

Steroid Withdrawal Effects Following Long-term Topical Corticosteroid Use

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Background: Concerns about topical steroid withdrawal (TSW) are leading some patients to cease long-term topical corticosteroid (TCS) therapy. Diagnostic criteria for this condition do not exist.

Objective: The aim of this study was to examine the demographics and outcomes in adult patients who believe they are experiencing TSW following discontinuation of chronic TCS overuse.

Methods: This was a retrospective cohort study of patients in an Australian general practice presenting with this clinical scenario between January 2015 and February 2018.

Results: Women represented 56% of the 55 patients seen, and ages ranged from 20 to 66 years (mean, 32.9 years; median, 30.0 years). Seventy-six percent had an original diagnosis of atopic dermatitis. Sixty percent had used potent TCSs on the face, and 42% had a history of oral corticosteroid use for skin symptoms. Burning pain was reported in 65%; all had widespread areas of red skin; and so-called “elephant wrinkles,” “red sleeve,” and the headlight sign were seen in 56%, 40%, and 29%, respectively.

Conclusions: Patients with a history of long-term TCS overuse may experience symptoms and signs described in TSW on stopping TCSs. Diagnostic criteria, reflecting the histories and examination findings of the patients studied, are suggested in this article with the aim to advance discussion and research into TSW.

Topical corticosteroids (TCSs) are the first-line treatment of many dermatological disorders including chronic conditions such as atopic dermatitis and, as a result, can be used for many years. With a reported 1 in 3 people using the Internet for medical advice,¹ some patients on long-term TCS therapy may become concerned that they are at risk of topical steroid withdrawal (TSW) and consider ceasing TCS treatment.

Topical steroid withdrawal, which has also been called red skin syndrome,² topical steroid addiction,³ and TCS addiction/withdrawal syndrome,⁴ has been found to be a distinct adverse effect of TCS overuse, especially where there has been long-term inappropriate use of moderate to potent TCSs on the face or genital area.⁴ The diagnosis is not yet widely accepted; it is omitted from the TCS adverse effect sections in some publications,^{5,6} and its significance is downplayed when it is mentioned in others.^{7,8} Comments

in the literature include TSW is “poorly defined”⁹ and merely “steroid phobia.”¹⁰

Topical steroid withdrawal diagnostic criteria do not exist; however, research into TSW does.^{2,4,11–14} Atopy is considered a risk factor for developing this condition.² Two distinct morphological syndromes have been described. The erythematous type is most commonly seen in patients with atopic dermatitis, and ~80% of patients with atopic dermatitis fall into this category.⁴ The papulopustular type is more often present in patients who used TCSs for cosmetic purposes or pigmentary conditions.⁴ Prior to ceasing TCSs, patients with TSW may have evidence of skin damage such as atrophy with striae and telangiectasia^{2,3} (Fig. 1A). Symptoms seen in TSW include burning pain, severe itch, shedding skin/desquamation (Fig. 1B), edema, serous exudate/ooze, skin sensitivity, insomnia, and depression.^{2–4,11} Signs that are commonly seen in these patients are discussed in Table 1. Although these are not specific to TSW, their presence, in addition to a classic history, supports the diagnosis. Biopsies have been reported to show spongiotic dermatitis,² parakeratosis,¹⁸ and insufficient corneal layer formation.¹⁸ Treatment options include use of moisturizers, cold compresses/ice, simple analgesics, over-the-counter antihistamines, and low-dose doxepin and short-term use of hydroxyzine. Occasionally, gabapentin, phototherapy, or immunosuppressants might be prescribed.² Limited use of sleeping aids and anxiolytics may be appropriate in some cases.² Tetracycline antibiotics and calcineurin inhibitors have been reportedly used in patients with the papulopustular type of TSW.⁴ Psychological therapy may be

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required² and is sometimes more pertinent later in the clinical course (when the patient appears to be doing well).

The study sought to identify the demographics and investigate outcomes in presenting patients concerned that they could be experiencing TSW following their cessation of long-term TCS overuse. The results were taken into consideration when drafting the proposed TSW diagnostic criteria set out in Box 1.

Box 1. Suggested Diagnostic Criteria for TSW: A Starting Point for Discussion and Future Research

Consider TSW when the following essential criteria are fulfilled; the diagnosis becomes more likely when more of the key diagnostic criteria are also present.

