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Cutaneous and Systemic Adverse Events Associated With Topical Corticosteroid Use: A Targeted Literature Review

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ABSTRACT

Background: Topical corticosteroids (TCS) have been used to treat chronic inflammatory skin conditions since initial approval in 1950, which was followed by reports of cutaneous and systemic adverse events (AEs) over the succeeding decades.

Methods: A targeted literature review was performed to identify case-report and observational-study publications from August 2015 to 2025 that reported TCS-associated adverse events (AEs).

Results: The 42 publications included identification of clinically meaningful cutaneous (69.0%) and systemic AEs, including hypothalamic-pituitary-adrenal axis suppression or adrenal insufficiency (40.5%) and Cushing syndrome (47.6%). AEs ranged from mild to severe and nonserious to serious, and reports implicated prolonged (≥12 months, 45.2%) or high-potency (69.0%) TCS use.

Conclusion: Overall, these results identified an opportunity to assess TCS access requirements and the need for additional clinician awareness and education to improve TCS prescribing practices, including monitoring of AEs and cumulative steroid exposure. Improving access to anti-inflammatory therapies that have demonstrated short- and long-term safety and efficacy in clinical trials and are not steroids for patients with chronic dermatoses should be prioritized. Often, gaining access to these alternative treatments requires step-through TCS therapy or other utilization management requirements, which unnecessarily puts patients at risk for steroid-associated AEs and delays positive treatment outcomes.

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INTRODUCTION

Since the 1950s, topical corticosteroids (TCS) have been used to treat chronic inflammatory dermatoses such as atopic dermatitis, psoriasis, and seborrheic dermatitis.[1] Since their introduction, evidence associating TCS with cutaneous and systemic adverse events (AEs) has accumulated, particularly related to misuse, prolonged use, high-potency formulations, and application to high-risk areas.[1,2]

Concern over steroid-associated AEs may manifest as steroid phobia[1] and can cause hesitancy among patients and caregivers to maintain an appropriate treatment plan, thus exacerbating or prolonging symptoms.[3,4] TCS side effects from use in children may be impacted by higher body surface area-to-weight ratios, relatively immature cutaneous immune environment and skin barrier, and a higher likelihood of occlusive application, each of which increases systemic exposure.[2,5]

MATERIALS AND METHODS

A targeted literature review was performed to identify case-report and observational-study publications reporting AEs associated with TCS use. Titles and abstracts published from August 2015 in PubMed were searched in September 2025 with search term

categories of treatment, application, adverse effect, and type of publication (Table 1). All search terms were used in combination (eg, ["corticosteroids" OR "hydrocortisone"] AND ["topical" OR "cutaneous"] AND ["side effect" OR "toxicity"] AND ["case report" OR "case series"]). Three reviewers (SS, BS, and RH) screened and reviewed publications. Non-human and non-English reports and those without safety outcomes were excluded, as well as those in which the relationship of the reported AE to TCS was unclear or confounded by other risk factors. Cushingoid skin findings and oral mucosal events were considered cutaneous events. Serious AE classifications were clinician-derived based on details of the case(s) included in the report. Steroid potency classes VI and VII were grouped as low, classes III to V as medium, and class I to II as high. In cases where ≥1 potency group was included in a report, the highest was used; in cases where the potency group could not be determined because the concentration or formulation was missing, the lowest was used. Publication tallies were not mutually exclusive; many reported ≥1 event leading to some totals >100%.

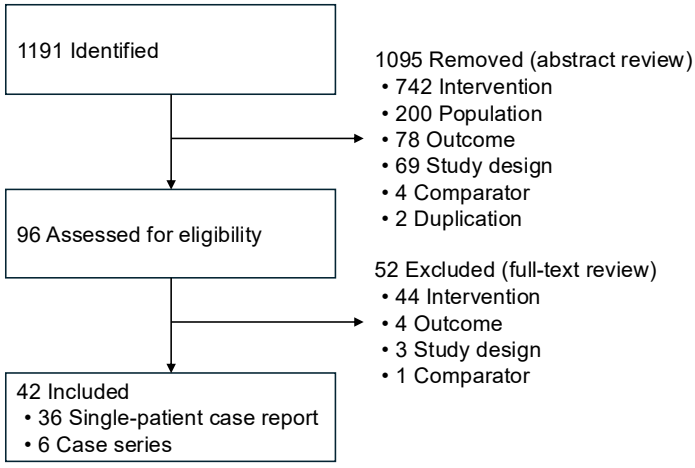
RESULTS

Overall, 1191 publications were identified, 96 were reviewed, and 42 (representing a total of 83 patients) were included in this report (Figure 1); the majority of publications (78.8%) were single-patient case reports (Table 2).

