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A Comparative Study of Safety, Efficacy and Pharmacotherapeutic Adherence to Hydroquinone vs Tranexamic Acid in Patients with Melasma in A Tertiary Care Teaching Hospital

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ABSTRACT

Background: Melasma is a common acquired hyperpigmentation disorder that predominantly affects women and has a significant impact on quality of life. Various topical agents are used for its management, among which Hydroquinone remains the standard treatment, while Tranexamic Acid has emerged as a promising alternative. The present study was undertaken to compare the efficacy, safety, and pharmacotherapeutic adherence of topical Hydroquinone 4% and topical Tranexamic Acid 5% in patients with melasma.

Materials and Methods: This observational comparative study was conducted in the Department of Pharmacology in collaboration with the Department of Dermatology, Venereology and Leprosy at G.S.V.M. Medical College and associated L.L.R. Hospital, Kanpur. A total of 84 patients were enrolled, of whom 80 completed the study and were included in the final analysis. Fifty patients received topical Hydroquinone 4% (Group A) and 30 patients received topical Tranexamic Acid 5% (Group B). Efficacy was assessed using the Melasma Area and Severity Index (MASI) score at baseline, 3, 6, 9, and 12 months. Pharmacotherapeutic adherence was evaluated using the 4-item Morisky Medication Adherence Scale (MMAS-4), while safety was assessed through monitoring of adverse drug reactions (ADRs). Statistical analysis was performed using SPSS software, with $p < 0.05$ considered statistically significant.

Results: The majority of participants were females (92.0% in the Hydroquinone group and 93.3% in the Tranexamic Acid group), with a mean age of 36.00 ± 8.88 years and 37.00 ± 8.79 years, respectively. Both treatment groups demonstrated significant reductions in MASI scores from baseline ($p < 0.05$). The Hydroquinone group showed a greater reduction in MASI score from 21.95 ± 3.01 at baseline to 13.71 ± 3.26 at 12 months, compared with a reduction from 21.98 ± 2.59 to 16.10 ± 3.29 in the Tranexamic Acid group. Intergroup comparison revealed significantly better efficacy with Hydroquinone at 12 months ($p = 0.01$). Adherence was high in both groups, with mean MMAS-4 scores of 3.30 ± 0.65 and 3.52 ± 0.51 in the Hydroquinone and Tranexamic Acid groups, respectively. Adverse drug reactions were observed in 4 patients (8.0%) receiving Hydroquinone, leading to treatment discontinuation, whereas no ADRs were reported in the Tranexamic Acid group.

Conclusion: Both Hydroquinone 4% and Tranexamic Acid 5% were effective in the treatment of melasma. Hydroquinone demonstrated superior efficacy in reducing MASI scores, while Tranexamic Acid exhibited an excellent safety profile and slightly better adherence. Tranexamic Acid may serve as a safe and well-tolerated alternative for long-term management of melasma.

***Keywords**: Melasma, Hydroquinone, Tranexamic Acid, MASI score, Pharmacotherapeutic Adherence, Adverse Drug Reactions, Hyperpigmentation.*

INTRODUCTION

Melasma is a common acquired hypermelanosis characterized by symmetrical brown to gray-brown macules and patches distributed predominantly over sun-exposed areas of the face. It is one of the most frequently encountered pigmentary disorders in dermatological practice and has a significant psychosocial impact due to its chronic, recurrent, and cosmetically disfiguring nature (1,2). The condition is particularly prevalent among women and individuals with darker skin phototypes, especially in tropical and subtropical regions where ultraviolet radiation exposure is high (1,3).

The pathogenesis of melasma is multifactorial and complex. Various factors such as genetic predisposition, ultraviolet radiation, hormonal influences, pregnancy, oral contraceptive use, thyroid disorders, and certain medications have been implicated in its development (2,3). Exposure to sunlight remains one of the most important aggravating factors, stimulating melanogenesis and contributing to recurrence even after successful treatment (1).