Essential criteria:

1. History of long-term regular TCS use (months to years) where TCSs were initially effective, but over time, either increased amounts or potencies (or both) were required to reduce severity of skin symptoms
2. Itch
3. Erythema

Key diagnostic criteria:

1. History of atopy, especially atopic dermatitis
2. History of TCS use on the face, especially potent TCSs
3. History of oral prednisone use for skin symptoms
4. Burning pain on the skin
5. Skin sensitivity to previously tolerated skin products
6. Excessive skin exfoliation (shedding)
7. Oozing skin
8. Edema, especially of the eyelids or ankles
9. Elephant wrinkles of the extensor elbows and anterior kneesⁱ
10. Red sleeve signⁱⁱ

Additional supporting features that may be present:

1. Sleep disturbance
2. Mood disturbance
3. Skin pain, other than burning pain
4. Papules and pustules
5. Headlight sign

ⁱElephant wrinkles: a descriptive term for apparent thickened skin with a reduction in skin elasticity, demonstrated, for example, on the anterior knees and/or extensor elbows, although not limited to these areas.

ⁱⁱRed sleeve sign: a descriptive term for a rebound eruption to either the upper or lower limb ending abruptly at the margin of the dorsal and palmar (or solar) border.

METHODS

Patients presenting with possible TSW following discontinuation of chronic TCS overuse were assessed in an Australian suburban general practice, and suspected cases were reported to the Therapeutic Goods Administration for inclusion in the Australian Adverse Drug Reaction Database. From this record, patients who presented concerned about TSW during the period from January 1, 2015, to February 28, 2018, were identified, and their medical files were reviewed to retrieve demographic data and history. Ethics approval for this study was obtained from the Royal Australian College of General Practitioners National Research and Evaluation Ethics Committee.

RESULTS

Sixty-nine patients were identified from the record; 14 patients were younger than 18 years at the time of first presentation and were excluded from the study. The age range of the 55 remaining patients was 20 to 66 years (mean, 32.9 years; median, 30.0 years). Patients gave histories of increasing amounts of TCSs used and/or increasing TCS potencies over months to years, where TCSs had helped initially but were later needed more often to reduce skin symptoms. Characteristics of the patients are detailed in Table 2, and clinical features are recorded in Table 3. Length of TCS use varied from 6 months to 40+ years. Continuous daily use was reported in a minority of patients. An accurate assessment of the total duration of TCS use was not possible in the patients because of large variations in frequency of use over time. Following TCS cessation, 23 patients consulted a dermatologist; 4, an immunologist; 2, an endocrinologist; 7, a psychologist; and 6, an alternative health practitioner. One attended an ophthalmology clinic regularly for severe atopic keratoconjunctivitis. Skin biopsies were obtained from 4 patients, and the resulting histopathologic reports all mentioned spongiosis and parakeratosis. Recommencement of TCSs occurred in 12 patients (22%). Three of these patients changed their minds and decided to discontinue TCS use a second time.

DISCUSSION

Confirming the diagnosis of TSW was problematic because with an absence of diagnostic criteria, TSW could be considered the most likely diagnosis only based on history and examination findings. The differential diagnosis of TSW includes atopic dermatitis itself and allergic contact dermatitis (often to an ingredient in the vehicle of topical agents) as primary considerations. However, the full differential diagnosis of atopic dermatitis must also be invoked at times, including cutaneous T-cell lymphoma, psoriasis, scabies, and other entities, which can present with eczematous skin. Many of the symptoms seen in TSW may also be seen in severe atopic dermatitis; however, others are more typical of TSW and were thus helpful in differentiating between the 2 diagnoses. Burning pain was reported in 65%; excessive skin desquamation, in 75%; swelling, in 65%; and skin sensitivity, in 47%. Signs that have been reported



Figure 1. A, Skin atrophy with telangiectasia and striae. This patient was unable to remain off TCSs. B, Excessively dry skin on the upper limb with desquamation and shedding. C, Red sleeve with erythema of an extremity, in this case, the upper limb, ending abruptly at the dorsal border. D, Red sleeve with erythema ending abruptly at the palmar border of the upper limb. E, A clear nose in an otherwise red face. In this patient, the perioral area was not spared, as is classically described in the headlight sign when seen in TSW.² F, Facial erythema ending at the midcheek with (relatively) clear skin from the midcheek to the left ear, as described in the headlight sign. G, Elephant wrinkles: thickened skin with a reduction in skin elasticity seen here to the extensor elbow.

commonly (but not necessarily exclusively) in TSW were seen in a number of patients: diffusely red skin, 100%; elephant wrinkles, 56%; red sleeve, 40%; and the headlight sign, 29%. Because of difficulty in accessing patch testing, exclusion of allergy to TCSs, or components of TCSs, was not possible in this population. Had it been readily available, however, patch testing would have been

