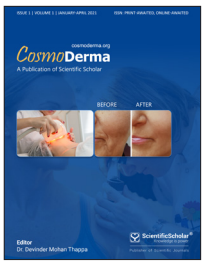
www.cosmoderma.org

ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

CosmoDerma



Review Article

Allergic contact dermatitis caused by topical corticosteroids: A review for clinicoepidemiological presentation, evaluation, and management aspects

Vikram K. Mahajan[1], Vikas Sharma[1], Neeraj Sharma[1], Monika Chandel[1], Rohit Verma[1]

[1]Department of Dermatology, Venereology and Leprosy, Dr. Radhakrishnan Government Medical College, Hamirpur, Himachal Pradesh, India.

***Corresponding author:**
Vikram K. Mahajan, Dermatology, Venereology and Leprosy, Dr. Radhakrishnan Government Medical College, Hamirpur, Himachal Pradesh, India.

vkm1@rediffmail.com

Received: 10 November 2023
Accepted: 22 December 2023
Published: 08 February 2024

DOI
10.25259/CSDM_233_2023

Quick Response Code:

ABSTRACT

Dermatitis medicamentosa or contact dermatitis to topically applied medicaments, active ingredients or excipients, is encountered frequently in clinical practice and should be suspected in patients showing resistance to treatment despite adequate therapy and in patients, who complain of intolerance to a particular treatment. Topical corticosteroids are prescribed mostly in dermatology for their anti-inflammatory, antiproliferative, and immunosuppressive actions to treat various inflammatory dermatoses. These may act as allergens and produce immunoglobulin E-mediated immediate hypersensitivity (anaphylaxis, urticaria, angioedema, bronchospasm, vomiting, and cardiovascular collapse) or T-cell-mediated allergic contact dermatitis (ACD). Although it occurs less often and is not life threatening, ACD negatively impacts the quality of life by worsening preexisting dermatitis. The prevalence of hypersensitivity to these allergens varies across regions and periods of time depending on the clinical practice, prescribing habits, and types of cases studied. Over-the-counter availability of corticosteroids in multiple formulations in recent years may further compound the problem due to their indiscriminate and extensive use. Although about one-third of all cases of contact dermatitis are initiated or perpetuated by topical medicaments, the occurrence of contact dermatitis due to corticosteroids remains undersuspected. This is perhaps due to their anti-inflammatory and immunosuppressive properties that make it difficult to doubt and prove contact sensitivity that may be from a corticosteroid itself or to the additives and vehicles in the formulation. Patch testing can help identify the culprit agents in ACD but early diagnosis depends on clinical suspicion. Sensitization in contact dermatitis exhibits cross-reactivity patterns based on corticosteroid structure. Clinicoepidemiological presentation, evaluation, and management aspects of contact hypersensitivity reactions to corticosteroids are reviewed.

Keywords: Adverse cutaneous drug reaction, Budesonide, Contact hypersensitivity, Corticosteroids, Dermatitis medicamentosa, Drug allergy, Hydrocortisone, Patch test, Standard battery, Tixocortol pivalate

INTRODUCTION

Corticosteroids are widely used topically or systemically in dermatology for their anti-inflammatory, antiproliferative, and immunosuppressive actions. These may act as allergens and produce delayed (T-cell mediated) or immunoglobulin E-mediated immediate hypersensitivity (anaphylaxis, urticaria, angioedema, bronchospasm, vomiting, and cardiovascular collapse) with a prevalence of 0.3–0.5%.[1] In comparison, delayed hypersensitivity or allergic contact dermatitis (ACD) from topical corticosteroids is uncommon and not life threatening but negatively impacts the quality of life due to therapeutic failure and/or worsening of preexisting dermatitis.[2,3] Topical corticosteroids, alone or in combination with antimicrobials, antifungals, local anesthetics or

keratolytics, are used with great benefit for eczemas, lichen planus, psoriasis, and other steroid-responsive dermatoses, which do not respond satisfactorily to other treatments. Their potency depends on the lipophilicity of the compound and the extent of absorption into the deeper layers. Local adverse effects such as skin atrophy, hypopigmentation, telangiectasia, striae, acneiform eruptions, hypertrichosis, perioral dermatitis, bacterial/fungal infections, and miliaria/vesiculations after prolonged topical use or when used under occlusion are well reported. Although side-effects commonly experienced are burning and stinging, irritation, itching, erythema, dryness, and occasional worsening of primary dermatosis following topical application, the occurrence of corticosteroid-induced ACD remains under-recognized despite the fact that these were designated contact allergen(s) of the year 2005.[4] Their anti-inflammatory and immunosuppressive properties perhaps make it difficult to suspect and prove contact sensitivity from them. Since corticosteroids are almost indispensable in dermatology therapeutics, it remains imperative to identify both the offending and the alternative formulations that can be used safely. We, herein, review the clinicoepidemiological presentation, evaluation, and management aspects of corticosteroid contact sensitivity.

