ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 09 | September - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ORAL TRANEXAMIC ACID WITH MODIFIED KLIGMAN'S REGIMEN VERSUS MODIFIED KLIGMAN'S REGIMEN ALONE IN TREATMENT OF MELASMA: A COMPARATIVE STUDY.

Dermatology

Dr Pooja Mudenur MBBS, Post Graduate, Department Of Dermatology, Venereology And Leprosy, JJM Medical College, Davanagere, Karnataka

Dr. Mangala H C MBBS, MD DVL, Professor, Department Of Dermatology, Venereology And Leprosy, JJM Medical College, Davanagere, Karnataka 577004

Dr. Sugareddy MBBS, DVD, DNB In DVL, Professor And HOD, Department Of Dermatology, Venereology And Leprosy, JJM Medical College, Davanagere, Karnataka 577004

ABSTRACT

Background: Melasma is an acquired hyperpigmentation disorder predominantly affecting sun-exposed areas, particularly in women of reproductive age. It significantly impacts quality of life due to its cosmetic and psychological effects. Despite various treatments, including topical agents and procedural therapies, consistent results remain challenging. Tranexamic acid, an antifibrinolytic agent, has emerged as a promising systemic therapy for melasma. This study evaluates the efficacy of oral tranexamic acid in combination with the modified Kligman's regimen compared to the modified Kligman's regimen alone. **Aims:** To compare the efficacy and safety of oral tranexamic acid combined with the modified Kligman's regimen versus the modified Kligman's regimen alone in melasma treatment. **Materials And Methods:** This randomized, open-label, prospective, interventional, comparative study was conducted in the Department of Dermatology, Venereology, and Leprosy at a tertiary care center in central Karnataka, from August 2023 to February 2025. Fifty patients meeting the inclusion criteria were randomly divided into two groups of 25. Group A received oral tranexamic acid 500 mg and modified Kligman's formula nightly for 12 weeks, while Group B used only the modified Kligman's formula. Clinical images and modified Melasma Area Severity Index (mMASI) scores were recorded to evaluate responses. Results: A significant difference ($P < 0.05$) was observed between the groups at 0 and 12 weeks, with an 84.3% reduction in MASI score in Group A and 69.6% in Group B. **Limitations:** Small sample size and lack of follow-up. **Conclusion:** Oral tranexamic acid 500 mg for 12 weeks is an effective adjunct therapy for managing melasma alongside standard treatment.

KEYWORDS

Melasma, Tranexamic Acid, Kligman's Regimen

INTRODUCTION

Melasma is a chronic acquired disorder characterized by symmetrical hyperpigmented macules and patches predominantly on sun-exposed areas of the face[1]. Women of reproductive age are frequently affected and is associated with hormonal influences, ultraviolet radiation, and genetic predisposition. The condition significantly impairs quality of life because of its cosmetic disfigurement and the psychological distress it often induces[2].

Studies indicate a higher prevalence in individuals with darker skin phototypes (Fitzpatrick III-V) living in tropical climates. The psychological burden underscores the need for effective and sustainable management strategies.

The pathophysiology of melasma is multifactorial, involving melanocyte hyperactivity, ultraviolet-induced damage, and altered dermal vascularity[2]. The role of hormonal influences, including estrogen and progesterone, is particularly pronounced. Despite various treatment modalities such as topical depigmenting agents, chemical peels, and laser therapy, achieving consistent and sustained results remains challenging. Relapse is common, often necessitating combination therapies to address different aspects of the disease mechanism.

The treatment of melasma by tranexamic acid (trans-4-aminomethylcyclohexanecarboxylic acid; TA) is a novel concept. The use of tranexamic acid in melasma was an accidental discovery by Nijo et al. in 1979 in a patient with urticaria[3]. This drug, widely used as an antifibrinolytic agent has been found to inhibit plasminogen–keratinocyte interaction leading to a decrease in the tyrosinase activity, thereby resulting in decreased melanin synthesis from the melanocytes.[4-7]

Several studies have reported its efficacy and safety when administered orally or topically. Meanwhile, the modified Kligman's regimen—a combination of hydroquinone, tretinoin, and a mild corticosteroid—remains a cornerstone for treating hyperpigmentation[8]. However, the synergy of combining these therapies has been less extensively explored. Early trials suggest a potential for enhanced efficacy, making it a valuable focus of investigation.

This study aims to evaluate the combined efficacy of oral tranexamic acid with the modified Kligman's regimen versus the latter alone. We hypothesize that the addition of oral tranexamic acid will result in a more significant reduction in melasma severity and improved patient satisfaction, addressing the limitations of monotherapy.

