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Research Article

An Analysis of Literature on Topical Steroid Withdrawal in Dermatology

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Topical steroids have been used to treat a variety of dermatological conditions and are one of the most commonly prescribed drugs in dermatology. These are Food and Drug Administration (FDA)-approved medications for treating diseases such as eczema, vitiligo, atopic dermatitis, discoid lupus erythematosus, and more. The mechanism of action of topical corticosteroids consists of anti-inflammatory, anti-mitotic, and immunosuppressive effects. Patients on topical corticosteroid treatments must be monitored carefully as there is a potential for adverse effects, especially in treatments lasting longer than several weeks. While when properly prescribed and monitored topical corticosteroid usage is considered safe, there have been growing concerns surrounding topical corticosteroid abuse, phobia, and withdrawal. Current research has focused on new therapeutic strategies and management protocols to improve long-term patient outcomes and mitigate the adverse effects of these drugs. In this narrative review, we describe the recent findings of clinical manifestations, patient perspectives in the literature, current knowledge, and misinformation and abuse pertaining to topical steroids.

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Background

Topical corticosteroids are one of the oldest and most commonly used treatments for skin conditions. Topical corticosteroids were not discovered serendipitously, but rather the result of a series of painstaking studies and a recognition of their possible applications to dermatologic therapies (Witten,1992). Topical use of cortisone was attempted as early as 1950. The successful use of hydrocortisone, a natural glucocorticoid hormone, was first demonstrated by Sulzberger and Witten in 1952 (Witten,1992, Mukhopadhyay and Kwatra, 2017). The use of

prednisolone and fluorohydrocortisone was first reported in 1955 (Witten,1992). This was then followed by the introduction of triamcinolone in 1958 which resulted in higher potency and lower adverse effects. (Robinson,1958). Topical betamethasone was first introduced in 1964. Betamethasone valerate 0.1% was then successfully formulated in 1967 after many chemical modifications. This was a significant milestone as clinicians previously depended on systemic corticosteroids to treat difficult dermatoses such as psoriasis (Witten,1992).

Today many classes and potencies exist amongst different topical corticosteroids. The evolution of topical corticosteroids brought the inevitable question of comparison of efficacy and potency

(Mukhopadhyay and Kwatra, 2017). The vasoconstriction assay, which measures the corticosteroid's cutaneous vasoconstrictive properties would become the benchmark for the evaluation of topical corticosteroid potency (Mckenzie and Stoughton, 1962, Place et al, 1970). The United States System classifies topical corticosteroids into seven classes based on their performance on the vasoconstriction assay. Class I super-high potency corticosteroids include clobetasol propionate 0.05% in any vehicle, betamethasone dipropionate 0.05% ointment, halobetasol propionate 0.05% ointment and fluocinonide 0.1% cream and should not be used for longer than 3 weeks (Stacey SK, McEleney M., 2021). Class II high-potency corticosteroids include amcinonide 0.1% ointment, desoximetasone in any vehicle, and diflorasone diacetate 0.05% cream and should not be used for longer than 12 weeks (Stacey SK, McEleney M., 2021). Examples of conditions treated with Class I and II corticosteroids include psoriasis, alopecia areata, lichen planus, discoid lupus, and vitiligo (Stacey SK, McEleney M., 2021). Class III medium to high potency corticosteroids includes fluticasone propionate 0.005% ointment, amcinonide 0.1% cream, and betamethasone dipropionate 0.05% cream and should not be used for longer than 12 weeks (Stacey SK, McEleney M., 2021). Class IV and V medium to high potency corticosteroids include betamethasone valerate 0.1% and triamcinolone acetonide 0.025% (Stacey SK, McEleney M., 2021). Examples of conditions treated with Class II, III, and IV corticosteroids include atopic dermatitis, scabies, and asteatotic eczema (Stacey SK, McEleney M., 2021). Class VI low potency corticosteroids include desonide 0.05% in any vehicle, hydrocortisone butyrate 0.1% cream, and alclometasone dipropionate 0.05% cream or ointment (Stacey SK, McEleney M., 2021). Class VII least potent corticosteroids include hydrocortisone 1% and 2.5% in any vehicle (Stacey SK, McEleney M., 2021). Class VI and VII treatments have no specified limit for the duration of use and are most commonly used for treating conditions like phimosis, facial dermatitis, and intertrigo (Stacey SK, McEleney M., 2021).