TABLE 1. Topical Steroid Withdrawal Signs

Red skin	The most common sign reported in TSW, seen in 92% of cases ⁴ (hence the name “red skin syndrome ² ”). Can be severe and widespread. ^{3,11,15} It typically occurs within days to weeks of ceasing long-term TCS overuse, ⁴ spreading from the original site of intractable eczema, with gradual extension into areas of the skin where TCSs may have never been applied. ^{3,11}
Red sleeve ¹⁶	A descriptive term for a rebound eruption to either the upper or lower limb ending abruptly at the margin of the dorsal and palmar (or solar) border ³ (Figs. 1C, D); skin to the palms and soles tends to be clear in all but the most severely affected patients with TSW. ³
Headlight sign ²	Clear nose and perioral skin in an otherwise red face ² (Fig. 1E); erythema often ends at the midcheek with normal skin present from the midcheek to the ears ¹⁷ (Fig. 1F)
Elephant wrinkles ¹⁶	A descriptive term for apparent thickened skin with a reduction in skin elasticity, demonstrated, eg, on the anterior knees and/or extensor elbows, ¹⁶ although not limited to these areas (Fig. 1G); can take many months to resolve

impractical in a number of patients because of their widespread red skin.

Suggested diagnostic criteria for TSW were devised following analysis of the 55 patient histories and clinical features (Box 1). All patients seen fulfilled the suggested essential criteria. Forty (73%) of the 55 patients met 5 or more of the key diagnostic criteria, and 48 (87%) of the 55 patients met 4 or more. Had these features been assessed prospectively and proactively, however, it is believed that significantly higher proportions of patients would have fulfilled 5 or more of the key diagnostic criteria.

The female preponderance noted elsewhere with TSW, while seen in this population, was less pronounced at 56% (31/55) of the total group. This might be because none of the patients in this sample had used TCSs for cosmetic purposes, which may be more commonly observed in women. Instead, 76% had an initial dermatological diagnosis of atopic dermatitis, whereas in Hajar and colleagues⁴ systematic review of TSW, where 81% of cases were female, only 33% commenced TCS use for atopic dermatitis. The problem of TCS misuse for cosmetic purposes as reported in Africa¹⁹ and Asia^{20–22} (particularly India^{23,24}) does not appear to exist in Australia.²⁵

The numbers of children presenting with possible TSW were higher than previously reported in the literature, and younger adults

TABLE 3. Clinical Features Seen in the Study Population

	All Patients (N = 55), n (%)
Symptoms	
Itch	55 (100)
Sleep disturbance	50 (91)
Shedding skin	41 (75)
Ooze	40 (73)
Burning pain	36 (65)
Swelling	36 (65)
Mood disturbance	33 (60)
Skin sensitivity	26 (47)
Pain, other than burning	17 (31)
Signs	
Red skin	55 (100)
Elephant wrinkles	31 (56)
Red sleeve	22 (40)
Headlight sign	16 (29)

were more commonly seen compared with older adults. Of the 69 cases seen over the study period, 14 (20%) were younger than 18 years (and were excluded from the analysis). This proportion was higher than the 7% found by Hajar et al.⁴ This could represent increasing parental internet research into TCSs over recent years and corresponding growing caretaker anxieties about long-term TCS use in children. The median age of adults presenting was 30.0 years. Younger patients have a greater propensity to seek health information online than older adults,¹ and so it is possible that they are more aware and, as such, more concerned about possible TSW than their senior counterparts.

Obtaining thorough and accurate histories of TCS use was difficult; in many cases, TCS use fluctuated over the years with break periods in between, and their TCS use spanned decades. Patients were frequently unclear about the potencies and/or names of TCSs used in the past. Details of TCS use in childhood could not be determined even when their parent(s) accompanied them to their appointment (which was not an infrequent occurrence as parents were often involved in the care and support of their adult children following their cessation of TCSs). Identifying total years of TCS use was problematic as many patients reported significant periods with little or no TCS use (eg, during their teenage years or following a move overseas) before resuming and then increasing their regular TCS use. It has been reported that TSW can occur with as short as 4 to 6 weeks of frequent TCS use.² However, the patients in this study reported much longer (but highly variable and thus difficult to quantify) periods of regular TCS use.

