Section: DVL

Original Research Article

INTRALESIONAL TRANEXAMIC ACID FOR MELASMA TREATMENT: EFFICACY AND SAFETY IN A 12-WEEK PROSPECTIVE PILOT STUDY

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Abstract

Background: Melasma is a frequent dermatological condition, especially in women of reproductive age, often triggered or intensified after pregnancy. It presents as hyperpigmented patches on the face, leading to cosmetic concerns and potential psychological impact. Tranexamic acid (TA), known for its antifibrinolytic properties, has recently been investigated for its utility in treating melasma. This pilot study aims to evaluate the efficacy of intralesional TA in improving melasma, as measured by the modified Melasma Area and Severity Index (mMASI). **Objective:** To assess the effectiveness of intralesional TA in the treatment of melasma by monitoring changes in the mMASI score over a 12-week period. **Material & Methods:** This prospective observational study enrolled 58 patients with varying distributions of melasma (centrofacial, malar, and mandibular). Patients were treated with 4mg/ml of TA, injected intradermally at 1cm intervals using an insulin syringe, and this procedure was repeated weekly for 12 weeks. Alongside TA treatment, patients were advised to use daily sunscreen and photoprotection. NSAIDs and antibiotics were administered as needed. The mMASI score was evaluated at 4, 8, and 12 weeks, supplemented by serial photographic documentation. **Results:** Of the participants, 72% presented with centrofacial melasma, 21% with malar, and 7% with mandibular melasma. After 12 weeks of intralesional TA therapy, a significant improvement in melasma was observed ($P<0.05$), indicating the effectiveness of this treatment modality. **Conclusion:** Intralesional TA represents a promising, affordable, and minimally invasive treatment option for melasma, showing efficacy in both dermal and mixed-type melasma resistant to other treatments. This therapy poses minimal adverse effects, making it a viable option for long-term management of this chronic and often recalcitrant condition. Further studies with larger sample sizes and longer follow-up periods are warranted to validate these findings.

INTRODUCTION

Melasma is a chronic, acquired dermatological condition characterized by symmetrical hyperpigmented patches, predominantly affecting women of reproductive age. The condition is particularly common post-pregnancy, suggesting hormonal influences in its pathogenesis. Melasma manifests as brown or tan patches primarily on sun-exposed areas of the face and neck. Despite its prevalence, the exact pathogenesis of melasma remains elusive, with multiple contributing factors proposed. These include ultraviolet (UV) radiation exposure, hormonal imbalances (often associated with pregnancy or contraceptive use), genetic predisposition, thyroid disease, and the use of certain cosmetics and phototoxic drugs.[1] Epidemiologically, melasma is globally distributed but shows a higher prevalence in certain ethnic

groups, particularly those of Asian and Middle Eastern descent.[2]

The management of melasma poses a significant challenge due to its recurrent nature and resistance to conventional treatments. Among various therapeutic options, Tranexamic acid (TA) has emerged as a promising agent. TA, a synthetic derivative of the amino acid lysine, is primarily known for its antifibrinolytic properties in preventing excessive bleeding. However, in the context of melasma, TA operates through a different mechanism. It inhibits the conversion of plasminogen to plasmin by blocking the plasminogen activator. This inhibition leads to a decrease in the production of free arachidonic acid and, consequently, a reduction in prostaglandin (PG) levels. Prostaglandins are known to play a role in melanogenesis, the process of melanin formation in the skin. By reducing PG production, TA effectively lowers melanocyte tyrosinase activity, which is crucial for melanin synthesis. Additionally, TA has been noted to reduce the levels of vascular endothelial growth factor (VEGF) and endothelin-1 (ET-1), both implicated in the increased vascularity often observed in melasma lesions.

Traditionally, TA has been administered orally or intravenously for its systemic effects. However, its use in these forms is limited by potential adverse effects and contraindications linked to its thrombolytic properties, which can increase the risk of thromboembolic events.[3,4] These risks necessitate the exploration of alternative delivery methods that can localize the effect of TA while minimizing systemic exposure. The current study focuses on the intralesional administration of TA as a novel approach for melasma treatment. This method involves directly injecting TA into the melasma lesions, thereby targeting the affected areas more precisely and reducing systemic absorption.

This pilot study aims to evaluate the efficacy of intralesional TA in improving melasma, as quantified by changes in the modified Melasma Area and Severity Index (mMASI) score. The mMASI is a validated clinical tool used to assess the severity of melasma, considering factors such as area coverage and darkness of pigmentation. By monitoring changes in the mMASI score over a 12-week treatment period, this study seeks to provide insights into the effectiveness and safety of intralesional TA as a treatment modality for melasma, especially in cases resistant to other forms of therapy.

