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EFFICACY AND SAFETY OF ORAL TRANEXAMIC ACID WITH GLYCOLIC ACID 35% SOLUTIONVS ORAL TRANEXAMIC ACID WITH MODIFIED JESSNER'S SOLUTION IN TREATING MELASMA: A COMPARATIVE STUDY

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Keywords:

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ABSTRACT: Background: Melasma is a frequent hyper pigmentary disorder characterized by the presence of brown to grey patches on the face. For melasma management, various modalities available that includes kojic acid, azelaic acid, Kligman's regimen, peels like glycolic acid, trichloroacetic acid (TCA), jessner's etc are in use but unsatisfactory results, recently tranexamic acid (TA) has added to treatment armamentarium for resistant melasma. **Objective:** To know the efficacy of oral tranexamic acid with glycolic acid 35% peel verses oral tranexamic acid with modified jessner's peel in treating melasma. **Materials and Methods:** Present study includes 60 patients with melasma, divided into group A and group B. Group A treated with glycolic acid peel and oral TA and group B treated with modified jessners peel with oral TA. Severity of melasma was assessed after 4th, 8th and 12th weeks after combination treatment using mMASI score. **Results:** Present study mean age affected 43.2+/-5.4 years, predominantly affected were females (75%). There is a significant difference in the severity of melasma between both groups at the end of 4th week (group A 12.2+/-1.4, group B 13.5+/-2.2), at the end of 8th the week (group A 10.4+/-2.1, group B 12.1+/-1.8) and at the end of 12 weeks (group A 8.9+/-2.4, group B 10.2+/-3.1) according to mMASI score. **Conclusion:** Oral tranexamic acid with glycolic acid 35% peel proved to be superior in efficacy and safety in treating melasma compared to oral tranexamic acid with modified jessner's peel.

INTRODUCTION: Melasma is a chronic acquired pigmentary disorder characteristically presents as brown to grey-brown patches commonly involving the mid face, malar area, and rarely the mandibular area [1]. Fitzpatrick IV/V skin types are most commonly affected and predominantly seen in women in their early twenties and sometimes in males less than 10% [2].

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The pathophysiology of melasma is complex and key etiological factors include genetics (30%), UV exposure including visible light and infrared radiation, drugs such as oral contraceptive pills (OCP'S), hormonal replacement therapy (HRT) used at menopause and few cosmetic agents, associated with autoimmune thyroid disease [3].

These inducers cause hyper functional melanocytes and increase amounts of melanin. Melasma is a great cosmetic concern causing social stigma and it may cause depression as the quality of life is dear ranged [4]. Till date the main stay of treatment lies with the topical depigmenting agents such as hydroquinone, tranexamic acid, kojic acid, alpha-arbutin, liquorice extracts, vit -c, resorcinol and

peeling agents such as alpha hydroxy acids (AHA) glycolic acid GA (35% to 50%) and Trichloroacetic acid TCA (15% to 35%), azelaic acid 20% individually or in combination with salicylic acid and lactic acid [5]. None of them have produced satisfying results nor could prevent the relapsing nature of the disease [6, 7]. Tranexamic acid (TA) is recently used [19] to treat resistant melasma [8]. TA is a derivative of amino acid lysine. It is used as an antifibrinolytic agent, but later repurposed for management of melasma as it inhibits the interaction between keratinocyte and plasminogen and decreases tyrosinase action, resulting in less melanin production. Chemical peels cause controlled epidermal regeneration with superficial exfoliation of skin based on strength of peel, depth of peel, number of coats and type of peel. Various chemical peeling agents have been used as an adjunctive in treatment of melasma. Oral tranexamic acid alone or along with topical depigmenting agents or comparing various chemical peels in melasma are present till date. Very few studies exist in literature where both oral tranexamic acid and peeling agents are combined together in treating melasma [9, 10]. Present study was conducted on 60 patients to compare the efficacy of oral tranexamic acid with GA35% peel vs oral tranexamic acid with modified jessners peel in melasma.