MATERIALS AND METHODS

Study Design And Setting

It is a randomized, open-label, prospective, interventional, comparative study, conducted at the Department of Dermatology, Venereology, and Leprosy, at a tertiary care center in Central Karnataka, from August 2023 to February 2025. The study was approved by the Institutional Review Board (IRB) and conducted following STROBE guidelines for observational studies.

Study Population

Fifty patients diagnosed with melasma were enrolled based on predefined inclusion and exclusion criteria. Female patients aged 18-50 years with clinical and dermoscopic evidence of melisma were included in the study. Patients with comorbid conditions such as diabetes mellitus, hypertension, thyroid disease, and renal impairment were excluded from the study. Patients with a history of thrombotic events, stroke, or myocardial infarction were also excluded. Additionally, pregnant women, lactating mothers, and those taking oral contraceptives were not included in the study. Patients with sensitive skin, characterized by a burning sensation or allergies to topical creams, as well as those with continuous exposure to excessive sunlight or photosensitivity disorders such as systemic lupus erythematosus (SLE) and porphyria, were excluded. Individuals who had undergone any surgery within the past three months were also not eligible. Informed consent was obtained from all participants.

Randomization And Intervention

Patients were randomly assigned to two groups, **Group A** received oral tranexamic acid (500 mg once daily) along with the modified Kligman's regimen (hydroquinone 4%, tretinoin 0.05%, and fluocinolone acetonide 0.01%) applied for 12 weeks in the night (Short contact application of 4 hours) . **Group B** received only the modified Kligman's regimen applied nightly for 12 weeks (Short contact application of 4 hours). Sunscreen application was advised in both the groups.

Outcome Measures

Baseline assessments included clinical photographs and modified

Melasma Area Severity Index (mMASI) scoring. Follow-up evaluations were performed at weeks 0 and 12, documenting changes in mMASI scores and any adverse effects.

Statistical Analysis

Data were analyzed using SPSS version 26. The Wilcoxon signed-rank test was used for intragroup comparisons, and the Mann-Whitney U test assessed differences between groups. A P-value < 0.05 was considered statistically significant.

RESULTS

Patient Demographics

All 50 enrolled patients completed the study (Group A: 25, Group B: 25). The mean age of participants was 32.4 ± 5.6 years, with no significant difference in baseline characteristics between groups. Table 1 and 2 shows the age distribution and type of melasma respectively.

Table 1. Age Distribution

Age Group	Group A (n=25)	Percentage A	Group B (n=25)	Percentage B
18-25	5	20.0%	4	16.0%
26-35	10	40.0%	11	44.0%
36-45	7	28.0%	6	24.0%
46-50	3	12.0%	4	16.0%

Table 2. Type Of Melasma

Melasma Type	Group A (n=25)	Percentage A	Group B (n=25)	Percentage B
Epidermal	12	48.0%	10	40.0%
Dermal	5	20.0%	6	24.0%
Mixed	8	32.0%	9	36.0%

Efficacy Outcomes

At week 12, a significant reduction in mMASI scores and improvement in GSS were observed in both groups.

- **Group A**: Mean mMASI score reduced from 12.8 ± 3.2 to 2.0 ± 1.4 (84.3% reduction, P < 0.001).
- **Group B**: Mean mMASI score reduced from 12.5 ± 3.1 to 3.8 ± 1.7 (69.6% reduction, P < 0.05).

Intergroup comparison showed a statistically significant difference favoring Group A (P = 0.018).

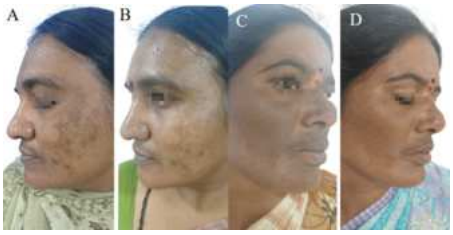


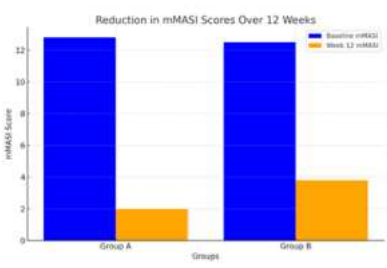
Figure: A and B show patient of Group A on weeks 0 and 12 respectively; C and D show patient of Group B on weeks 0 and 12 respectively.

Safety And Adverse Effects

Six patients in Group A reported mild gastrointestinal discomfort and three experienced transient headaches. In Group B, two patients reported mild skin irritation. No serious adverse events were observed.