Topical Steroid Addiction

Topical Steroid Addiction (TSA) is a condition in which cessation of topical corticosteroid (TCS) treatment causes more severe or varied cutaneous symptoms than which existed prior to treatment. It is important to note that adverse effects of TCS are not limited to cutaneous symptomology and can also be

systemic in nature. Examples of these adverse effects include peripheral edema, Cushing syndrome, ocular hypertension, and hyperglycemia (Stacey SK, McEleney M., 2021). TSA is also known as Red Skin Syndrome (RSS), Red Burning Skin Syndrome (RBSS), and Topical Steroid Withdrawal Syndrome (TSWS). As the naming implies, the skin is described as being “addicted” or “resistant” to the TCS. It occurs most commonly in adult women applying mid- or high-potency TCS to the face or genital region and is associated with increased frequency and duration of treatment (Arnold et al., 2018, Juhász et al., 2014, Manchanda et al., 2014). Evidence points to an increased incidence in younger patients, as well as in prolonged and excessive use of TCS (Arnold et al., 2018, Juhász et al., 2014).

While the pathogenesis of the reaction is still poorly understood, there are several potential mechanisms that have been suggested. For example, patients who are resistant to TCS have a low ratio of GR- α to GR- β ; alteration in the glucocorticoid receptor (GR) expression pattern on the surface of cells (Arnold et al., 2018, Juhász et al., 2014). Vasodilatory mechanisms have also been implicated in the redness that is normally seen. TCS decreases the production of nitric oxide (NO), which inhibits the vasodilatory action of the blood vessels. Once the TCS is discontinued, a rebound effect may happen wherein NO levels rise and cause excessive vasodilation (Arnold et al., 2018, Juhász et al., 2014).

The addicted skin typically appears almost normal or well-controlled by TCS prior to withdrawal. Prurigo-like eruptions or other difficult-to-control lesions are seen in some patients, which are usually mistaken as manifestations of atopic dermatitis by both dermatologists and patients alike. The condition usually manifests as one of two subtypes: the erythematoedematous type, which is characterized by erythema, scaling, papules and nodules, desquamation, and edema; and the papulopustular type, which has more prominent pustules, papules, and nodules and less common occurrences of burning and edema. Rebound eruptions have also been reported in areas without prior lesions or TCS application, although the cause has yet to be proven (Arnold et al., 2018, Fukaya et al., 2014). TSA has started to become more of a patient concern and has started to gain increased traction on social media as well. As of yet, there are no standard diagnostic criteria for the condition (Arnold et al., 2018).

Treatment of Topical Steroid Withdrawal

Treatment for topical steroid withdrawal, also known as TCS addiction or withdrawal syndrome, is best done as soon as symptoms of prolonged use, such as erythema, burning, or itching, appear ([Hwang et al., 2022](#)). Dermoscopy, in addition to a physical examination, can help dermatologists confirm the diagnosis, distinguish it from other causes, and determine the approximate length of TCS abuse to offer a better prognosis ([Sethi et al., 2021](#)). The most common first step in treatment in documented cases is to stop using TCS ([Arnold et al., 2018](#)). The other known management strategy involves reducing doses and frequency of application, weekly maintenance therapy, once-daily applications, and avoiding occlusion ([Mehta et al., 2016](#)). More severely addicted patients, however, are unable to reduce the dosage or potency of their TCS at all as doing so causes a sudden rebound effect. As a result, in some cases, patients must stop either gradually or abruptly. Time may be the most helpful "medication" for these patients in this state, along with psychological support and the prevention of more dire consequences like sepsis ([Fukaya et al., 2014](#)).