Objective: This study was done to compare the efficacy and safety of oral tranexamic acid with GA 35% peel verses oral tranexamic acid with modified jessner's peel in treating melasma.

MATERIAL AND METHODS: This comparative study was conducted at a MNR medical college and hospital in India from June 2021 to December 2022.

Study Design: Interventional Randomized, single-blinded study. The study is interventional, as therapy was given to patients as a part of the study in the form of two combinational therapies.

Study Location: This study was carried out at Department of Dermatology at MNR Medical College and Hospital, Sanga reddy, Telangana, India.

Study Duration: June 2021 to December 2022

Sampling Procedure: Simple random sampling

Sample size: 60 patients

Sample size Calculation: As per the study done by Sheth *et al* 10the prevalence of melasma in Southeast Asia is variable. It is high as 40%. At a confidence level of 85%, taking error as 10%, the minimum sample size obtained was 50. So, we included 60 patients considering a few dropouts.

Subjects & Selection Method: The study population was included from patients who were coming to an outpatient unit of the Dermatology unit with skin hyperpigmentation.

Melasma was diagnosed clinically and confirmed by using woods lamp which clearly differentiated epidermal, dermal and mixed type of melasma. Patients were divided into two groups by randomization method. Group A (n=30) patients received a combination of oral tranexamic acid 500mg once a day with GA peel 35%. Group B (n=30) patients received a combination of oral tranexamic acid 500mg once a day with Modified jessner's peel. Peeling sessions were done for every 3-4weeksfor a duration of 3 months. Oral tranexamic acid 500mg once daily after dinner is given for 3 months. Both groups received sunscreen with spf>30 daily every 3 hours during daytime. The study is single-blinded, in which the investigator knows what combination the patient is getting. Patients don't know what combination they are receiving. Both combinations were made to look similar to avoid bias.

Inclusion Criteria:

1. Patients aged 20-50 years are diagnosed with melasma.
2. Patients with epidermal, dermal and mixed type were included in the study.
3. Either gender.
4. Patients who provided informed consent.

Exclusion Criteria:

- Pregnant and lactating women.
- Patients on topical depigmenting agents for the last 6 weeks.

- ❖ Patients with coagulopathies, anti-coagulant medication and hypersensitivity to drug.
- ❖ Patients with active infections and open wounds.
- ❖ Patients with dermal and mixed melasma.
- ❖ Patients with unrealistic expectations.

Materials and Methods: Patients coming to OPD with melasma were examined with woods lamp and classified into epidermal, dermal and mixed types, which were included in the study. A detailed history regarding family, intake of oral contraceptive pills or on any hormonal replacement therapy (HRT) and recent history of stroke or any cardiovascular risk were noted. General physical examination and systemic examination was done. Basic investigations like complete blood picture, PT/ APTT/ INR were done and those with deranged parameters were excluded from the study.

Melasma area severity index (MASI) [11] was calculated before initiation of treatment and at the end of each session. Clinical photographs were taken before the start of treatment and after every session of peeling. Informed consent was taken and randomly placed the patients in 2 different groups A and B. Patients were asked not to apply any topical depigmenting agents over the course of the treatment apart from sunblock.

Group A patients were treated with GA 35% solution (sesderma) on the day of initiation of oral TXA, after degreasing the patient a single pass of solution was applied for 3-5 min or until frosting is seen. Group B patients were treated with modified jessner's solution (Sesderma) on the day of initiation of oral TXA, after cleansing the skin, solution was applied as 1-3 coats for 5-6 min or until erythema, irritation or frosting is seen.

Procedure of Chemical Peel:

- ➢ Degreasing the skin with alcohol swab or with acetone.
- ➢ Covering the sensitive areas of the face like peri-orbital, periocular and nasolabial folds with vaseline.
- ➢ Application of the peel with cotton bud over the face making sure there is no spillage or dripping down to other areas.
- ➢ Throughout the session the patient asked weather he is comfortable, or any sense of irritation or tingling is present.
- ➢ Once the desired duration and depth is achieved, we clean the entire face with cotton and normal saline.
- ➢ Immediately post peel we apply a mild emollient and sunscreen over the entire face.