TABLE 1.

Search Strategy	
Term Category	**Specific Search Terms**
Treatment	Corticosteroids OR Glucocorticoids OR Topical Steroid OR Topical Corticosteroid OR Hydrocortisone OR Betamethasone OR Clobetasol OR Mometasone OR Fluocinolone OR Fluticasone OR Desonide OR Desoximetasone OR Triamcinolone
Application	Administration, Topical OR Administration, Cutaneous OR Topical OR Cutaneous OR Dermal
Adverse effect	Chemically Induced Disorders OR Adverse Drug Reaction Reporting Systems OR Drug-Related Side Effects and Adverse Reactions OR Safety OR Side Effect OR Adverse Effect OR Adverse Event OR Adverse Reaction OR Complication OR Toxicity OR Skin Atrophy OR Striae OR Telangiectasia OR HPA Axis Suppression OR Cushing Syndrome OR Glaucoma OR Cataract OR Topical Steroid Withdrawal OR TSW
Type of publication	Case Reports OR Case Report OR Case Series

FIGURE 1. PRISMA diagram.



Note: A full list of included references can be provided upon request.
PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

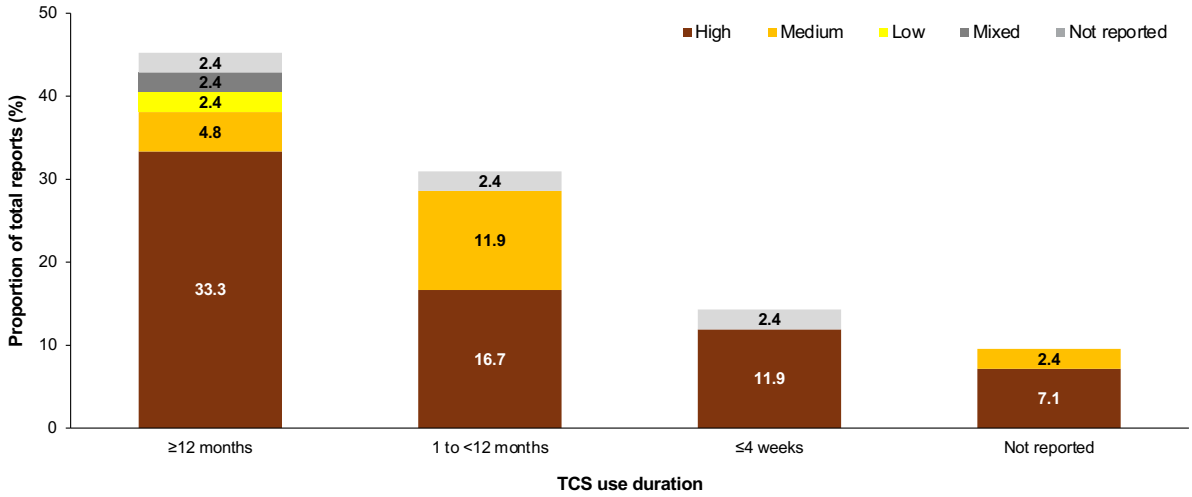
TABLE 2.

Report Characteristics		
		n (%) [N=42]
Patient age group	Adults only	21 (50.0)
	Children only	19 (45.2)
	Adults and children	2 (4.7)
Type	Single-patient case report	36 (85.7)
	Case series	6 (14.3)
Setting	Outpatient (dermatology or primary care)	17 (40.5)
	Emergency department visit (not admitted)	6 (14.3)
	Inpatient or hospitalization	3 (7.1)
	Not reported	16 (38.1)
Geographic location	Japan	4 (9.5)
	Mexico	4 (9.5)
	France	3 (7.1)
	India	3 (7.1)
	Italy	3 (7.1)
	United States	3 (7.1)
	Australia	2 (4.8)
	Morocco	2 (4.8)
	Nepal	2 (4.8)
	Pakistan	2 (4.8)
	Saudi Arabia	2 (4.8)
	Turkey	2 (4.8)
	Argentina	1 (2.4)
	Chile	1 (2.4)
	Croatia	1 (2.4)
	Denmark	1 (2.4)
	Germany	1 (2.4)
	Ireland	1 (2.4)
	Spain	1 (2.4)
	Not reported	8 (19.0)
TCS potency	High	29 (69.0)
	Medium	5 (11.9)
	Low	2 (4.8)
	Mixed	4 (9.5)
	Not reported	3 (7.1)
Frequency of TCS use	At least once daily	14 (33.3)
	Weekly/monthly	8 (19.0)
	Variable	19 (45.2)
	Not reported	1 (2.4)
Duration of TCS use	≥12 months	19 (45.2)
	1 to <12 months	13 (31.0)
	≤4 weeks	6 (14.3)
	Not reported	4 (9.5)

