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The Use of Tranexamic Acid to Prevent and Treat Post-Inflammatory Hyperpigmentation

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ABSTRACT

The risk of post-inflammatory hyperpigmentation (PIH) in patients undergoing dermatologic procedures is well known. It is especially common after laser procedures and chemical peels but can be seen with any procedure. PIH is also a sequela of acne, burns, and other trauma. High-risk patients are thought to have excessive production and abnormal distribution of melanin within the skin that triggers PIH, but the exact pathophysiology is unknown.[1] We define high-risk patients as Fitzpatrick skin types 3–5, those with existing PIH, or a history of PIH.[1,2]

Tranexamic acid (TXA) is an antifibrinolytic medication prescribed to treat bleeding and is also used off-label to treat melasma. TXA is contraindicated in patients with hypercoagulable conditions, renal impairment, vision impairment disorders, pregnancy, breast-feeding, or on hormone therapies.[3,4,5]

From 2015–2020, we have used TXA off-label to successfully treat and/or prevent PIH in approximately 82 high-risk patients after injuries or prior to procedures that disrupt the epidermis. We also have used TXA to prevent PIH after acute injuries such as irritant dermatitis, thermal burns, and abrasions. We now consider TXA treatment for all at risk patients prophylactically before undergoing microneedling, cryotherapy, cryolipolysis, chemical peels, and laser treatments.

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CASE 1

A 38-year-old woman with Fitzpatrick skin type 3 complained of a burning 20 minutes after the application of topical anesthetic cream: benzocaine 20%, lidocaine 8%, and tetracaine 4% (BTL cream, Sincerus Pharmaceuticals, Pompano Beach, FL). Removal of BTL cream showed evidence of significant inflammation (Figure 1). Past medical history was significant for severe PIH in the same location after irritation from a chemical peel.

FIGURE 1. Irritation after removal of anesthetic cream in Case 1.

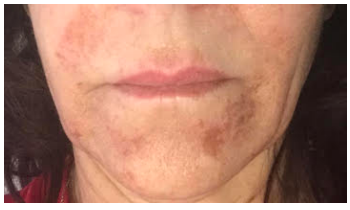
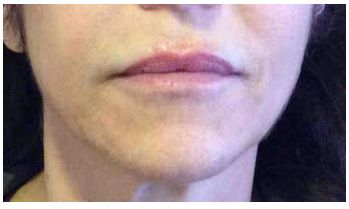


FIGURE 2. Eight weeks after injury in Case 1.

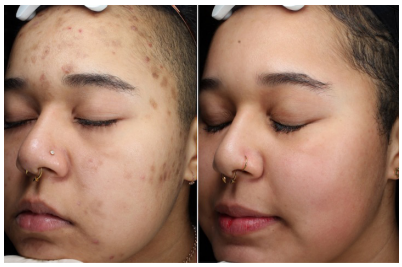


The patient had no contraindications for oral TXA. Given the high concern for PIH, she was prescribed TXA 650 mg daily and clobetasol 0.05% cream twice daily. The clobetasol cream was discontinued after one week and TXA was discontinued after eight weeks. Sixteen weeks later, she presented with normal-appearing skin. Her previous similar episode of PIH had been treated with clobetasol 0.05% cream for 2 weeks followed by hydroquinone 4% and monthly light chemical peels, leading to resolution only after six months. We believe the addition of TXA was responsible for her quick recovery without PIH, and without multiple chemical peels or prolonged use of hydroquinone (Figure 2).

CASE 2

A 20-year-old woman with Fitzpatrick skin type 4, presented with acne, acne excorie, and PIH (Figure 3, left side). She was treated with topicals (sunscreen and tretinoin 0.05%) and daily spironolactone 100 mg. A series of light chemical peels was planned. She was prophylactically prescribed oral TXA 650 mg daily for her ongoing excoriation and concern that the peels would exacerbate her current PIH. Over a period of 2.5 years, she completed nine exfoliative chemical peels (Vitalize peels, Allergan, Irvine, CA) without any complications (Figure 3, right side). She did not develop any new PIH during this time despite continued excoriation.

FIGURE 3. Before and after treatments in Case 2.



DISCUSSION

Skin dyschromias such as melasma, lentigos, and PIH are dermatologic conditions that can have significant negative impacts on the quality of life of affected patients.[1,2] Ironically, many of the procedures that treat pigment disorders can also cause irritation with the subsequent worsening or development of PIH. Prophylactic use of sunscreens, topical corticosteroids, and topical depigmenting agents have been used in an attempt to prevent and treat PIH with varying success.[2] PIH with or without treatment can take many months or even years to fully resolve. We believe this is because established topical treatments cannot be used after injury until the skin has re-epithelialized and the pathogenesis of hyperpigmentation has already been set in motion. TXA can be administered orally immediately after injury. Once the skin is healed, all patients are also counseled to use sun protection and established topical treatments[2] may be used in combination with TXA. The exact mechanism of TXA in reducing melanogenesis is unknown. It blocks melanocyte and keratinocyte interactions by inhibiting plasmin and mimicking lysine to prevent plasminogen from binding to keratinocytes. This decreases the inflammatory arachidonic acid and prostaglandins that stimulate melanocytes.[5,6,7] TXA is structurally similar to tyrosinase and may work by competitively antagonizing the enzyme.[7] TXA inhibits ultraviolet induced plasmin activity and reduces ultraviolet melanogenesis.[3,7,8] TXA has been shown to inhibit melanogenesis through activating autophagy in cultured melanoma cells.[8] Kim et al showed TXA treated melanocytes exhibited decreased melanin content and tyrosinase activity in lasered cells, adding to the rationale for using TXA to prevent or treat PIH after procedures.[9]

Three studies have looked at TXA for the prevention of PIH. TXA 650 mg daily was given to 32 Japanese women before Q-switched ruby laser (QSRL) for the treatment of senile lentigos (SL). This prospective randomized study found no significant difference between the treatment and placebo group with regard to PIH. This protocol may have been suboptimal due to small sample size, TXA dose, or duration of treatment.[3] Another prospective randomized study looked at the effect of 1500 mg daily of oral TXA on 40 patients undergoing SL treatment with Q-switched 532-nm Nd:YAG laser. This dose was not effective in preventing PIH compared with placebo. However, oral TXA did speed resolution of PIH when continued up to six weeks post-treatment.[4] The third study found a single dose of intradermal TXA injection (50 mg/mL) was mildly successful in reducing PIH after SL removal with a Q-switched 532-nm Nd:YAG laser when compared with placebo (0.9% normal saline) injection.[5]

We use oral TXA at a dose of 650 mg daily until the injury is fully healed and no PIH is present. This time period ranges from 2 weeks to several years in the case of ongoing treatment. We counsel patients to stop treatment for 48 hours prior to periods of immobility such as air or car flights over 4 hours and to avoid dehydration.

A recent extensive review and meta-analysis of nonsurgical patients treated with TXA without known hypercoagulability or risk factors for hypercoagulability such as drug interactions, active bleeding, cancer, past blood clots, or hormone therapy showed no increased risk of venous or arterial blood clots.[10]

A randomized, controlled study of acute TXA treatment to prevent and treat PIH would be extremely difficult to undertake given the individual variation of its expression, even within the same individual with the same type of injury. Until alternative studies can be completed, adding oral TXA to one's armamentarium in the setting of acute skin injury to prevent PIH in at-risk patients is safe and appears effective.

DISCLOSURES

The authors have no conflicts.

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