Patients were called at the end of 4th week, 8th, and 12th weeks. Follow up was done for 3 months. The data was subjected to statistical analysis and then a conclusion was drawn.

Parameters Assessed:

- Age
- Gender
- Duration of disease
- Type of Melasma
- Severity of melasma

Type of melasma was assessed by clinical examination and wood lamps examination. Severity of melasma was assessed by melasma area severity index (mMASI) score as depicted in **Fig. 1.**

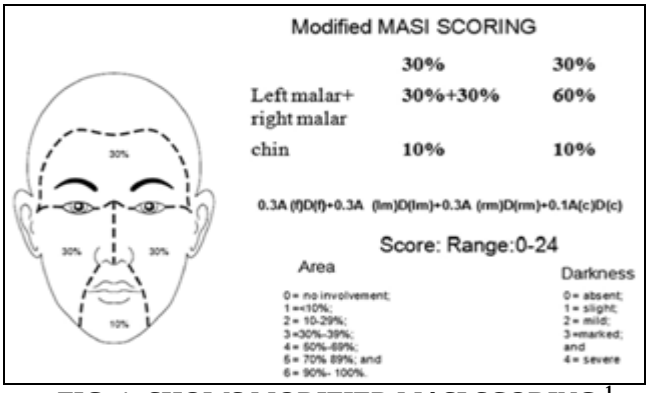

FIG. 1: SHOWS MODIFIED MASI SCORING [1]

Statistical Analysis: Epi info software version was used to analyze data 7.2.5. Results were noted as percentages and mean with standard deviation. Comparison between categorical parameters and numerical parameters between two groups was done using chi square test and student t test. Results were presented in tabular forms and graphs in pie and bar diagrams. P value below 0.05 is considered significant.

RESULTS: The current study included 60 patients with melasma.

Demographic Variables: Most common age group affected is 35-40yrs and gender affected is female in both groups as shown in **Table 1**. Hence the comparison is justifiable.

TABLE 1: DEMOGRAPHIC VARIABLES IN BOTH GROUPS

Demography	Group A(n=30)	Group B(n=30)	P value
Mean age	43.2±5.4 years	44.1±2.1 years	0.39
Gender (females)	22	23	0.08

Mean Duration of Disease: There is no significant difference in the mean duration of disease between two groups as depicted in graph 1. (p=0.41). Age of patients ranged from 19 to 58 years.

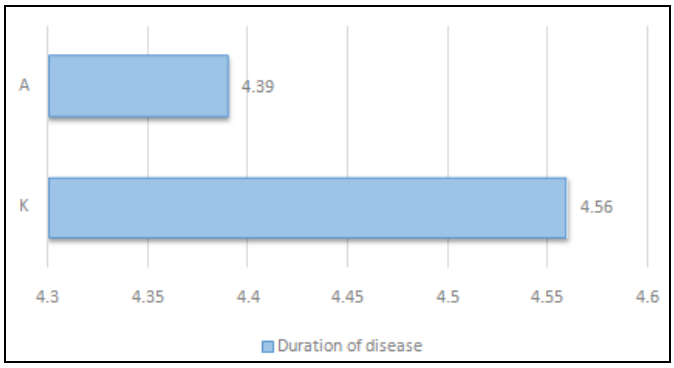

FIG. 2: DURATION OF DISEASE IN TWO GROUPS

Type of Melasma: Most of the patients had epidermal type of melasma, as shown in graph 2.