TCS, topical corticosteroid.

Reports included adults (50.0%) and children (45.2%) with global representation across 19 countries. TCS were the primary exposure; clobetasol, betamethasone, and hydrocortisone were the most commonly reported TCS, and high-potency formulations (class I-II[6]) were frequently (69.0%) implicated. TCS were applied at least once daily in 33.3% of the reports. Duration of TCS use was chronic (≥12 months) and intermediate (1 to <12 months) in 45.2% and 31.0% of the reports, respectively. TCS applied under occlusion were associated with AEs in 5 (11.9%) reports. One-third (13/42; 33.3%) of reports involved chronic application of high-potency TCS (Figure 2).

FIGURE 2. Duration of use by TCS potency.



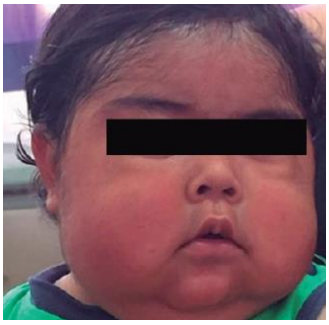
Note: There was one study where duration was not reported and TCS potency was unclear.
TCS, topical corticosteroid.

FIGURE 3. AEs by potency of associated TCS.

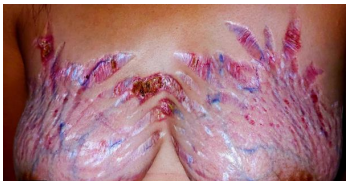
AE group[a]	Proportion of total reports (%)	Frequent events reported	Associated potency of TCS[b]
Local cutaneous events	69.0	Skin atrophy, striae, telangiectasia, hypopigmentation	High (29%); Medium (18%); Low (5%)
Cushing syndrome or features	47.6	Moon face, truncal obesity, buffalo hump, weight gain	High (20%); Medium (14%); Low (3%)
HPA axis suppression or adrenal insufficiency	40.5	Low cortisol/ACTH, failed stimulation tests, adrenal crisis risk	High (17%); Medium (10%); Low (3%)
Hypertension, osteopenia, osteoporosis, cardiac, or metabolic abnormalities	33.3	Hypertension, osteopenia, osteoporosis, infections, metabolic abnormalities	High (14%); Medum (11%); Low (1%)
Serious AEs	28.6	Sepsis, adrenal crisis, hospitalization, rare fatal outcomes	High (67%); Medium (17%); Mixed (8%)
Ocular complications	16.7	Glaucoma, vision loss, corneal abscess, central serous retinopathy	High (7%); Medium (3%); Mixed (1%)
Topical steroid withdrawal/rebound flare	9.5	Erythema, burning, desquamation, severe pruritus	High (4%); Medium (1%); Low (1%)

[a]AE groups not mutually exclusive; multiple AEs may have been noted in an individual report. [b]Proportions calculated based on the number of reports identifying TCS potency/total reports (or, in the case of serious AEs, total serious AE reports); potency not reported for 1% of reports that included local cutaneous events, 8% of those including serious AEs, and 1% those reporting topical steroid withdrawal/rebound flare. High potency: class I and II; medium potency: class III–V.
ACTH, adrenocorticotropic hormone; AE, adverse event; HPA, hypothalamic-pituitary-adrenal; NA, not available; TCS, topical corticosteroid.

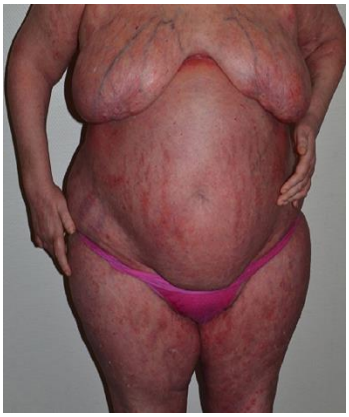
FIGURE 4. Examples of TCS-associated adverse events from included reports.