Table 3. Reduction In mMASI Scores Over 12 Weeks

Group	Baseline mMASI	Week 12
Group A	12.8 ± 3.2	2.0 ± 1.4
Group B	12.5 ± 3.1	3.8 ± 1.7



Graph 1: Reduction in mMASI over 12 weeks in Group A and B

DISCUSSION

Our study demonstrates that tranexamic acid oral tablets combined with the topical modified Kligman's regimen provides superior improvement in melasma compared to topical therapy alone. Previous studies demonstrated, tranexamic acid efficiently acts in melasma by inhibiting melanogenesis through its anti-plasmin activity. According to study by K.Minni, et.al[9], 65.6% patients had marked improvement in oral Tranexemic acid with kligman regimen group by 12th week in contrast to only 27.1% in modified kligman regimen group.

Tranexamic acid acts by interfering with the plasminogen activator system, reduction of melanocyte stimulation and vascular components in melasma and the minimum risk of adverse effects with oral tranexamic acid makes it a plausible treatment option for melasma[10]. GI irritation and hypomenorrhea are most common side effects [11]. Gold standard therapy for melasma currently is Triple combination creams (TCC) and is more effective than dual combination therapy and Hydroquinone or kojic acid (KA) alone[12,13,14].The modified Kligman's regimen is currently standard therapy, working through depigmentation (hydroquinone), epidermal turnover (tretinoin), and inflammation control (fluocinolone acetonide).

Significantly reduced mMASI scores in Group A highlights the potential of tranexamic acid as an adjunctive therapy for melasma. The treatment in our study was well tolerated with minimal adverse effects, making it a considerable option for long-term management.

Limitations And Future Directions

Limitations include the relatively small sample size and single-center design, which may affect generalizability. Future research should explore longer follow-up periods, varied dosages of tranexamic acid, and multicenter trials to optimize efficacy and safety.

Financial Support And Sponsorship

Nil.

Conflicts Of Interest

There are no conflicts of interest.

REFERENCES:

1. Grimes PE. Melasma: Etiologic and therapeutic considerations. Arch Dermatol. 1995;131(12):1453–7.
2. Handel AC, Miot LD, Miot HA. Melasma: a clinical and epidemiological review. An Bras Dermatol. 2014;89(5):771–82.
3. Nijo S. Treatment of melasma with tranexamic acid. The Clin Rep 1979;13:3219–31.
4. Lee JH, Park JG, Lim SH, et al. Localized IDM of tranexamic acid for treatment of melasma in Asian patients: A preliminary clinical trial.Dermatol Surg 2006;32:626-31.
5. Maeda K, Tomita Y. Mechanism of the inhibitory effect of tranexamic acid on melanogenesis in cultured human melanocytes in the presence of keratinocyte-conditioned medium. J Health Sci 2007; 53:389–96.
6. Wang N, Zhang L, Miles L, Hoover-Plow J. Plasminogen regulates pro-opiomelanocortin processing. J Thromb Haemost 2004; 2:785-96.
7. Zhang L, Li Y, Zhang Y, et al. Oral tranexamic acid in the treatment of melasma: A review. Dermatol Ther. 2020;33(6):e14188.
8. Sheth VM, Pandya AG. Melasma: a comprehensive update: Part II. J Am Acad Dermatol. 2011;65(4):699–714.
9. Minni K, Poojary S. Efficacy and safety of oral tranexamic acid as an adjuvant in Indian patients with melasma: a prospective, interventional, single.centre, triple.blind, randomized, placebo.control, parallel group study. Journal of the European Academy of Dermatology and Venereology. 2020 Jun 22;34(11):2636–44
10. Dyba J, Chan FC, Lau KK, Chan AKC, Chan HHW. Tranexamic Acid is a Weak Provoking Factor For Thromboembolic Events: A Systematic Review Of The Literature. Blood. 2013 Nov 15;122(21):3629–9
11. Taraz M, Niknam S, Ehsani AH. Tranexamic acid in treatment of melasma: A comprehensive review of clinical studies. Dermatologic Therapy. 2017 Jan 30;30(3): e12465
12. Gong Z, Lai W, Zhao G, Wang X, Zheng M, Li L, et al. Efficacy and Safety of Fluocinolone Acetonide, Hydroquinone, and Tretinoin Cream in Chinese Patients with Melasma: A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Parallel-Group Study. Clinical Drug Investigation. 2015 May 20;35(6):385–95
13. Walaiorn Pratchyapruit, Niramol Vashrangsi, Jirot Sindhavananda, Tagami H. Instrumental analysis of the pattern of improvement and that of recurrence of melasma in Thai females treated with Kligman-Willis triple combination therapy: confirmation by using its two different formulae. Skin Research and Technology. 2011 Jan 24;17(2): 226–33
14. Reyhaneh Astaneh, Effat Farboud, Nazemi MJ. 4% hydroquinone versus 4% hydroquinone, 0.05% dexamethasone and 0.05% tretinoin in the treatment of melasma: a comparative study. International Journal of Dermatology. 2004 Jun 8;44(7):599–601