

Innovative approaches in melasma management: unveiling the multifaceted potential of tranexamic acid

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ABSTRACT

Tranexamic acid (TXA) has emerged as a promising therapeutic agent for melasma due to its multifaceted action on vascular, inflammatory, and melanogenic pathways. This review investigates the current evidence supporting the efficacy and safety of oral, topical, and intradermal routes of TXA administration. Oral TXA demonstrates notable effectiveness, achieving a 50–60% reduction in Melasma Area and Severity Index (MASI) scores, while topical formulations offer comparable benefits with an improved safety profile. Intradermal administration allows for rapid, localized effects, with MASI score improvements ranging from 55–65%. Moreover, combinatory regimens particularly with fractional CO₂ lasers or antioxidants like ascorbic acid have shown synergistic effects, offering new hope for recalcitrant cases. Despite these promising developments, challenges remain. The absence of comprehensive long-term safety data and the inadequate representation of varied communities in clinical studies necessitate immediate concern. Future research should emphasize longitudinal follow-up, genetic predispositions, and ethnic-specific responses. Ultimately, integrating advanced delivery systems with patient education and adherence strategies is vital for optimizing and sustaining TXA's therapeutic benefits in melasma management.

KEYWORDS

tranexamic acid, melasma, MASI, hyperpigmentation, topical therapy

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1. INTRODUCTION

Melasma is a chronic dermatological condition characterized by hyperpigmented macules often found on sun-exposed areas, most seen in women of reproductive age and individuals with Fitzpatrick skin types III to V and substantially impacts psychological well-being; it is most common in individuals of Hispanic, Asian, Middle Eastern, and African descent due to genetic predisposition and higher baseline levels of melanin. Melasma pathophysiology incorporates genetic susceptibility, hor-

monal triggers, ultraviolet radiation, and vascular dysfunction, with hormonal changes in pregnancy and usage of oral contraceptives worsening the condition. At the vascular, inflammatory, and melanogenic levels, the antifibrinolytic drug (TXA) is effective in treating melasma. The system can adopt a variety of administration methods (e.g., safer topical formulations and efficient intradermal microinjections) to mitigate systemic adverse effects and improve patient satisfaction compared to systemic treatments [1].

2. MECHANISMS OF ACTION OF TRANEXAMIC ACID

TXA effects on melasma include modulation of multiple pathophysiological pathways. One major mechanism is through inhibition of plasminogen activation. TXA also inhibits the plasmin-mediated release of pro-inflammatory mediators, including the vascular endothelial growth factor (VEGF) and prostaglandins, by blocking lysine-binding sites on plasminogen, thereby reducing inflammation and vascular proliferation. It acts not only on inhibiting plasminogen activation but also on the keratinocyte–melanocyte signalling events, which makes it well matched for the complex pathogenesis of melasma. Finally, TXA inhibits melanogenesis also because of the negative effects on α -MSH and endothelin-1. This promotes the stability of melanocyte-keratinocyte interactions, leading to reduced amounts of melanin, and directly targeting one key mechanism of melasma pathogenesis. Furthermore, TXA exerts its vascular-modulating effects through dermal stabilization of blood vessels and reduces erythema and pigmentation related to the proliferation of blood conductors [2].

3. CLINICAL APPLICATIONS OF TRANEXAMIC ACID

Research by Ebrahim et al. shows that TXA is a safer topical agent than hydroquinone, owing to less irritation and side effects. [3]. Recently, Pazyar and Bani-Hani [4] have demonstrated that intradermal TXA, particularly when combined with ascorbic acid, can improve the effectiveness of melasma treatment. Furthermore, TXA has shown improved pigment clearance when combined with other treatment methods such as niacinamide, lasers, and kojic acid, which has been shown in study by Park et al. [5]. Combination therapies harness synergistic effects and target diverse mechanisms of TXA, as well as preventing melanin synthesis to enhance the response of the skin to treatment.

4. COMPARISON OF MASI REDUCTION AND TREATMENT OUTCOMES

Intralesional tranexamic acid (TXA) was shown to markedly decrease the Melasma Area and Severity Index (MASI) score, significantly more than topical 4% hydroquinone in terms of rapid, targeted improvement and limited side effects, making it an efficient and safe option in the management of melasma. The psychosocial impact of melasma is significant, especially in younger, married patients. Intralesional TXA has been shown to improve quality of life to a greater extent than alternative treatments [6]. Effective, safe, and patient-preferred options are critical in the management of melasma.