Cushing syndrome in a boy aged 14 months treated with topical hydrocortisone acetate 1% cream and clotrimazole, followed by betamethasone dipropionate cream 0.05% for 10 months for dermatitis of the scalp and perineal area. Image used with permission per CC BY-NC 4.0 from Hansen S, et al. Iatrogenic Cushing's syndrome in an infant due to prolonged use of topical corticosteroids. Case report. Article in Spanish. *Rev Chil Pediatr.* 2018;89(3):368-372.



Striae, atrophy, telangiectasia, and visible veins with crusting and ulceration in a pregnant female aged 18 years following prolonged use (≈6 months) of Zalim lotion (ie, phenol, tincture iodine, and crystalviolet) and clobetasol propionate 0.05%. Image used with permission per CC BY-NC 4.0 from Mathur M, et al. Misuse of topical over-the-counter medication: a case report. *Clin Case Rep.* 2024;0:e8949.



Severe cutaneous atrophy, diffuse telangiectasias, faciotruncal obesity, broad purple abdominal striae, and limb muscle wasting in a female aged 38 years with Netherton syndrome using topical betamethasone for ≈10 years to treat severe pruritus. Additional diagnoses upon examination included osteoporosis, Cushing syndrome, corticotropic insufficiency, and inframammary, axillary, and intergluteal superinfected intertrigo. Image from Valette C, et al. Fatal outcome of Netherton syndrome due to excessive use of topical corticosteroids in an adult patient. Article in French. *Ann Dermatol Venereol.* 2020;147(1):36-40.

TCS, topical corticosteroid.

Local, cutaneous AEs were noted in 69.0% of reports and were largely associated with prolonged (>1 month [per label]) or high-potency TCS use (Figure 3). Among published reports of cutaneous AEs, 37.9% described striae, 34.5% cushingoid cutaneous changes, 31.0% hypertrichosis/hirsutism, 24.1% purpura/ecchymosis, 20.7% skin atrophy, 20.7% secondary skin infection, 20.7% hypopigmentation, 17.2% telangiectasia, and 13.8% acne/acneiform eruptions. Resolution of cutaneous AEs varied across reports; mild atrophy and erythema were considered partially reversible with TCS discontinuation; however, other AEs (ie, striae and telangiectasia) persisted. Systemic AEs were typically associated with high-potency TCS use, occlusion, extensive body surface area exposure, or prolonged (>1 month [per label]) duration of exposure. Systemic AEs included hypothalamic-pituitary-adrenal axis suppression/adrenal insufficiency (40.5%); Cushing syndrome or features (47.6%); hypertension, osteopenia, osteoporosis, and cardiac or metabolic abnormalities (33.3%); and ocular complications (eg, glaucoma, visual impairment, and corneal infection; 16.7%; Figure 3 and Figure 4). Topical steroid withdrawal syndrome was described in 9.5% of publications.

Cases were from outpatient (40.5%), inpatient (7.1%), and emergency (16.6%) settings, indicating that AEs occurred across the spectrum of mild to severe and nonserious to serious (serious AEs were noted in 28.6% of reports). Many cases involved inappropriate use patterns (ie, self-medication [individual treatment without medical guidance], over-the-counter access [varies by country], excessive dosing [additional applications than prescribed], prolonged use without medical supervision, and application to high-risk areas [eg, face and diaper region of children, including reapplication with diaper changes]).

DISCUSSION

Inappropriate TCS use is at least in part related to unclear and inconsistent instructions on frequency and duration of use.[7] Most often, patients are directed to apply TCS based on "fingertip units"; however, this comes with a wide variation on number of applications per day and an inconsistent approach to reducing application frequency over time.[7] Repeated prescription renewals without reassessment may unintentionally extend exposure to TCS beyond the originally planned treatment period, particularly among patients with chronic relapsing disease. Overall, these patterns suggest that AEs are not driven by TCS potency alone but rather by management gaps and cumulative corticosteroid exposure. Collectively, corticosteroid potency, treatment duration, application frequency, body surface area treated, anatomical location, occlusion, repeated treatment courses, and lack of follow-up with patients to ensure appropriate use each contributed to development of AEs.