Several therapeutic modalities have been employed for the management of melasma, including topical depigmenting agents, chemical peels, laser therapies, and systemic medications. Despite numerous available treatment options, complete and sustained remission remains difficult to achieve, and recurrence is common (4). Therefore, effective treatment should not only improve pigmentation but also possess an acceptable safety profile and encourage long-term adherence.

Hydroquinone is considered the gold standard topical treatment for melasma. It acts primarily by inhibiting tyrosinase, thereby reducing melanin synthesis and suppressing melanocyte metabolic processes (4,5). Numerous studies have demonstrated its effectiveness in reducing pigmentation and improving clinical outcomes. However, prolonged use of hydroquinone may be associated with adverse effects such as erythema, burning sensation, irritation, contact dermatitis, and rarely exogenous ochronosis, which may limit patient compliance and long-term utility (5,6).

Tranexamic acid, originally developed as an antifibrinolytic agent, has recently gained attention as a promising treatment for melasma. It inhibits the plasminogen-plasmin system, thereby reducing melanocyte activation and decreasing ultraviolet-induced pigmentation. Topical, oral, and intradermal formulations of tranexamic acid have shown favorable outcomes in several clinical studies (7–9). In addition to its efficacy, tranexamic acid has demonstrated a relatively favorable safety profile, making it an attractive alternative to conventional depigmenting agents (8,9).

Successful treatment of melasma depends not only on efficacy but also on patient adherence to therapy. Since melasma often requires prolonged treatment and strict photoprotection, patient compliance plays a critical role in determining therapeutic outcomes (10). Assessment of pharmacotherapeutic adherence is therefore an important component when comparing treatment modalities in real-world clinical practice.

Although both hydroquinone and tranexamic acid are widely used for the treatment of melasma, comparative data regarding their efficacy, safety, and patient adherence remain limited. Therefore, the present study was undertaken to compare topical Hydroquinone 4% and topical Tranexamic Acid 5% in patients with melasma attending a tertiary care teaching hospital.

MATERIALS AND METHODS

Study Design and Setting

This observational comparative study was conducted in the Department of Pharmacology in collaboration with the Outpatient Department of Dermatology, Venereology and Leprosy at G.S.V.M. Medical College and associated L.L.R. Hospital, Kanpur, Uttar Pradesh, India. The study was designed to evaluate and compare the efficacy, safety, and pharmacotherapeutic adherence of topical Hydroquinone 4% and topical Tranexamic Acid 5% in patients with melasma.

Study Population

Patients attending the Dermatology Outpatient Department with a clinical diagnosis of melasma were screened for eligibility. Participants were recruited according to predefined inclusion and exclusion criteria after obtaining written informed consent.

Inclusion Criteria

Patients fulfilling the following criteria were included in the study:

- Clinically diagnosed cases of melasma.
- Age between 18 and 65 years.
- Willingness to provide written informed consent and comply with follow-up visits.

Exclusion Criteria
Patients were excluded if they had:

- Pregnancy or lactation.
- Known hypersensitivity to hydroquinone or tranexamic acid.
- Active skin infections or other dermatological disorders affecting assessment.
- Use of topical depigmenting agents within the preceding three months.
- Coagulation disorders.
- Significant comorbid illnesses.
- Refusal to participate in the study.

Sample Size and Sampling Technique
The sample size was calculated using Yamane's formula with a 95% confidence level and an acceptable margin of error. The calculated sample size was 80 participants. A total of 84 eligible patients were initially enrolled. Four patients receiving hydroquinone were subsequently excluded due to adverse drug reactions. Thus, 80 patients completed the study and were included in the final analysis.

Participants were allocated into two groups according to the treatment prescribed by the treating dermatologist:

- Group A (Hydroquinone Group): Patients prescribed topical hydroquinone 4% cream applied at night along with SPF 40 sunscreen during daytime. Fifty-four patients were initially enrolled, of whom four were excluded due to adverse drug reactions, resulting in 50 patients for final analysis.
- Group B (Tranexamic Acid Group): Patients prescribed topical tranexamic acid 5% cream applied at night along with SPF 40 sunscreen during daytime. Thirty patients were enrolled and completed the study.