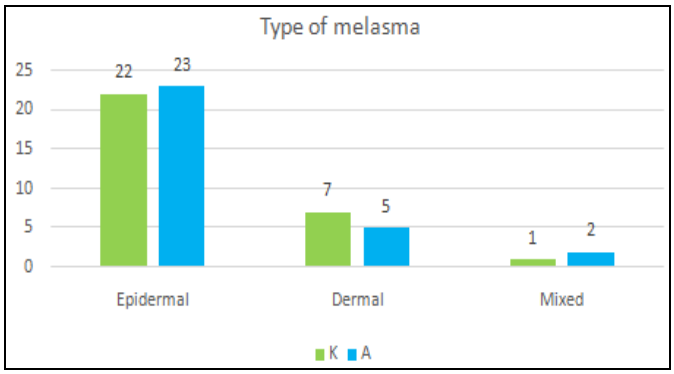

FIG. 3: SHOWS TYPE OF MELASMA IN EACH GROUP

Severity of Melasma: There is no significant difference in the baseline mMASI score among two groups (p=0.59) as depicted in graph 3.

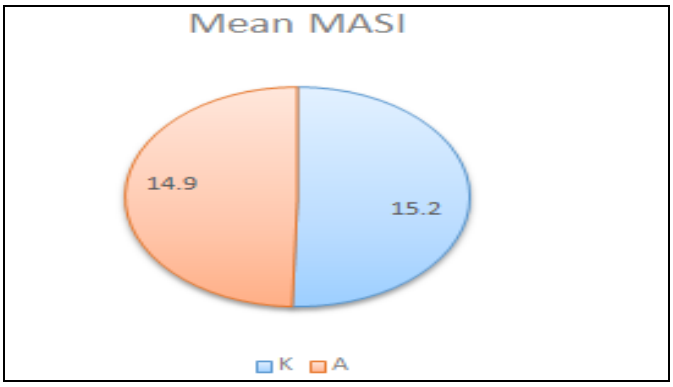

FIG. 4: SHOWS BASELINE SEVERITY OF MELASMA

Severity of Melasma after Treatment: There is a significant difference in the severity of melasma between both groups at the end of 4th, 8th and 12th weeks. It was less in group A patients, as summarized in **Table 2.**

TABLE 2: SHOWS SEVERITY OF MELASMA AFTER TREATMENT

Severity of melasma (mean MASI score)	Group A	Group B	P value
4th week	12.2±1.4	13.5±2.2	0.04
8th week	10.4±2.1	12.1±1.8	0.001
12th week	8.9±2.4	10.2±3.1	0.02

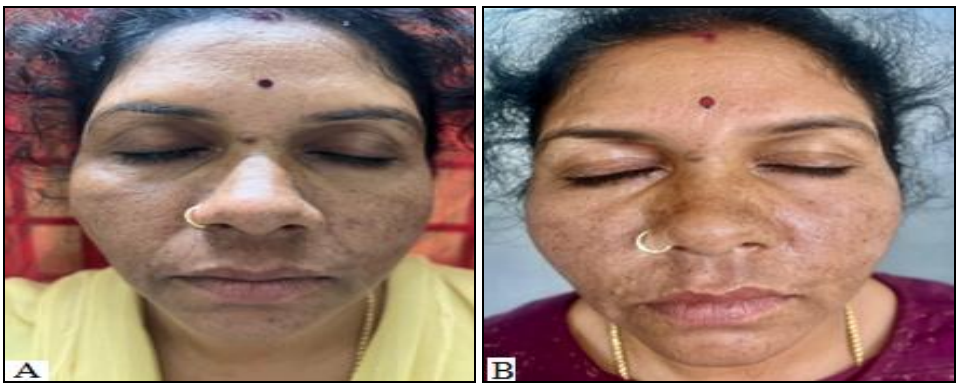

FIG. 5: PHOTOGRAPH SHOWING MELASMA AT BASELINE (A) AND AT 12 WEEKS (B)OF TREATMENT WITH ORAL TRANEXAMIC ACID AND MODIFIED JESSNERS PEEL