This review is limited in sample size compared to the expansive number of corticosteroid prescriptions filled,[8] and for which case reports can provide heterogenous information, often in unstructured and inconsistent formats. Use of case-based evidence introduces bias toward more severe or atypical AEs, and overall AE occurrence may be underrepresented from lack of reporting in published literature.

Overall, these findings support a broader framework for TCS use that emphasizes cumulative exposure rather than isolated treatment episodes. Taken together, these data underscore the need to optimize TCS prescribing practices by selecting appropriate TCS potency, limiting treatment duration, reassessing recurrent prescriptions, and minimizing unnecessary cumulative corticosteroid exposure. Findings highlight a need for ongoing monitoring of cutaneous and systemic adverse effects and standardized approaches for documenting cumulative steroid exposure. Additionally, there is an opportunity to discuss the risk-benefit balance and overall cost burden of all topical treatments, including direct and indirect costs of related AEs. Topical therapies that are not steroids are recommended in treatment guidelines and are valuable therapy options.[9,10] Policies requiring treatment with TCS prior to implementing newer and more targeted non-steroid treatments can inadvertently prolong corticosteroid exposure, increasing patient risk for steroid-associated AEs and delaying positive treatment outcomes. Modern steroid-sparing treatments have been assessed using current regulatory standards that support consistent, long-term use in chronic inflammatory dermatoses. More appropriate access to advanced targeted topical treatments with demonstrated safety and efficacy profiles, in addition to standardized drug labels in this treatment space, are warranted.

DISCLOSURES

Adam J. Friedman has served as a consultant, advisor, speaker for and/or received grants from AbbVie, Arcutis, Galderma, Hoth Therapeutics, Incyte, Johnson & Johnson, Kenvue, L'Oréal, La Roche-Posay, LEO Pharma, Lilly, MicroCures, MINO Labs, Novartis, Pfizer, Sanofi-Regeneron, Takeda, UCB, and Zylö Therapeutics.

Peter Lio has served as an advisor, consultant, speaker for and/or owns stock in AbbVie, Alphyn Biologics, Almirall, Amyris, Apogee Therapeutics, Arcutis, Astria Therapeutics, Castle Biosciences, Codex Labs, Concerto Biosciences, Dermavant, Galderma, Incyte, Kenvue, LEO Pharma, Lilly, Lipidor, La Roche-Posay/L'Oréal, Merck, Micreos, MyOr Diagnostics, Nektar Therapeutics, Nia Health, Pelthos Therapeutics, Novartis, Pfizer, Phyla Skincare, Pierre-Fabre, Regeneron/Sanofi Genzyme, Sibel Health, Skinfix, Song Lab Skincare, Soteri Skin, Stratum Biosciences, Sun Pharma, Theraplex, Thimble Health, Topaz Biosciences, Unilever, Verdant Scientific, Verrica, and Yobee.

Lawrence F. Eichenfield has served as a consultant, investigator, and/or member of board of directors for AbbVie, Acrotech Biopharma, Almirall, Amgen, Apogee Therapeutics, Arcutis, Attovia, Castle Biosciences, CorEvitas, Dermavant, Dermira, Forte Biosciences, Galderma, Incyte, Janssen, Johnson & Johnson, LEO Pharma, Lilly, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi-Genzyme, Target RWE, TRex Bio, and UCB.

Lisa Weiss has served as a speaker and/or consultant for Arcutis, Galderma, Incyte, Johnson & Johnson, LEO Pharma, Organon, Sun Pharma, Sanofi/Regeneron, UCB, and Verrica.

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Douglas DiRuggiero has served as an advisory board member and/or speaker for AbbVie, Amgen, Arcutis, Galderma, Incyte, Johnson & Johnson, LEO Pharma, Lilly, Novartis, Sanofi-Regeneron, Sun Pharma, Takeda, and UCB.

Melissa S. Seal, Scott Snyder, Brett Stephenson, and Robert Higham are employees of Arcutis Biotherapeutics, Inc.

Alexandra K. Golant has served as a consultant, investigator, and/or speaker for AbbVie, Amgen, Apogee Therapeutics, Arcutis, BMS, Boehringer Ingelheim, Dermavant, Galderma, Incyte, Janssen, LEO Pharma, Lilly, Pfizer, Regeneron, Sanofi, and Takeda.

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