Study Procedure
All enrolled patients received counselling regarding the chronic and recurrent nature of melasma, the expected duration of treatment, and the importance of strict photoprotection. A broad-spectrum sunscreen (SPF 40) was prescribed to all participants and advised to be applied 15 minutes before sun exposure.

The study duration was 12 months. Baseline clinical evaluation was performed followed by follow-up assessments at 3, 6, 9, and 12 months.

Outcome Assessment
Efficacy Assessment
The primary efficacy endpoint was the change in Melasma Area and Severity Index (MASI) score from baseline.
The MASI score was calculated by evaluating four facial regions: forehead, right malar region, left malar region, and chin. Assessment included the extent of area involvement, darkness, and homogeneity of pigmentation. MASI scores were recorded at baseline and at each follow-up visit.

Pharmacotherapeutic Adherence Assessment
Medication adherence was assessed using the 4-item Morisky Medication Adherence Scale (MMAS-4). The questionnaire evaluated medication-taking behavior, including forgetfulness, carelessness, discontinuation when symptoms improved, and discontinuation when symptoms worsened.

Scores were categorized as follows:

- High adherence: score of 4
- Medium adherence: score of 2–3
- Low adherence: score of 0–1

MMAS-4 assessments were performed during each follow-up visit.

Safety Assessment
Safety and tolerability were evaluated by monitoring adverse drug reactions (ADRs) throughout the study period. Patients were assessed for local and systemic adverse effects including erythema, burning sensation, itching, irritation, and hypersensitivity reactions.

The causality of ADRs was assessed using the Naranjo Adverse Drug Reaction Probability Scale, while severity was evaluated using the Modified Hartwig Severity Scale.

Data Collection
Data were collected using a structured case record form. Baseline demographic and clinical variables including age, sex, duration of illness, family history, and baseline MASI score were recorded.

At each follow-up visit (3, 6, 9, and 12 months), the following parameters were assessed:

- MASI score
- MMAS-4 adherence score
- Occurrence of adverse drug reactions

All collected data were entered into a master database using Microsoft Excel and subsequently verified for completeness and accuracy.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of G.S.V.M. Medical College, Kanpur, prior to patient recruitment (approval dated 24 June 2024). Written informed consent was obtained from all participants before participation in the study. Participants were informed about the study objectives, procedures, potential benefits, and risks. Confidentiality of patient information was maintained throughout the study, and participants were free to withdraw from the study at any stage without affecting their routine medical care.

Statistical Analysis

Data were using Statistical Package for the Social Sciences (SPSS) software. Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages.
Comparisons between the Hydroquinone and Tranexamic Acid groups were performed using the unpaired Student's t-test for continuous variables and appropriate categorical tests where applicable. Statistical significance was considered at a p-value of less than 0.05.

RESULTS AND OBSERVATIONS

Table 1. Age Distribution of Participants by Study Group

Age Group (Years)	Hydroquinone Group (n=50)	Tranexamic Acid Group (n=30)
<20	0	0
20–39	30	19
40–59	19	10
≥60	1	1
Total	50	30

Table 1 presents the age distribution of participants in the Hydroquinone and Tranexamic Acid treatment groups. In the Hydroquinone group (n = 50), 30 (60%) participants were aged 20–39 years, 19 (38%) were aged 40–59 years, and 1 (2%) was aged ≥60 years. In the Tranexamic Acid group (n = 30), 19 (63.3%) participants belonged to the 20–39 years age group, 10 (33.3%) were aged 40–59 years, and 1 (3.3%) was aged ≥60 years. No participants in either group were younger than 20 years.

The age distribution was comparable between the two treatment groups. The majority of participants in both groups were in the 20–39 years age category, accounting for 60% of the Hydroquinone group and 63.3% of the Tranexamic Acid group. Approximately one-third of participants belonged to the 40–59 years age group, while only a small proportion were aged 60 years or older. The absence of participants below 20 years of age and the similar distribution across age categories indicate good baseline comparability between the treatment groups with respect to age (Table 1).