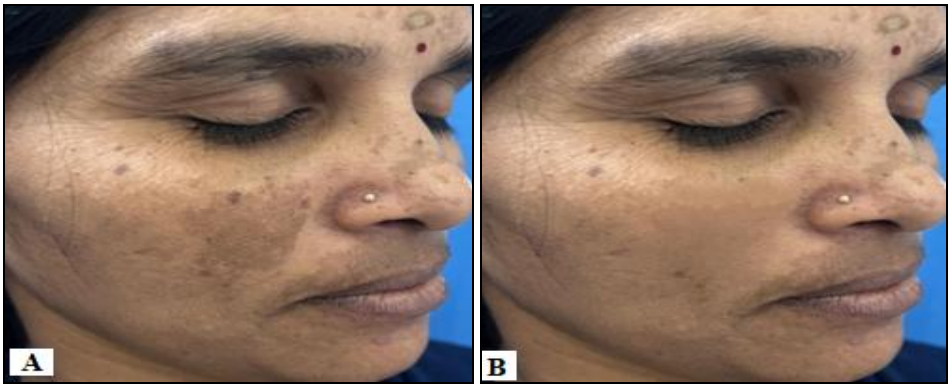

FIG. 6: PHOTOGRAPH SHOWING MELASMA AT BASELINE (A) AND AT 12 WEEKS (B) OF TREATMENT WITH ORAL TRANEXAMIC ACID AND GA PEEL

Side Effects: Side effects were seen in 11 patients overall. As summarized in **Table 3.** These are minor and self-limited. Gastritis is the most common side effect which occurred due to oral tranexamic acid. Most common immediate side effects seen with chemical peels were burning sensation, pruritis, erythema, edema. Delayed side effects are persistant erythema, acneiform eruption, hyperpigmentation and hypopigmentation.

TABLE 3: SHOWS SIDE EFFECTS IN BOTH GROUPS

Side effects	Group A	Group B
Gastritis	4	5
Palpitations	1	Nil
Menstrual disturbances	Nil	1

DISCUSSION: Melasma is a frequent acquired skin condition of symmetric hyperpigmentation, commonly occurring over the face. It shows higher prevalence in females and darker skin types. Various treatment options used for melasma include topical therapies with tretinoin, hydroquinone, and triple combination creams. Oral therapies include tranexamic acid, glutathione and Polypodium leucotomos. Tranexamic acid is a fibrinolytic agent that is repurposed recently to treat melasma. The usual effective dose for treating melasma is 250 mg twice or thrice a day for at least 3months duration. Combination therapies like procedures and topical or oral therapies had become modality of choice for many patients. The present study is focused on management of melasma where we have included 60 patients with clinically diagnosed cases of melasma, divided into two groups. Group A and group B included 30 patients each. They were given oral tranexamic acid 500 mg once a day with GA 35% peel and oral TXA 500 mg once a day with jessner's peel. There is no significant difference in the mean age, gender between two groups Age ranged from 19 to 58 years. The epidermal type is most commonly seen, followed by dermal type of melasma. There is no significant difference in baseline MASI score between two groups. But the score is significantly less in group A patients at the end of 4th, 8th and 12th weeks after treatment in our study.

Safoora *et al* [12] identified that 82.8% of affected patients with melasma as females. Their study included 65 melasma patients. In concordance to our study where we included 60 melasma patients and 91.6% were females. Arun Achar *et al* [13] *et al* conducted a study in 312 patients where on woods lamp examination dermal type of melasma was seen in 54.48% and epidermal and mixed type of melasma was seen in 21.47% and 24.07% of the cases respectively. In concordance to our study of 60 patients where epidermal melasma was seen in 75% followed by dermal in 20% and mixed in 5% of the cases.

