Exploring the controversy and pathogenesis of Topical Steroid Withdrawal Syndrome

Background

Topical glucocorticoids (more commonly termed topical corticosteroids; TCS) are first line therapy for management of numerous skin conditions. Topical Steroid Withdrawal (TSW) is a controversial diagnosis advocated by patients with prolonged TCS exposure who report severe systemic reactions upon treatment cessation. Although the disease may be confused for eczematous disorders or dismissed outright, there have been no systematic clinical or mechanistic studies to either refute or support TSW as molecularly distinct from other dermatopathies. This study aimed to clinically differentiate TSW symptomatology, delineate abnormal molecular pathways, and investigate potential therapeutic agents.

Methodology

Results

Fig 1. Representative images of TSW-associated symptoms

Fig 2. Symptom resolution plot depicting prolong symptom profile for majority of patients. Proposed diagnostic criteria (1 major + 3 minor) with 92% sensitivity.

Fig 3. Serum cytokines profile in TSW is similar to AD with elevated proinflammatory cytokines

Fig 4. Skin microbiota signatures in TSW differ significantly from controls

Fig 5. Skin tissue metabolomics demonstrate relative upregulation of nicotinic acid and downregulation of tryptophan metabolism when compared to HC

Fig 6. RNA-seq data shows increased expression of complex 1 of the electron transport chain in TSW patients

Fig 7. Complex 1 transcripts are upregulated in healthy individuals 4 hours after treatment with topical steroids

Fig 8. Mice treated with nicotinic acid have increased ear thickness (left) and inflammation around hair follicles (middle), differing from AD mouse model where entire ear is involved (right)

Fig 9. WGS showed VUS in TTN (likely insignificant); Expanded analysis identified FMO2 and PAX6 (CADD>20 present in 12/16 pts)

Fig 10. Complex 1 inhibitors berberine and metformin decrease mitochondrial stress and cell proliferation

Fig 11. Treatment with complex 1 inhibitors berberine and metformin reduce subjective symptom severity in case series (N=12)

Conclusions

Citations