Table 2. Gender Distribution of Participants by Study Group

Gender	Hydroquinone Group (n=50)	Tranexamic Acid Group (n=30)
Male	4 (8.0%)	2 (6.7%)
Female	46 (92.0%)	28 (93.3%)
Total	50 (100%)	30 (100%)

Table 2 shows the gender distribution of participants in the two study groups. In the Hydroquinone group (n = 50), 4 (8.0%) participants were male and 46 (92.0%) were female. Similarly, in the Tranexamic Acid group (n = 30), 2 (6.7%) participants were male and 28 (93.3%) were female.

A marked female predominance was observed in both treatment groups. Females constituted more than 90% of the study population, whereas males represented only a small proportion of participants. The gender distribution was comparable between the Hydroquinone and Tranexamic Acid groups, indicating that both groups were well matched with respect to gender at baseline (Table 2).

Table 3. Duration of Illness

Group	Duration of Illness (Years) Mean ± SD
Hydroquinone Group (n=50)	**0.5 ± 1.5**
Tranexamic Acid Group (n=30)	**0.2 ± 1.0**

Table 3 presents the duration of illness among participants in the two study groups. The mean duration of illness in the Hydroquinone group (n = 50) was **0.5 ± 1.5 years**, while the mean duration of illness in the Tranexamic Acid group (n = 30) was **0.2 ± 1.0 years**.

The average duration of illness was relatively short in both groups. Participants in the Hydroquinone group had a slightly longer mean duration of illness compared to those in the Tranexamic Acid group. However, the overall duration of illness was low in both groups, suggesting that most participants had relatively recent onset of the condition. The baseline duration of illness appeared broadly comparable between the two treatment groups (Table 3).

Table 4. Mean Age of Participants

Group	Number of Patients (n)	Mean Age (Years) ± SD
Hydroquinone Group	**50**	**36.00 ± 8.88**
Tranexamic Acid Group	**30**	**37.00 ± 8.79**

Table 4 shows the mean age of participants in the two study groups. The Hydroquinone group included 50 participants with a mean age of **36.00 ± 8.88 years**, while the Tranexamic Acid group included 30 participants with a mean age of **37.00 ± 8.79 years**.

The mean age of participants was similar in both treatment groups. Participants in the Tranexamic Acid group were, on average, slightly older than those in the Hydroquinone group; however, the difference was minimal. The comparable mean age and standard deviation values indicate that the two groups were well matched with respect to age, reducing the likelihood of age-related bias in treatment outcome comparisons (Table 4).

Table 5. Family History of Melasma

Family History	Hydroquinone Group (n=50)	Tranexamic Acid Group (n=30)
Present	**24 (48.0%)**	**14 (46.7%)**
Absent	**26 (52.0%)**	**16 (53.3%)**
Total	**50 (100%)**	**30 (100%)**

Table 5 presents the distribution of family history of melasma among the study participants. In the Hydroquinone group (n = 50), a positive family history of melasma was reported by 24 (48.0%) participants, while 26 (52.0%) had no family history. In the Tranexamic Acid group (n = 30), 14 (46.7%) participants reported a positive family history, whereas 16 (53.3%) had no family history of melasma.

The proportion of participants with and without a family history of melasma was similar in both treatment groups. Approximately half of the participants in each group reported a positive family history, suggesting a possible genetic predisposition among a substantial proportion of cases. The comparable distribution of family history between the Hydroquinone and Tranexamic Acid groups indicates that both groups were well balanced with respect to this baseline characteristic (Table 5).