Other therapeutic modalities suggest the use of dupilumab in the management of TCS withdrawal in the setting of moderate to severe atopic dermatitis, and it is deserving of additional study ([Arnold et al., 2018](#)). Occasionally gabapentin, phototherapy, or immunosuppressants might be prescribed. Limited use of sleeping aids and anxiolytics may be appropriate in some cases. Tetracycline antibiotics and calcineurin inhibitors have been reportedly used in patients with the papulopustular type of TSW. Simple analgesics, over-the-counter antihistamines, cold compresses or ice, moisturizers, and other psychological aids should be taken into consideration ([Sheary, 2018](#)). Physician awareness and patient education will continue to be the cornerstones of addressing this expanding issue until newer and safer topical corticosteroids are made available ([Mehta et al., 2016](#)). Proper patient education is a crucial future consideration ([Manchanda et al., 2017](#)).

Therapeutic Implications

Impacts and Effects of Prolonged Topical Steroid Usage

Corticosteroids mediate clinical effects due to their anti-inflammatory, vasoconstrictive, antiproliferative, and immunosuppressive properties, which are also involved in the mechanisms of their side effects. The advent and frequent use of more potent formulations over prolonged periods of time have caused the side effects and subsequent withdrawal syndromes to be more prevalent. Figure 1 summarizes some of the effects of long-term use. Atopy is considered a risk factor for developing TSA. There is also an increased incidence in female patients ([Manchanda et al., 2017](#), [Sethi et al., 2021](#), [Juhász et al., 2017](#)). The prevalence of positive contact allergies to topical corticosteroids is believed to be between 0.2% and 6%. Rebound eruptions can sometimes extend to areas of the skin where TCS has never been applied, sparing the hands and soles. The skin lesion basically resembles the original skin disease. The skin then becomes dependent on the TCS and shows signs of addiction or withdrawal once it is discontinued ([Arnold et al., 2018](#), [Juhász et al., 2017](#)). Some of the symptoms include erythema, pruritus, burning sensation, exudation, pustules, scaling, xerosis, epidermal thinning, and telangiectasias. Ocular side effects include posterior subcapsular cataracts and glaucoma. Systemic effects include diabetes mellitus/hyperglycemia, mineralocorticoid effects (edema, hypocalcemia, hypokalemia, hypertension), and adrenal suppression. These effects tend to be seen after extensive application to wide areas of the body ([Mehta et al., 2016](#), [Sheary, 2018](#), [Siegfried et al., 2016](#)). Side effects of TCS use on the face include steroid rosacea, acneiform eruptions, hypertrichosis, and demodicosis. These findings are also termed "topical steroid-induced facial rosacea dermatitis" (TSIFRD) or topical steroid-dependent face (TSDF) ([Manchanda et al., 2017](#)). Longer periods of application may increase the risk of experiencing adverse cutaneous and systemic side effects. There is limited data regarding the safety of mid to high-dose TCS prescribed for long-term use ([Juhász et al., 2017](#), [Fukuya et al., 2014](#), [Siegfried et al., 2016](#)). However, TSA can occur upon withdrawal of the medication after as little as 2 months of use or even less. The addicted skin becomes normal as time passes, and it can take anywhere from weeks to even years to resolve. In this regard, there is a great deal of

heterogeneity both in the progression and resolution of TSA.

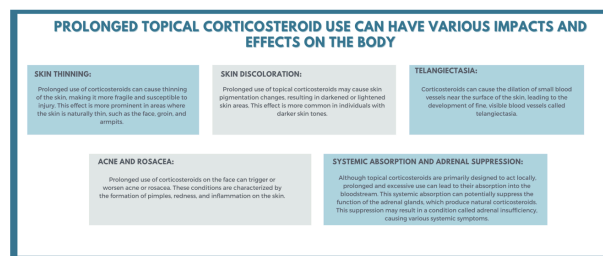


Figure 1. Prolonged Topical Corticosteroid Use Can Have Various Impacts And Effects On The Body