Wei-jen wang *et al* [14] according to their study the optimal dose of oral tranexemic acid was 250mg thrice daily for 12 weeks in treating epidermal melasma. Concordance to our study where we had good results with 500mg once daily dose for 12 weeks of tranexemic acid as it reduces the pill burden and encourages better outcome. Rashmi Kumari *et al* [15] identified that reduction in MASI scoring after 12 weeks in GA group was by 79% (from 26.6 to 5.6) and 73% reduction in TCA group (29.1 to 8.2) but the difference was not siginificant. In accordance with our study MASI was reduced in GA group after 12 weeks by 24.4% (13.5 to 10.2) and in TCA group by 27% (12.2 to 8.9) which was not statistically significant (P=0.59). In an era where topical depigmenting

agents became the first line of treatment, we wanted to nullify and reduce the long-term side effects of triple combination creams and increase the compliance and good treatment response with oral drug along with an adjunct of chemical peeling which is safer as it is supervised and controlled under dermatologist. But thorough screening of personal and familial risk factors of thromboembolism should be carried out before starting treatment with fibrinolytic agents like tranexamic acid. After completion of therapy, maintenance with regular sun protection is the utmost important measure we recommended to all patients. The study is self-sponsored. There were no conflicts of interest.

CONCLUSION: Oral tranexamic acid along with GA35% peel proved to be superior in efficacy and safety in treating Melasma compared to oral tranexamic acid with modified jessner's solution as per the MASI score.

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Consent for Publication: Not applicable.

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REFERENCES:

1. Mpofana N, Chibi B and Visser T: Treatment of melasma on darker skin types: a scoping reviews. Cosmetics 2023; 10.
2. Mahajan VK, Patil A and Blicharz L: Medical therapies for melasma. J Cosmet Dermatol 2022; 21: 3707–3728.
3. Spreading of dangerous skin-lightening products as a result of colourism: a review. Juliano CCA. Appl Sci 2022; 12: 3177.
4. Espósito AC, Cassiano DP and da Silva CN: Update on melasma-part I: pathogenesis. Dermatol Ther (Heidelb) 2022; 12: 1967–1988.
5. Page MJ, McKenzie JE and Bossuyt PM: The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: 0.
6. McKesey J, Tovar-Garza A, Pandya AG: Melasma treatment: an evidence-based review. Am J Clin Dermatol 2020; 21: 173-225.
7. Yeung H, Kahn B, Ly BC and Tangpricha V: Dermatologic Conditions in Transgender Populations. Endocrinol Metab Clin North Am 2019; 48(2): 429-440.
8. Zubair R, Lyons AB, Vellaichamy G, Peacock A and Hamzavi I: What's New in Pigmentary Disorders. Dermatol Clin 2019; 37(2): 175-181.
9. Glowka A, Olejnik A and Nowak I: The release studies of undecylenoyl phenylalanine through cellulose based membranes. Saudi Pharm J 2018; 26: 709–718.
10. Goh CL, Chuah SY, Tien S, Thng G, Vitale MA and Delgado-Rubin A: Double-blind, placebo-controlled trial to evaluate the effectiveness of *Polypodium leucotomos* extract in the treatment of melasma in Asian skin: A pilot study. J Clin Aesthet Dermatol 2018; 11(3): 14–19.
11. Zhang L, Tan WQ, Fang QQ, Zhao WY, Zhao QM, Gao J and Wang XW: Tranexamic Acid for Adults with Melasma: A Systematic Review and Meta-Analysis. Biomed Res Int 2018; 1683-414.
12. Aamir, Safoora and Riffat Naseem: "Oral tranexamic acid in treatment of melasma in Pakistani population: a pilot study. Journal of Pakistan Association of Dermatology 2016; 198-203.
13. Achar A and Rathi SK: Melasma: A clinico-epidemiological study of 312 cases. Indian J Dermatol 2011; 56: 380-2.
14. Wang WJ, Wu TY, Tu YK, Kuo KL, Tsai CY and Chie WC: The optimal dose of oral tranexamic acid in melasma: A network meta-analysis. Indian J Dermatol Venereol Leprol 2023; 89: 189-94.
15. Kumari R and Thappa DM: Comparative study of trichloroacetic acid versus glycolic acid chemical peels in the treatment of melasma. Indian J Dermatol Venereol Leprol 2010; 76: 447.
16. Bala HR, Lee S, Wong C, Pandya AG and Rodrigues M: Oral Tranexamic Acid for the Treatment of Melasma: A Review. Dermatol Surg 2018; 44(6): 814-825.

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