Table 6. Intra-group Analysis of Efficacy of Hydroquinone 4% (Group A)

Time Point	Mean MASI Score ± SD	p-value (vs Baseline)
Baseline	**21.95 ± 3.01**	**-**
3 Months	**19.72 ± 2.98**	**<0.05**
6 Months	**17.83 ± 2.96**	**<0.05**
9 Months	**15.67 ± 3.25**	**<0.05**
12 Months	**13.71 ± 3.26**	**<0.05**

Table 6 presents the intra-group analysis of the efficacy of Hydroquinone 4% (Group A) over a 12-month follow-up period. The mean MASI score at baseline was **21.95 ± 3.01**. A progressive reduction in MASI score was observed at each follow-up visit, decreasing to **19.72 ± 2.98** at 3 months, **17.83 ± 2.96** at 6 months, **15.67 ± 3.25** at 9 months, and **13.71 ± 3.26** at 12 months. The reduction in MASI score at all follow-up time points was statistically significant compared with baseline (**$p < 0.05$**).

Participants treated with Hydroquinone 4% demonstrated a steady and significant improvement in melasma severity throughout the study period. The mean MASI score decreased by **8.24 points** from baseline to 12 months, representing a substantial reduction in disease severity. The continuous decline in MASI scores at successive follow-up visits indicates sustained therapeutic efficacy of Hydroquinone 4%, with statistically significant improvement evident as early as 3 months and maintained up to 12 months (Table 6).

Table 7. Intra-group Analysis of Efficacy of Tranexamic Acid 5% (Group B)

Time Point	Mean MASI Score ± SD	p-value (vs Baseline)
Baseline	**21.98 ± 2.59**	**-**
3 Months	**20.50 ± 2.67**	**<0.05**
6 Months	**18.98 ± 2.85**	**<0.05**
9 Months	**17.58 ± 3.06**	**<0.05**
12 Months	**16.10 ± 3.29**	**<0.05**

Table 7 presents the intra-group analysis of the efficacy of Tranexamic Acid 5% (Group B) over a 12-month follow-up period. The mean MASI score at baseline was **21.98 ± 2.59**. A gradual reduction in MASI score was observed during follow-up, declining to **20.50 ± 2.67** at 3 months, **18.98 ± 2.85** at 6 months, **17.58 ± 3.06** at 9 months, and **16.10 ± 3.29** at 12 months. The reduction in MASI score at each follow-up visit was statistically significant compared with baseline (**$p < 0.05$**).

Participants treated with Tranexamic Acid 5% showed a consistent and statistically significant improvement in melasma severity throughout the study period. The mean MASI score decreased by **5.88 points** from baseline to 12 months, indicating a favorable therapeutic response. The progressive decline in MASI scores at successive follow-up visits demonstrates sustained efficacy of Tranexamic Acid 5%, with significant improvement evident from 3 months onward and maintained up to the end of the 12-month follow-up period (Table 7).

Table 8. Comparison of Mean MASI Scores Between Groups During Follow-up

Time Point	Hydroquinone 4% (Mean ± SD)	Tranexamic Acid 5% (Mean ± SD)	p-value
Baseline	**21.95 ± 3.01**	**21.98 ± 2.59**	**-**
3 Months	**19.72 ± 2.98**	**20.50 ± 2.67**	**0.963**
6 Months	**17.83 ± 2.96**	**18.98 ± 2.85**	**0.230**
9 Months	**15.67 ± 3.25**	**17.58 ± 3.06**	**0.090**
12 Months	**13.71 ± 3.26**	**16.10 ± 3.29**	**0.010**

Table 8 compares the mean MASI scores between the Hydroquinone 4% and Tranexamic Acid 5% groups during the 12-month follow-up period. At baseline, the mean MASI scores were comparable between the Hydroquinone group (**21.95 ± 3.01**) and the Tranexamic Acid group (**21.98 ± 2.59**). During follow-up, both groups demonstrated progressive reductions in MASI scores. At 3 months, the mean MASI scores were **19.72 ± 2.98** and **20.50 ± 2.67** in the Hydroquinone and Tranexamic Acid groups, respectively (**$p = 0.963$**). At 6 months, the corresponding values were **17.83 ± 2.96** and **18.98 ± 2.85** (**$p = 0.230$**), while at 9 months they were **15.67 ± 3.25** and **17.58 ± 3.06** (**$p = 0.090$**). At 12 months, the mean MASI score was significantly lower in the Hydroquinone group (**13.71 ± 3.26**) compared with the Tranexamic Acid group (**16.10 ± 3.29**), with a statistically significant difference (**$p = 0.010$**).

