexamic acid group 39 (22%) cases had side effects and in Hydroquinone group 83 (46.9%) cases had side effects. While in Tranexamic acid group 138 (78%) cases did not have any side effect and in Hydroquinone group 94 (46.9%) cases had no side effects. The frequency of side effects was significantly less in Tranexamic acid group as compared to hydroquinone group, p-value  $< 0.05$  (**Table 2**).

Mean duration of illness in Tranexamic acid group was  $6.45 \pm 3.10$  months and in Hydroquinone group was  $6.50 \pm 3.02$  months.

**Table 1** Mean comparison of MASI (baseline) and MASI score after 4 weeks

		Mean	S. D	Minimum	Maximum	p-value
MASI (baseline)	Tranexamic acid	36.14	6.85	26.00	48.00	0.358
	Hydroquinone	36.61	6.81	26.00	48.00	
	Total	36.37	6.83	26.00	48.00	
MASI score after	Tranexamic acid	23.68	7.96	6.00	41.00	$<0.001$
	Hydroquinone	19.32	8.33	5.00	40.00	
	Total	21.50	8.43	5.00	41.00	

**Table 2** Frequency distribution of side effects

		Study groups		Total
		Tranexamic acid	Hydroquinone	
Side effects	Yes	39(22.0%)	83(46.9%)	122(34.5%)
	No	138(78.0%)	94(53.1%)	232(65.5%)
Total		177(100.0%)	177(100.0%)	354(100.0%)

Chi-square = 24.214 ; P-value  $< 0.001$

In this study the mean age of cases in Tranexamic acid group was  $35.42 \pm 10.68$  years and in Hydroquinone group was  $36.25 \pm 10.42$  years.

In Tranexamic acid there were 13 (7.3%) male and 164 (92.7%) female cases and in Hydroquinone group there were 26 (14.7%) male and 151 (85.3%) female cases.

## **Discussion**

In current study the mean MASI score at last follow up in Tranexamic acid group was  $23.68 \pm 7.96$  and in Hydroquinone group was  $19.32 \pm 8.33$ . The mean MASI score was statistically less in Hydroquinone group as compared to Tranexamic acid group,  $p$ -value  $< 0.01$ . In Tranexamic acid group 39 (22%) cases had side effects and in Hydroquinone group 83 (46.9%) cases had side effects. One randomized trial showed that with TA, mean MASI score was  $22.60 \pm 10.37$  while with hydroquinone, mean MASI score was  $19.48 \pm 10.93$ . Although the difference was insignificant ( $p=0.31$ ). But in terms of side effects, 23.1% patients of TA group while 51.3% patients of hydroquinone group showed side effects (erythema, skin irritation, dryness of skin or hypertrichosis). Significant side effects were noted for hydroquinone compared with TA ( $p = 0.01$ ). Authors concluded that the topical TA is as effective as hydroquinone but more safe medication for the treatment of melasma.<sup>8</sup> These findings are almost similar to current study.

Recently a randomized double-blinded clinical trial was performed on 60 women who suffered from melasma. The patients were then randomly assigned via computerized randomization to two groups: group A received TXA 5% (topically twice a day for 12 weeks in the location of the melasma) and group B (received hydroquinone

2% with the same treatment order). No side effects were detected in group A, but 10% of those in group B complained of drug-related side effects including erythema and skin irritation ( $p=0.131$ ). Regarding the level of patient satisfaction, the patients in group A had a significantly higher level of satisfaction 33.3% compared with 6.7% in group B ( $p = 0.015$ ).<sup>9</sup>

Similarly, in 2015, another study was done to compare therapeutic effects of liposomal tranexamic acid and conventional hydroquinone on melasma. Thirty women with bilateral melasma were enrolled in a split-face trial lasting 12 weeks. Patients blindly applied 5% topical liposomal TA and 4% hydroquinone cream, to the designated sides of the face twice daily in addition to the assigned sunscreen in the morning. Skin pigmentation was measured using MASI (Melasma Area and Severity Index) at each visit separately for each side at the base line and every month until one month after treatment course. The mean MASI scores significantly reduced in both treated sides ( $P < P=0.001$ ) after 12 week. A greater decrease was observed with 5% liposomal TA, although this difference was not statistically significant. Irritation occurred in three patients with hydroquinone, while no serious adverse events occurred with TA. Thus, on the basis of these results, topical liposomal TA can be used as a new, effective, safe, and promising therapeutic agent in melasma.<sup>10</sup>

Moreover another double-blind split-face trial was performed to evaluate the efficacy and safety of topical solution of TA and compare it with combined solution of hydroquinone and dexamethasone as the gold standard treatment of melasma in Iranian women. After 12 weeks a significant decreasing trend was observed in the MASI score of both groups with no significant difference between them during the study ( $P < 0.05$ ). No differences were seen in patient's

and investigator's satisfaction of melasma improvement between two groups ( $P < 0.05$ ). However, the side effects of hydroquinone + dexamethasone were significantly prominent compared with TA ( $P = 0.01$ ). So, this study's results concluded that the topical TA is an effective and safe medication for the treatment of melasma.<sup>8</sup>

### **Conclusion**

This study concludes that MASI score was significantly reduced in hydroquinone group but cases in topical tranexamic acid group developed less side effects. So, further studies are required to establish the use of topical tranexamic acid.

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