The number of younger people presenting with possible TSA has appeared to increase. This could be attributed to numerous rationales. For one, younger patients may be more likely to research information online and are hence more aware of the adverse effects of TCS. Another possibility is due to the increasing number of patients who use this treatment for acne, this is seen more often in younger patients. It is also possible that these patients find TCS treatment effective and utilize it outside of its intended use or at a different frequency than suggested. TSA for children has additional effects to consider. For instance, the treatment of atopic dermatitis (AD) is one of the main uses of TCS ([Manchanda et al., 2017](#)). Because of the high prevalence of childhood-onset AD and its chronic nature, treatment tends to be prolonged and involves a large surface area, thus increasing the risk of TSA. Some of the other effects include hypothalamic-pituitary axis suppression and the development of avascular necrosis of the developing femoral head; these have been implicated as possible causes of slow growth in children with TSA ([Manchanda et al., 2017](#)). There is also a higher incidence of full-body TSA in children as compared to adults, although it tends to spare the palms and soles. Research also shows that children with severe AD and children under 18 months old will absorb high-potency TCS more readily than others ([Juhász et al., 2017](#), [Mehta et al., 2016](#), [Siegfried et al., 2016](#)). Therefore, great care should be taken when prescribing TCS to children and adolescents.

Some of the suggested key current diagnostic criteria to identify TSA include patient history; excessive skin exfoliation ("shedding") edema, especially of the eyelids or ankles; sleep and mood disturbances; the "Red Sleeve" sign; and elephant wrinkles (thickened

skin, especially the elbows, and knees) ([Sheary, 2018](#)). The most common dermoscopy findings seen on the faces of patients with TSA are brown globules, red diffuse areas, vessels, white structureless areas, hypertrichosis, and white hairs. Thus, it is recommended that patients presenting with the symptoms of TSA be examined using dermoscopy to differentiate the condition from other causes that can be mistaken for it, such as SLE or fungal infections ([Sethi et al., 2021](#), [Tatu, 2016](#), [Siegfried et al., 2016](#)). There are currently no widely established diagnostic criteria for TSW. More research is required to develop guidelines for the prevention and diagnosis of TSA in the future.

Patient Perspectives on Topical Steroids

Patient perspectives on TCS use, and in some cases, TSW, can vary in the literature. According to a systematic review of published trials on the long-term safety of topical corticosteroids, $\leq 5\%$ of patients reported discontinuation due to adverse effects (DAEs) ([Sheary, 2018](#)). Transient delivery of systemic steroids is very effective, despite the fact that the majority of patients reject this therapy approach. Some patients believe using TCS will prevent their eczema from healing. Rehabilitation from TCS addiction is impossible to obtain without "undertreatment" meaning a reduction in dosage ([Fukaya et al., 2014](#)). Furthermore, both case studies and observational literature have revealed that many cases of TSW were diagnosed by the patients themselves, as there are no established diagnostic criteria. In the setting of moderate to severe atopic dermatitis, experience reveals that dupilumab was an effective treatment that was well tolerated by the patients, and it merits further study alongside other potential treatments ([Arnold et al., 2018](#)). Given the heterogeneity in presentation, manifestation, and even duration of TSW, it is likely that several different treatment pathways will need to be elucidated.

According to a study, over half of the participants believed that potent TCS performed better in the trials than mild TCS and that extremely potent topical corticosteroids performed better than potent topical corticosteroids ([Juhász et al., 2014](#)). In addition to this, many patients noted treatment compliance is hindered and risk is increased with an absence of clear guidance on the appropriate usage of TCS ([Juhász et al., 2014](#)). Hence, it is clear that there must be a patient education component to any proposed solutions to TSW.

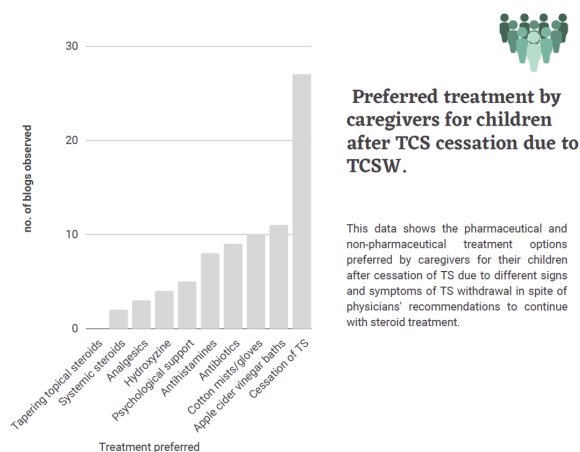


Figure 2. Preferred Treatment by Caregivers for Children After Topical Corticosteroid Cessation Due to Topical Steroid Withdrawal Syndrome