Table 1 shows some of the melasma treatment modalities that are available and the need to choose the modalities that are effective, safe, cheap and which are preferable by the patients.

5. COST ANALYSIS AND RECURRENCE

TXA is inexpensive (\$10-50/month), but recurrence rates are 20% to 40% after stopping treatment. On the other hand, laser-assisted TXA, the most expensive option, runs in the range of \$500 and \$1,500 per session and has the lowest recurrence rates between 10 and 20 percent. The wide variation in costs underscores the need for patient-centered treatment plans that incorporate cost, effectiveness, and patient values [4-8].

6. ADVANCE DELIVERY SYSTEMS

The highest treatment efficacy was achieved through combination therapies, especially those involving fractional laser-assisted delivery of TXA, with MASI reductions reaching 70–75% [5]. This synergistic benefit results from enhanced drug penetration and dual targeting of vascular and pigmentary pathways, such combinations should be reserved for refractory or recurrent melasma cases and be evaluated on a case-by-case basis. Similarly, innovative techniques that improve cutaneous absorption of TXA such as using assisted transdermal delivery methods—have demonstrated encouraging clinical results in melasma treatment. These approaches enhance localized drug action while reducing systemic exposure, offering a balanced profile of efficacy and safety in appropriately selected patients [8].

Table1. Comparison of Melasma Area and Severity Index (MASI) reduction across treatments.

Treatment type	Average MASI reduction (%)	Duration for improvement	Additional notes
Oral tranexamic acid	50–60%	12 weeks	Highly effective but with minimal risk of thromboembolic events in predisposed individuals
Topical tranexamic acid	40–50%	8–12 weeks	Safe with minor side effects like redness
Intradermal tranexamic acid	55–65%	6–8 weeks	Rapid results but mild injection site pain
Hydroquinone	45–55%	12 weeks	Effective but may cause skin irritation or PIH (post-inflammatory hyperpigmentation)
Laser + tranexamic acid	70–75%	4–6 weeks	Outstanding results but expensive and limited accessibility in some areas

7. PATIENT ADHERENCE; SAFETY OF IA TXA STACKING IN MELASMA THERAPY

The local Tranexamic Acid (TXA) formulations have been shown to be well tolerated with very few side effects that may enhance the adherence of patients, however since they need to be applied daily, this may act as a barrier. How about oral TXA, which is systemic, leading to GI upsets and rarely thrombotic events, or intradermal injections which, while effective, are painful, may cause discomfort and require regular attendance at the clinic, potentially affecting patient preferences and compliance? Telling patients about the benefits and drawbacks of each treatment in detail is very crucial for improving adherence and outcomes. Results in the included studies, adherence rates to prescribed treatment ranged from 45% to 93% (median 64%) for topical agents and 35% to 91% (median 66%) for oral agents, with median response rates of 65% for topical agents and 40% for oral agents. Adequate risk mitigation can be achieved through patient screening, protection against UV exposure, adjustment of the laser parameters for skin type, and the selection of appropriate sunscreens that will minimize irritation and maximize both the safety and effectiveness of treatment [3,4,7-9].

However, in response to the potential thromboembolic risk of oral TXA, the failure to implement risk stratification with thorough risk assessment is concerning. This involves assessing patients' history for clotting disorders, family history of thromboembolism, and performing pre-treatment laboratory tests such as D-dimer levels and coagulation pro-

files. Although some risks can be mitigated by the simple prescription of low-dose aspirin, and the recommendation of compression stockings for high-risk patients. However, the long-term safety and efficacy of TXA has not been adequately addressed and previous studies have primarily reported short-term outcomes and did not consider late adverse events or long-term use consequences. The antifibrinolytic effects of TXA dictate an ongoing evaluation of coagulation variables in at-risk patients. Therefore, investigating genetic factors affecting the development of melasma and responsiveness to TXA is important because it might enable more personalized treatment strategies [10].

8. CONCLUSION

Oral, topical, and intradermal formulations of tranexamic acid modulate inflammation, angiogenesis, and melanogenesis, providing effective treatment of melasma. Oral TXA is usually well-tolerated but does require careful screening for thromboembolic risk. To ensure long-term safety, advanced delivery systems, and combination therapies should be prioritized in future research since they can not only improve efficacy but also reduce recurrence.

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CONFLICT OF INTEREST STATEMENT

This study has not received any external funding; The authors declare that there are no conflicts of interest. All data referenced in this review are de-

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