Both treatment groups showed gradual improvement in melasma severity over the study period, as evidenced by decreasing MASI scores. Although the Hydroquinone group consistently demonstrated lower mean MASI scores than the Tranexamic Acid group during follow-up, the differences were not statistically significant at 3, 6, or 9 months. However, by the end of 12 months, Hydroquinone 4% achieved a significantly greater reduction in MASI score compared with Tranexamic Acid 5% (**$p = 0.010$**). These findings suggest that while both treatments were effective, Hydroquinone 4% provided superior long-term efficacy in reducing melasma severity (Table 8).

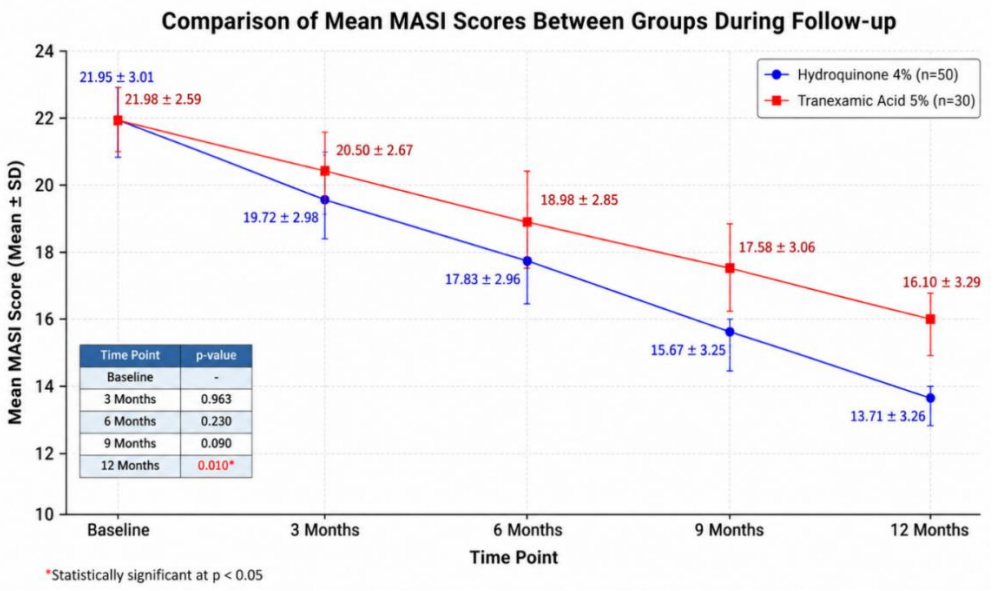

Table 9. Comparison of Pharmacotherapeutic Adherence (MMAS-4 Score)

Treatment Group	Mean MMAS-4 Score ± SD	Adherence Classification
Hydroquinone 4%	**3.30 ± 0.65**	**High Adherence**
Tranexamic Acid 5%	**3.52 ± 0.51**	**High Adherence**

Table 9 presents the comparison of pharmacotherapeutic adherence between the two treatment groups as assessed using the Morisky Medication Adherence Scale-4 (MMAS-4). The mean MMAS-4 score in the Hydroquinone 4% group was **3.30 ± 0.65**, while the Tranexamic Acid 5% group demonstrated a mean score of **3.52 ± 0.51**. Both groups were classified as having **high adherence** to the prescribed treatment regimen.

High treatment adherence was observed in both study groups. The Tranexamic Acid 5% group showed a slightly higher mean MMAS-4 score compared to the Hydroquinone 4% group, indicating marginally better adherence. However, both groups achieved scores consistent with high adherence, suggesting good compliance with therapy throughout the study period. This high level of adherence may have contributed positively to the treatment outcomes observed in both groups (Table 9).