MATERIALS AND METHODS

This was a prospective observational study conducted over a period of 12 weeks. It involved 60 patients diagnosed with Melasma, of whom only 2 were dropouts. The study was carried out at Andhra Medical College, Visakhapatnam, during the period from October 2022 to March 2023.

Inclusion Criteria

The participants included in the study were Patients with inclusion criteria of females with age 18-50yrs with having II-IV skin types and with clinical diagnosis of Melasma and who are willing to participate in the study were included.

Exclusion Criteria

Patients who were on topical treatment, having history of hormonal therapy, OC pills usage and H/O hypersensitivity. Patients with bleeding disorders, on anticoagulants therapy were excluded and also Patients with Herpes, warts, dermatoses and patients with unrealistic expectations were excluded from the study.

Ethical Considerations

Informed consent of the patients were taken and confidentiality of the patients were maintained. Institutional ethics committee approval was taken before starting the study.

Procedure

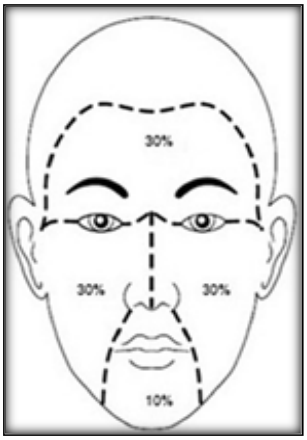
Baseline examination of the patient with woods lamp, investigations, photographs and baseline modified MASI (baseline) were taken. Followed by applying topical anaesthesia for 45min, 4mg/ml Tranexemic acid (TA) was injected intradermally into the melasma lesion at 1cm intervals by using insulin syringe. This Procedure repeated weekly for 12 weeks. Daily sunscreen, photoprotection was advised. If necessary, NSAIDS and antibiotics were given. Reviewed mMASI at 4, 8, 12 weeks and 1 month follow up with serial photographs.

Modified Melasma Severity Index score(mMASI)[5]

Location of Melasma	Scoring	Calculation for total score
Fore head	(0.3) (A) (D)	Fore head mMASI score + Left malar mMASI score + Right malar mMASI score + Chin mMASI score = Total mMASI score
Left malar	(0.3) (A) (D)	
Right malar	(0.3) (A) (D)	
Chin	(0.1) (A) (D)	

Scoring system: A, Area of involvement rated 0 to 6: 0 indicates absent; 1, <10%; 2,10% to 29%; 3, 30% to 49%; 4, 50% to 69%; 5, 70% to 89%; 6, 90% to 100%. D, Darkness rated 0 to 4: 0 indicates absent; 1, slight; 2, mild; 3, marked; 4, severe.

Total mMASI score range is 0 to 24 and calculated by adding scores for 4 areas of the face.



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Clinical Efficacy

(mMASI before treatment – mMASI aftetreatment) ×100
mMASI before treatment

Excellent response: >75% fall in mMASI
Very Good: 50-75% fall in mMASI
Good: 25-50% fall in mMASI
Poor: <25% fall in mMASI

Analysis of Data

Data was entered and analysed in Microsoft excel sheet. Variables were expressed in percentages. P value of < 0.05 was taken as significance.

RESULTS

The study enrolled a total of 58 patients diagnosed with melasma, who were treated with intralesional Tranexamic acid (TA). The distribution of melasma types among these patients varied, with 72% (42 patients) exhibiting centrofacial melasma, 21% (12 patients) with malar melasma, and 7% (4 patients) presenting with melasma in the mandibular area. The efficacy of the treatment was evaluated based on the reduction in the modified Melasma Area and Severity Index (mMASI) scores over the 12-week treatment period.

The response to treatment was categorized into three levels based on the percentage reduction in mMASI scores: very good response (50-75% reduction), good response (25-50% reduction), and poor response (<25% reduction). Among the patients with centrofacial melasma, a very good response was observed in 31 patients, indicating a substantial improvement in over half of the cases in this group. In the malar melasma group, 4 patients showed a very good response, while one patient with mandibular melasma also fell into this category.

Furthermore, a good response, characterized by a 25-50% reduction in mMASI, was noted in 8 patients with centrofacial melasma. This response rate highlights a significant improvement, though less pronounced than those in the very good response category. Additionally, 3 patients with malar melasma and 2 with mandibular melasma exhibited a good response to the treatment.

However, the treatment was less effective for some patients. A poor response, defined as less than a 25% reduction in mMASI scores, was observed in 3 patients with centrofacial melasma. This minimal change indicates a resistance to the treatment in a small subset of patients with this melasma type. Similarly, 5 patients with malar melasma and one with mandibular melasma also showed a poor response, suggesting variability in the efficacy of intralesional TA across different melasma locations.