In Hajar and colleagues⁴ systematic review, 97% of patients had a history of TCS use on the face,⁴ and this was a common, but not universal, finding among patients in this study as well. Eighty-four percent had used TCS on the face, and 60% of all patients reported using potent TCSs on their face. The higher incidence of TCS use on the face in Hajar and colleagues' review might reflect the larger proportion of patients with a history of using TCSs for reasons other

TABLE 2. Characteristics of the Study Population

	All Patients (N = 55), n (%)
Sex	
Female	31 (56)
Age first presented with concerns about TSW, y	
18–24	12 (22)
25–34	23 (42)
35–44	12 (22)
≥ 45	8 (15)
Initial indication for TCS use	
Atopic dermatitis	42 (76)
Contact dermatitis	8 (15)
Nonspecific rash	5 (9)
Location of TCS use (included, but not limited to)	
Face	46 (84)
Genital area	2 (4)
Potency of TCS use to the face*	
Mild	4 (7)
Moderate	4 (7)
Potent	33 (60)
Unknown	5 (9)
Use of oral corticosteroids for skin symptoms in the past	
Yes	23 (42)
Age TCSs were first used, y	
≤ 5	26 (47)
6–12	8 (15)
13–20	4 (7)
≥ 21	13 (24)
Unknown	4 (7)

*TCS potency was based on the classifications used in the Australian Medicine Handbook 2018.

than atopic dermatitis, as many of those conditions affect the face primarily (cosmetic/pigmentary use, “facial rash,” acne, rosacea, and perioral dermatitis were some of the initial indications for TCS use in Hajar and colleagues’ study). In this Australian study, only 13 (23.6%) of the 55 patients had used TCSs for a purpose other than atopic dermatitis.

A history of prior use of oral corticosteroids for skin symptoms was commonly seen, with 42% (23/55) of the patients reporting use of oral corticosteroids for this purpose. Previous US research reported oral corticosteroid prescriptions to be “commonplace” in 5.9%²⁶ of patients seen by a dermatologist for their atopic dermatitis. It is likely that a history of oral corticosteroid use indicates a more severe clinical picture with a consequent increased risk of TCS overuse and therefore TSW.

Topical corticosteroids were first used before the age of 13 years in 62% (34/55) of the patients, consistent with the high incidence of atopic dermatitis in childhood. However, cases still occurred in patients where TCSs were commenced in adulthood; 24% of the patients in this study reported not using TCSs until 21 years or older.

Twelve patients (22%) in this study resumed TCS use; however, 3 of them discontinued TCSs again at a later date. Twenty-two percent is likely to be an underestimate as it would be expected that some patients would not return for follow-up if they elected to recommence TCSs. This figure was higher than the 5% and 13% reported in 2 previous articles by Rapaport and Rapaport.^{2,14} This may be due in part to limited access to other therapies. Ten patients in this study were offered immunosuppressant therapy by their dermatologist or immunologist (5 of these reported taking it). One was given the option of participating in a trial using a biologic treatment. Another factor could be cost-of-living pressures, with many people unable to have a period of weeks (or months) off work as would be required for some patients experiencing TSW.

Although this exploratory study has a number of limitations, it does provide real-world evidence about the demographics of patients who cease long-term TCS overuse and the outcomes these patients experience. Clarifying histories of long-term TCS use is problematic. The ad hoc nature of presentations in the community makes comparisons between patients at similar stages difficult. In addition, this particular study cannot answer the most commonly asked question, “How long will TSW last for me?” Prospective studies over several years, following patients with differing TCS use histories, will be required to provide evidence-based time frame estimates for these patients.

CONCLUSIONS

Although there are currently no diagnostic criteria for TSW, and the symptoms and signs described in this condition are somewhat non-specific, the combination of a typical history with characteristic features increases the likelihood of TSW. The proposed diagnostic criteria outlined in Box 1 reflect the findings from this study. A patient with a history of atopy, reporting prolonged TCS overuse, especially where such use has included the face and provided

diminishing clinical benefit over time, is classic. Use of oral corticosteroids for skin symptoms appears to be a common feature on history and should be considered a risk factor for TSW. Following TCS discontinuation, patients experiencing TSW will typically report burning pain, excessive skin exfoliation, edema, and/or skin sensitivity. Widespread red skin may be seen in addition to elephant wrinkles, red sleeve, and/or the headlight sign. A significant proportion of patients in this study chose to resume TCS use. However, where an informed, competent patient with the previously mentioned clinical presentation remains motivated to eschew further TCS treatment, it would be reasonable to explore appropriate non-steroidal options, monitor for complications, and provide (or arrange) any psychological support required.

More research into TSW is required to develop guidelines to assist with prevention, establish consensus diagnostic criteria, and recommend evidence-based management.

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