Misinformation and Abuse of Topical Steroids

Misinformation on the use of topical steroids is spreading rampantly which leads to emerging problems all over the world. TCSs are abused globally for rapid symptomatic relief in many skin disorders without proper knowledge of side effects that bring adverse health events. Many factors related to public awareness, professional education, the pharmaceutical industry, and limited government regulations contribute to this problem. Resistant dermatophytoses emerged due to the use of TCS as steroid cocktails (Shrestha et al., 2020). In a recent cross-sectional study, TCS in combination with antifungal and antibiotic cream was the most common form utilized in 58.1% of patients who developed dermatophytoses (Shrestha et al., 2020). It is worth noting that antibiotics have also been a topic of recent controversy in part due to their frequent over-prescribing leading to unprecedented levels of antibiotic resistance.

The application of TCS and counterfeit products for cosmetic purposes may also have detrimental effects on the skin. A common misconception is that only the most potent topical corticosteroids have a high potential for causing TCA. However, long-term use of the milder TCSs so-called “safe TCS” is not completely without risks (Ghosh et al., 2014). Concerning cosmetics, erroneous advice from social connections, pharmacies, and media promotions encourages purchasing counterfeit cosmetic products (CCP). Misguided individuals start to use CCP and

steroid-containing lightening creams and may continue until the abuse results in serious burning, hyper-, and hypopigmentation (Kabir Chowdhury, 2018). The most common side effects in a study from Bangladesh were acneiform eruptions followed by steroid dependency and steroid dermatitis resembling rosacea or red face, tachyphylaxis with telangiectasia, and atrophy (Kabir Chowdhury, 2018). A prospective multi-center clinic questionnaire in Iraq applied to 235 patients showed an interesting fact that acne and erythema were common while atrophy, dryness, telangiectasia, and hirsutism appeared solely on long-term use (Jaccob et al., 2020). A study from India recorded that tinea incognito and acne were the most prevalent adverse effects (Meena et al., 2017). Crucially, there is a lack of regulation and legislation in many countries surrounding the prescription of TCS, especially in counterfeit cosmetic products like fairness creams (Kabir Chowdhury, 2018).

Cultural factors and different availability of TCS may also influence health outcomes. A cross-sectional study on TCS abuse focused only on women in Madagascar suggesting that facial care was not yet a daily habit for Malagasy men (Sendrasoa et al., 2017). In this study, 49.8% of women surveyed had utilized TCS for cosmetic purposes, and 68% indicated they utilized TCS combined with handcrafted cosmetics (Sendrasoa et al., 2017). Respondents indicated “Pandalao” a handcrafted cosmetic combined frequently with TCS containing salicylic acid, peppermint oil, lanolin, mercury powder, and Vaseline was among the most utilized (Sendrasoa et al., 2017). Interestingly, many respondents did not have any primary dermatosis but utilized this product for the main purpose of lightening their skin color. In contrast, males (232/370; 62.70%) outnumbered females (138/370; 37.30%) in another clinical study from India examining cutaneous adverse effects (Meena et al., 2017). Among patients taking TCS, only 29.7% had been prescribed TCS by either a general practitioner or dermatologist (Meena et al., 2017). Low prices, massive marketing, and lack of restrictions bring quick profits to the manufacturers. The TCS abuse epidemic is aggravated by the immediate availability of over-the-counter CCP at local pharmacies, and cosmetics stores all across the country in certain places where limited restrictions apply such as Bangladesh, India, and Nepal (Jaccob et al., 2020, Shrestha et al., 2020, Kabir Chowdhury, 2018). Prescription restrictions help with reducing adverse effects as described in a cross-sectional study from Saudi Arabia that reported only 16.5% of the participants had any side effects due to TCS given

prescription restrictions for preventing TCS misuse in the kingdom ([Dhafiri et al., 2022](#)).