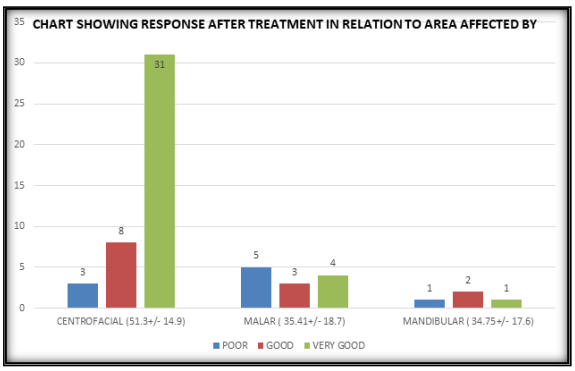
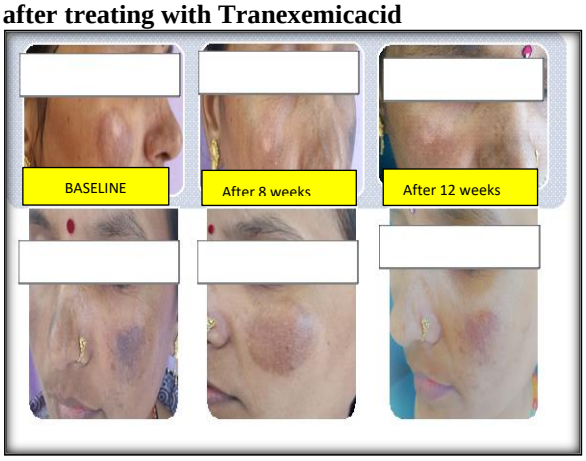


Figure 1: Chart Showing Response After Treatment in Relation to Area Affected by Melasma

p value = 0.005 significant difference was seen after treatment with Tranexemic acid. (which is <0.05)
There is significant improvement by the treatment with intralesional tranexamic acid treatment after 12 weeks of therapy (P<0.05). [Table 1]

Image showing Improvement of the Melasma after treating with Tranexemicacid



In the present study there were minimum adverse effects like erythema, wheal, localized burning sensation etc.

Table 1: Showing Improvement of the Melasma after treating with Tranexemicacid

	Baseline (MEAN mMASI)	End of Treament (MEAN mMASI)	Improvement
Our Study	13.4±2.45	7.9±1.2	41.04%

Table 2:

Side Effects	No. of Patients Effected	Percent
Localized Burning Sensation	46	79%
Wheal	32	55%
Erythema	26	45%

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DISCUSSION

Epidemiologically, melasma is found in all geographical and ethnic groups Melasma, though it is benign, it can cause extremely psychological distress and has been shown to have a significant impact on quality of life, social, and emotional wellbeing,[6] use of Contraceptive pills and pregnancy have shown the increase serum plasminogen activator that can activate the melanogenesis process. Other dermatological changes also seen to contribute to melasma include disruption of basement membrane, increased blood vessels, and solar elastosis. Number of mast cells may also be increased in the lesional dermis resulting dermal factors may be the cause behind the refractory nature of melisma.[7]

Present study included only females and most of the patients (72%) belongs to centrofacial Melasma followed by 21% patients were having Malar Melasma and 7% were having Mandibular area melasma. In the present study baseline mean mMASI shows 13.4±2.45, at the end of the treatment mean mMASI was 7.9±1.2 in which 41.04% improvement was seen and is significant ($p<0.05$). similar findings were seen in LEE JH, PARK JG et al,[8] where the mean baseline mMASI score was 13.22±3.02 , at the end of the treatment mean mMASI was 7.57±2.54 in which 42.7% improvement was seen which is also significant. But in a study done by Elfar NN et al,[9] comparative study between different therapeutic modalities with the best results in glycolic acid peeling followed by topical silymarin cream then the least response was in intradermal injection of tranexamic acid. Which is statistically significant. In agreement with the present study, Ayuthaya et al.[10] studied topical 5% tranexamic acid twice daily for 12 weeks for the treatment of epidermal type melasma in split face trial study showed improvement in Melasma, which is significant.

In another study Budamakuntla L et al,[11] where tranexamic acid was given in the microinjections, there was 35.72% improvement in the MASI score compared to 44.41% improvement by microneedling of tranexamic acid which is significant. Another study where tranexamic acid administration causes a significant reduction in epidermal melanin pigmentation, vessel numbers, and mast cell counts in Histological analysis done by Na et al.[12]

Regarding side effects present study showed 79% effected with localized burning sensation wheal was seen 55% followed by erythema in 45% similarly Elfar NN et al,[9] all patients (100%) were suffered with burning sensation and wheal followed by 25% of the patients suffered with erythema.