Table 10. Incidence of Adverse Drug Reactions and Discontinuation Rates

Safety Parameter	Hydroquinone 4% (n=50)	Tranexamic Acid 5% (n=30)
Patients Reporting ADRs	4 (8.0%)	0 (0.0%)
Reported Symptoms	Erythema, Irritation, Burning	None
Treatment Discontinuation Due to ADRs	4 (8.0%)	0 (0.0%)

Table 10 summarizes the incidence of adverse drug reactions (ADRs) and treatment discontinuation rates in the two study groups. In the Hydroquinone 4% group (n = 50), **4 (8.0%)** participants reported ADRs, which included **erythema, irritation, and burning sensations**. All four affected participants discontinued treatment due to these adverse effects, resulting in a discontinuation rate of **8.0%**. In contrast, no participants in the Tranexamic Acid 5% group (n = 30) reported any ADRs, and no treatment discontinuations were recorded.

The incidence of adverse drug reactions was observed only in the Hydroquinone 4% group, where a small proportion of participants experienced local cutaneous side effects. These adverse effects were sufficiently severe to result in treatment discontinuation among all affected participants. The absence of reported ADRs and treatment discontinuations in the Tranexamic Acid 5% group suggests a more favorable safety and tolerability profile. Overall, Tranexamic Acid 5% demonstrated better tolerability, whereas Hydroquinone 4% was associated with a higher risk of treatment-related adverse effects (Table 10).

DISCUSSION

The present study was conducted to compare the efficacy, safety, and pharmacotherapeutic adherence of topical Hydroquinone 4% and topical Tranexamic Acid 5% in patients with melasma over a period of twelve months.

Melasma predominantly affected females in the present study, accounting for 92.0% of patients in the Hydroquinone group and 93.3% in the Tranexamic Acid group. This finding is consistent with previous studies that have reported a

higher prevalence of melasma among women, largely attributed to hormonal influences, pregnancy, and oral contraceptive use (1–3). The mean age of participants was 36.0 ± 8.88 years in the Hydroquinone group and 37.0 ± 8.79 years in the Tranexamic Acid group, indicating that melasma most commonly affects individuals during their reproductive and perimenopausal years. Similar observations have been reported in earlier epidemiological studies (2,3). A positive family history of melasma was observed in nearly half of the participants in both groups. This finding supports the role of genetic predisposition in the development of melasma and is in agreement with previous reports highlighting familial clustering of the disease (2,3).

The primary efficacy outcome was assessed using the Melasma Area and Severity Index (MASI). Both treatment groups demonstrated a progressive reduction in MASI scores throughout the follow-up period, indicating significant clinical improvement. In the Hydroquinone group, the mean MASI score decreased from 21.95 ± 3.01 at baseline to 13.71 ± 3.26 at 12 months, representing approximately 38% improvement. In contrast, the Tranexamic Acid group demonstrated a reduction from 21.98 ± 2.59 to 16.10 ± 3.29, corresponding to approximately 27% improvement.

These findings suggest that both treatments are effective in reducing melasma severity; however, Hydroquinone produced greater improvement than Tranexamic Acid. The superior efficacy of Hydroquinone may be attributed to its direct inhibitory action on tyrosinase and melanin synthesis. Similar results have been reported in previous studies where hydroquinone-based regimens demonstrated substantial improvement in pigmentation scores (4–6).

Tranexamic Acid also showed significant improvement in MASI scores throughout the study period. Its beneficial effects may be explained by inhibition of plasmin activity, reduction of inflammatory mediators, and suppression of melanocyte stimulation induced by ultraviolet radiation (7–9). Although the magnitude of improvement was less than that observed with Hydroquinone, the clinical response remained significant and supports its use as an effective therapeutic alternative. Intergroup comparison revealed no statistically significant difference between treatment groups during the early stages of treatment. However, at the 12-month follow-up, Hydroquinone demonstrated significantly lower MASI scores than Tranexamic Acid ($p = 0.01$), indicating superior long-term efficacy. This finding suggests that prolonged treatment may enhance the comparative benefit of Hydroquinone in reducing pigmentation severity.

