Sir,

Topical steroid dependent/damaged face (TSDF) is defined as a semi-permanent or permanent damage to the skin of the face precipitated by the irrational, indiscriminate, unsupervised, or prolonged use of topical corticosteroids (TC) resulting in a plethora of cutaneous signs and symptoms and psychological dependence on the drug.[1] Once damaged, the management becomes challenging as the treatment options are very limited and results are unpredictable. We present a case of recalcitrant TSDF with excellent response to topical 10% tranexamic acid (TXA).

A 21-year-old girl ( Fitzpatrick type IV-V) presented with persistent erythema of the face with associated itching and burning sensation [Figure 1a and b]. On enquiring, she gave history of application of betamethasone dipropionate cream twice daily for past 5 months. She was advised by a local pharmacist to apply betamethasone dipropionate cream for her freckles. Since last 1 month, she has been experiencing a burning sensation on face and a persistent erythema. Patient was asked to stop the topical steroid application and was advised strict photoprotection. Topical tacrolimus 0.1% was prescribed at nighttime but was discontinued after 8 weeks due to minimal improvement of symptoms. Topical brimonidine 0.33% was given later, which showed initial improvement. The lesions, however, reappeared on discontinuation of therapy. Patient was then started on topical 10% TXA, which was prepared from injection TXA (100 mg/ml). The solution was dispensed in an ethylene/propylene copolymer plastic container and patient was educated to apply it with a cotton bud once daily at night. In addition, a physical sunscreen was also advised. Burning sensation decreased within 2 weeks. Erythema was assessed using a clinician erythema assessment scale[2] [Table 1] and it showed a 2-grade reduction (baseline grade-4) after 4 weeks [Figure 2a and b]. Treatment was continued till 8 weeks, after which it was stopped and patient was asked to continue using the sunscreen. There was no relapse in the next 4 weeks, after which the patient was lost to follow up.

The clinical picture of TSDF appears due to a combination of factors: dermal atrophy (TC inhibit collagen and hyaluronic acid synthesis by fibroblasts),[3] local immunosuppression, and inhibition of action of nitric oxide (NO).[4,5] On withdrawal of TC, endothelial NO is released causing vasodilation and erythema.[4,5]

TXA is a synthetic lysine-like molecule, which competitively inhibits the conversion of plasminogen into plasmin, thereby inhibiting the plasmin mediated angiogenesis.[2] In addition, it is known to inhibit vascular endothelial growth factor. Topical TXA has been used in the management of rosacea.[2,3] Tranexamic acid decreases the clinical signs of rosacea via inhibition of PAR-2 activation by serine protease and calcium influx in keratinocytes.[2] Additionally, it decreases erythema by decreasing pro-inflammatory cytokines (interleukin 6 and tumor necrosis factor alpha).[3]

Treatment of TSDF includes withdrawal of the topical corticosteroid, which itself can lead to the increased flushing and erythema due to released nitric oxide from the endothelia.[4,5] Oral anti-inflammatory antibiotics, topical

| Table 1: Clinician erythema assessment scale description |
|---------------------------------------------------------|
| Grade 1 | CEA scale description                               |
|---------|------------------------------------------------------|
| 0       | Clear skin with no signs of erythema                 |
| 1       | Almost clear, slight redness                         |
| 2       | Mild erythema, definite redness                      |
| 3       | Moderate erythema, marked redness                    |
| 4       | Severe erythema, fiery redness                       |

Figure 1: Dusky erythema over the face of a young girl (a); lateral view showing topical steroid induced erythema (b)

Figure 2: Improvement of the erythema after 4 weeks of topical 10% tranexamic acid application (a); lateral view showing improvement in erythema (b)
Inhibitory mechanisms of topical steroid dependent face

| Topical therapeutic modality | Mechanism of action |
|-----------------------------|---------------------|
| Topical tacrolimus/pimecrolimus | Calcineurin antagonist that causes immunosuppression and anti-inflammatory effect by blocking T-cell activation, thereby down-regulating interleukin (IL-2), IL-4, IL-10, and other cytokines. |
| Topical brimonidine | Alpha-adrenoceptor agonist and causes vasoconstriction of cutaneous microcirculation |
| Topical xylometazoline | Anti-inflammatory effect that interferes with neutrophil release of reactive oxygen species |
| Topical metronidazole | Anti-inflammatory effect through inhibition of the production of reactive proinflammatory oxygen species (hydroxy and super oxynradicals) from neutrophils. |
| Topical azelaic acid | Inhibit the innate inflammatory cascade by inhibiting demodex (which may increase due to immunosuppressive action of topical corticosteroids) |
| Topical ivermectin | Reduces bacterial superantigens that proliferate due to immunosuppressive action of topical corticosteroids, in addition to having anti-inflammatory properties |
| Topical clindamycin | Inhibits the conversion of plasminogen into plasmin, thereby inhibiting the plasmin mediated angiogenesis. In addition it inhibits vascular endothelial growth factor. It also causes inhibition of PAR-2 activation by serine protease and calcium influx in keratinocytes. Lastly, it decreases erythema by decreasing pro-inflammatory cytokines (interleukin 6 and tumor necrosis factor alpha) |
| Sunscreen | Protects against the Ultraviolet light damage and reduces trans-epidermal water loss. |
| Topical tranexamic acid | Infates with anti-inflammatory effect by blocking interleukin(IL)-2, IL-4, IL-10, and other cytokine. |

Metronidazole, topical tacrolimus/pimecrolimus, topical brimonidine, and topical xylometazoline has been used in past with variable results [Table 2]. Increasing evidence of TXA in the reduction of erythema prompted us to start the patient on 10% TXA. Commercially, TXA preparation as solo therapeutic agent is not available and hence has to be prepared from the injectable form. The preparation has to be stored in an ethylene/propylene plastic bottle. The preparation should be stored away from light and at room temperature.

Dryness was the only side-effect reported by our patient during the therapy. A moisturizer was prescribed to deal with dryness. A long-term follow-up could not be done in our patient, which is the limitation of this report. Our report shows a promising role of TXA in TSDF. However, further studies with increased sample size and long-term follow-up is needed to conclude the role of TXA in the management of TSDF.

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Conflicts of interest
There are no conflicts of interest.

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