Lueangarun et al13 research evaluates the effectiveness of intradermal TA injections over 48 weeks, suggesting sustained effectiveness. Konisky et al14 review explores various TA administration routes, including topical, oral, and injectable forms, offering a comprehensive perspective on their effectiveness and practicality. Bala et al15study focuses on oral TA, a non-invasive option, examining its systemic effects and overall efficacy. Collectively, these studies highlight TA's versatility in treating melasma and emphasize the need for more research on its long-term effects and optimal use in different forms.

CONCLUSION

Intralesional tranexamic acid emerges as a cost-effective and well-tolerated treatment option for melasma, demonstrating notable efficacy, particularly in cases resistant to other therapies. Its application, either as a standalone treatment or in combination with other modalities, shows promising results in managing both dermal and mixed forms of melasma, thereby offering a valuable addition to the current therapeutic arsenal for this challenging dermatological condition.

Recommendations: Future research should focus on investigating the efficacy of tranexamic acid at varied dosages and in conjunction with other therapeutic agents. This approach will help in optimizing treatment strategies and enhancing the overall management of melasma.

Conflict of interest: No conflicts of interest

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REFERENCES

1. Tse TW, Hui E. Tranexamic acid: An important adjuvant in the treatment of melasma. J Cosmet Dermatol 2013; 12:57-66.
2. Halder RM, Grimes PE, McLaurin CI, Kress MA, Kenney JA Jr. Incidence of common dermatoses in a predominantly black dermatologic practice. Cutis 1983; 32:388, 390.
3. Kim SJ, Park JY, Shibata T, Fujiwara R, Kang HY. Efficacy and possible mechanisms of topical tranexamic acid in melasma. Clin Exp Dermatol 2016; 41:480-5.
4. Calapai G, Gangemi S, Mannucci C, Miniullo PL, Casciaro M, Calapai F. Systematic review of tranexamic acid adverse reactions. J Pharmacovigil 2015; 3:1 7.
5. Pandya AG, Hynan LS, Bhore R, et al. Reliability assessment and validation of the Melasma Area and Severity Index (MASI) and a new modified MASI scoring method. J Am Acad Dermatol. 2011;64(1):78-83, 83. e1-83. e2.
6. Tran JM, Chan AW (2012) Quick diagnosis: melasma. University of Toronto Med J 89: 143-145.
7. Hernández-Barrera R, Torres-Alvarez B, Castanedo-Cazares JP, Oros-Ovalle C, Moncada B. Solar elastosis and presence of mast cells as key features in the pathogenesis of melasma. Clin Exp Dermatol 2008; 33:305-8.
8. Lee JH, Park JG, Lim SH, Kim JY, Ahn KY, KIM MY, Park YM. Localized intradermal microinjection of tranexamic acid for treatment of melasma in Asian patients: a preliminary clinical trial. Dermatologic surgery. 2006 May;32(5):626-31.
9. Elfar NN, El-Maghraby GM. Efficacy of intradermal injection of tranexamic acid, topical silymarin and glycolic acid peeling in treatment of melasma: A comparative study. J Clin Exp Dermatol Res. 2015;6(280):2.
10. Pinyapat Kanechorn Na Ayuthaya, Nucha Niumphradit, Aranya Manosroi & Artit Nakakes (2012) Topical 5% tranexamic acid for the treatment of melasma in Asians: A double-blind randomized controlled clinical trial, Journal of Cosmetic and Laser Therapy, 14:3, 150-154, DOI: 10.3109/14764172.2012.685478
11. Budamakuntla L, Loganathan E, Suresh DH, Shanmugam S, Suryanarayan S, Dongare A, Venkataramiah LD, Prabhu N. A randomised, open-label, comparative study of tranexamic acid

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microinjections and tranexamic acid with microneedling in patients with melasma. Journal of cutaneous and aesthetic surgery. 2013 Jul;6(3):139.
12. Na JI, Choi SY, Yang SH, Choi HR, Kang HY, Park KC, et al. Effect of tranexamic acid on melasma: A clinical trial with histological evaluation. J Eur Acad Dermatol Venereol 2013; 27:1035-9.
13. Lueangarun S, Sirithanabadeekul P, Wongwicharn P, Namboonlue C, Pacharapakornpong S, Juntongjin P et al. Intradermal Tranexamic Acid Injection for the Treatment of Melasma: A Pilot Study with 48-week Follow-up. J Clin Aesthet Dermatol.2020;13(8):36-39.
14. Konisky H, Balazic E, Jaller JA, Khanna U, Kobets K. Tranexamic acid in melasma: A focused review on drug administration routes. J Cosmet Dermatol. 2023 Apr;22(4):1197-1206. doi: 10.1111/jocd.15589.
15. Bala HR, Lee S, Wong C, Pandya AG, Rodrigues M. Oral Tranexamic Acid for the Treatment of Melasma: A Review. Dermatol Surg. 2018 Jun;44(6):814-825.

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