Medication adherence was assessed using the MMAS-4 scale. Both treatment groups exhibited high adherence levels. However, adherence was numerically higher in the Tranexamic Acid group (3.52 ± 0.51) compared to the Hydroquinone group (3.30 ± 0.65). Better tolerability and absence of treatment-limiting adverse effects may have contributed to improved adherence among patients receiving Tranexamic Acid. Previous studies have emphasized that treatment-related adverse effects significantly influence adherence and long-term therapeutic outcomes (10).

Safety assessment revealed notable differences between the two treatment groups. Four patients (8%) receiving Hydroquinone developed adverse drug reactions in the form of erythema, burning sensation, and irritation, leading to discontinuation of therapy. In contrast, no significant adverse reactions were observed among patients receiving Tranexamic Acid. These findings are consistent with previous reports documenting local irritant effects associated with Hydroquinone therapy (5,6).

The absence of significant adverse events in the Tranexamic Acid group highlights its excellent tolerability profile. Earlier studies have similarly reported favorable safety outcomes with topical tranexamic acid and minimal risk of local irritation (7–9). Therefore, Tranexamic Acid may be particularly useful in patients who are unable to tolerate Hydroquinone or require prolonged maintenance therapy.

Overall, the findings of the present study indicate that Hydroquinone 4% provides superior efficacy in reducing melasma severity, whereas Tranexamic Acid 5% offers a better safety profile and slightly higher treatment adherence. Both treatment modalities are effective and can be considered valuable options in the management of melasma. The choice of therapy should be individualized based on clinical severity, patient preference, tolerability, and long-term treatment requirements.

CONCLUSION

Both topical Hydroquinone 4% and topical Tranexamic Acid 5% were effective in reducing the severity of melasma over the 12-month study period. Hydroquinone demonstrated significantly greater improvement in MASI scores and superior therapeutic efficacy. However, Tranexamic Acid showed an excellent safety profile with no reported adverse drug reactions and slightly better pharmacotherapeutic adherence. Thus, Hydroquinone may be preferred when greater clinical improvement is desired, whereas Tranexamic Acid represents a safe and well-tolerated alternative for long-term management of melasma.

REFERENCES

1. Handel AC, Miot LD, Miot HA. Melasma: a clinical and epidemiological review. An Bras Dermatol. 2014;89(5):771-782.
2. Passeron T, Picardo M. Melasma, a photoaging disorder. Pigment Cell Melanoma Res. 2018;31(4):461-465.
3. Grimes PE. Melasma. Etiologic and therapeutic considerations. Arch Dermatol. 1995;131(12):1453-1457.
4. Westerhof W, Kooyers TJ. Hydroquinone and its analogues in dermatology. J Cosmet Dermatol. 2005;4(1):55-59.
5. Draelos ZD. Skin lightening preparations and the hydroquinone controversy. Dermatol Ther. 2007;20(5):308-313.
6. Torok HM. A comprehensive review of the long-term and short-term treatment of melasma with hydroquinone. Dermatol Nurs. 2006;18(1):57-66.
7. Kanechorn Na Ayuthaya P, Niumphradit N, Manosroi A, Nakakes A. Topical 5% tranexamic acid for treatment of melasma. J Cosmet Laser Ther. 2012;14(3):150-154.
8. Ebrahimi B, Naeini FF. Topical tranexamic acid as a promising treatment for melasma. Adv Biomed Res. 2014;3:89.
9. Lee JH, Park JG, Lim SH, Kim JY, Ahn KY, Kim MY. Localized intradermal microinjection of tranexamic acid for treatment of melasma. Clin Exp Dermatol. 2006;31(2):179-181.
10. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care. 1986;24(1):67-74.