A study conducted in Bosnia and Herzegovina demonstrated that prescribing information about TCS was inadequate in the majority of the prescriptions which may mislead patients ([Lovric et al., 2021](#)). It is crucial that patients are aware of the significant risks of TCS misuse and how to minimize the risk of developing TSW. Furthermore, a new phenomenon affecting compliance adversely, TCS phobia, has emerged partly due to the widespread abuse of TCS. TCS phobia in patients may cause irregular application, less than prescribed application, or complete refusal of TCS treatment as in the case of the childhood eczema study which found that 50% of parents requested non-steroidal prescriptions due to concerns regarding skin atrophy and stunted growth ([Ghosh et al., 2014](#)). There is also ongoing misinformation among healthcare professionals about TSW being a myth. Many providers question the prevalence or even existence of TSW because it remains a diagnosis of exclusion due to the lack of clear diagnostic criteria ([Nguyen et al., 2022](#)). Amongst entities such as the American Academy of Dermatology, there remains no current consensus on specific diagnostic criteria for TSW nor pathognomonic histologic findings defined ([Nguyen et al., 2022](#)). However, the UK Medicines and Healthcare Products Regulatory Agency (MHRA) and other renowned organizations such as the British Association of Dermatologists, the National Eczema Society, and the US National Eczema Association have recognized TSW ([Moss et al., 2023](#)). Measures that can be taken to alleviate TCS abuse with respect to healthcare professionals include raising awareness on the adverse effects and immediate actions to counteract them, avoiding home-made dilutions, combining prescriptions with antimicrobial and antifungal agents, prescriptions lacking adequate information, and resisting the temptation to prescribe TCS for undiagnosed rash which worsens the possibility of a correct diagnosis in the future ([Lovric et al., 2021](#), [Rathi and D'Souza, 2012](#)).

Conclusions

Prolonged topical corticosteroid use has become a major problem for patients as well as dermatologists. The introduction of more potent formulations over prolonged periods of time has resulted in side effects and subsequent withdrawal symptoms being more prevalent. Prolonged treatment for childhood-onset atopic dermatitis increases the risk of Topical Steroid

Addiction (TSA) or Topical Steroid Withdrawal (TSW) and full-body TSA. Injudicious TCS use over large body surface areas and over the face has also resulted in numerous complications encountered on a day-to-day basis ([Juhász et al., 2017](#), [Mehta et al., 2016](#), [Siegfried et al., 2016](#)).

Despite the development of TSA in the event of prolonged TCS use, it is imperative that the inflammatory and difficult dermatoses be treated appropriately and correctly. The increased prevalence of steroid phobia outlines the need for strategy/guidelines to both assess and combat steroid phobia ([Contento et al., 2021](#)). A strong provider-patient relationship is vital in reducing a patient's steroid phobia, enhancing their knowledge, and reducing their TCS use-related stress. The interactive provision of information adjusted to a patient's individual needs, as opposed to the one-way provision of information such as magazines and the internet is more effective in the development of steroid phobia. ([Song et al., 2018](#), [Masood et al., 2021](#), [Contento et al.](#))

There is growing public awareness and concern about TSA with many groups calling for earlier recognition, advocacy, and research into TSA ([Cotter et al., 2022](#)). Therefore, there is a need to mitigate the spread of misinformation on TCS usage, which can lead to unnecessary avoidance of important treatments for dermatologic conditions while creating unnecessary phobia ([Tracy et al., 2022](#)). Until newer and safer alternatives to TCS become available, judicious TCS use with proper patient education remains the mainstay in resolving this rising problem ([Mehta et al., 2016](#)). To combat misinformation and TCS abuse, a holistic approach should be adopted which comprises actions at all levels such as the legislation regarding the manufacture and selling of TCS compounds, inappropriate prescribing, raising public awareness on adverse effects of TCS abuse via social media campaigns, and advocating to achieve the desired health outcomes for all.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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