HISTORICAL ASPECTS

Historically, ACD from topical hydrocortisone was suspected first in 1959 soon after its introduction. Later in the year 1960, hydrocortisone aldehyde hydrate, a precursor and contaminant of hydrocortisone, was found to cause stronger patch test reactions than hydrocortisone itself in hydrocortisone sensitive patients with a high prevalence of positive patch test reactions to hydrocortisone (15% pet) in patients with stasis dermatitis and leg ulceration.[5] Tixocortol pivalate was identified in 1989 as a marker for topical hydrocortisone allergy and its efficacy to identify cross-reaction patterns more accurately was confirmed by intradermal testing with corticosteroids in a 1992 study.[6,7] In 1996, European Environmental and Contact Dermatitis Research Group observed that 2.6% of patients were positive to at least one of the five corticosteroids patch tested in a multicenter study of 7238 patients.[8] The majority of positive reactions were from budesonide (1.4%), tixocortol pivalate (1.3%), and hydrocortisone-17-butyrate (1%) in that order.

EPIDEMIOLOGY

There are no Indian data on the exact prevalence of corticosteroid contact allergy and not many studies are from Southeast Asia. Wattanakrai *et al*.[9] reported a positivity rate of 3.29% of Thai patients patch tested over 10 years. The overall prevalence was 2.9–4.8% of patients found allergic to one or more corticosteroids in European clinics.[10] Its prevalence is between 0.2% and 5% across regions and time periods and it was 1.1% in Spain,[11] 2.2% in Sweden,[12] 2.6% in Europe,[8] 2.7% in Denmark,[13] and 4.6% in the United States based on positive patch test studies.[14] Budesonide in 0.95% and tixocortol in 0.63% were the main allergens in Spain whereas it was tixocortol and budesonide in the United States.[11,15,16] The contact sensitivity rate from budesonide, tixocortol, and hydrocortisone-17-butyrate is also similar in Europe.[17] Of the 3594 patch-tested Danish patients, 2% had steroid allergy due to tixocortol-21-pivalate (0.8%), budesonide (1%), and hydrocortisone-17-butyrate and budesonide (1%) whereas budesonide and hydrocortisone-17-butyrate accounted for 67.7% of the positive results in a recent study of 185 patients.[13,17] The prevalence of corticosteroid contact allergy in Melbourne (Australian) was 0.55–5.98% in 1993–2002 and 0.52% of positive patch test reactions in a later retrospective study of 1153 patients.[18] The majority of positive reactions were from betamethasone-17-valerate, budesonide, betamethasone dipropionate 0.05%, tixocortol-21-pivalate, and triamcinolone acetonide. This low rate of contact sensitivity was attributed to local unavailability of corticosteroids with high sensitizing potential. Similarly, 22% of 41 Turkish patients showed positivity from one or more corticosteroids; mostly from tixocortol pivalate (six patients) followed by two patients each from triamcinolone acetonide, budesonide, alclometasone dipropionate, and dexamethasone-21-disodium phosphate while betamethasone-17-valerate caused positive reaction in one patient only.[19] Clinically, relevant positive patch test reactions in 7.4% of 257 Polish patients were mainly from budesonide, amcinonide, hydrocortisone-17-butyrate, betamethasone-17-valerate, clobetasol propionate, and prednisolone.[20] Similarly, 4.12% of 17978 patch-tested patients had one or more positive reactions to corticosteroids in a North American Contact Dermatitis Research Group study spanning 2007–2014.[21] Most positive reactions were from tixocortol-21-pivalate, budesonide, hydrocortisone-17-butyrate, clobetasole-17-propionate, and desoximetasone in order of frequency. This wide variation in the prevalence of corticosteroid contact sensitivity across regions is attributable to the nature of clinical practice, prescribing habits, availability of formulations and frequency of corticosteroid use, inability to expect the possibility of corticosteroid sensitivity, and timing and the diagnostic tests used.[22]

PREDISPOSING FACTORS

The patients with atopic dermatitis (all age groups), contact allergy from other allergens (nickel, potassium dichromate, phenylenediamine, and balsam of Peru), chronic actinic dermatitis, chronic hand/foot eczema, anogenital dermatitis, facial dermatitis, eyelid dermatitis, otitis externa or stasis dermatitis/leg ulcers are at risk of corticosteroid ACD mainly

due to proinflammatory nature of the drugs and compromised skin barrier.[5,23-29] Factors such as thin skin, flexures, and occlusion enhance the risk of corticosteroid sensitivity from increased penetration. Occlusion may increase pH of the skin and potential degradation of corticosteroids into aldehydes, the possible contact allergen. Female gender (F: M 3:1), age above 40 years, dermatosis of long duration, and self-medication with unsupervised on-and-off extended corticosteroid use are other potential risk factors.[13,16,22,29] Environmental and genetic predisposition too has been postulated.[30] Some corticosteroid-sensitive patients may also develop eruptions after administration of steroid hormones.[31,32]

SOURCES AND ROUTES OF EXPOSURE

Direct skin contact remains the commonest mode of sensitization. Respiratory tract (through inhalation), gastrointestinal tract (oral intake), and other mucosal surfaces such as nasal mucosa (from inhalers), and conjunctival mucosa (from ophthalmic formulations) are other routes of sensitization.[33-36] Contact dermatitis through airborne mechanism has occurred among companions of patients using budesonide inhalers.[37,38] Contact sensitization can occur from occupational exposure among pharmaceutical workers, pharmacists, nurses, and other healthcare providers.

COMMON CORTICOSTEROIDS IMPLICATED IN CONTACT SENSITIVITY

Non-halogenated corticosteroids, hydrocortisone and budesonide have been found to cause most reactions among patients, who are patch tested. Hydrocortisone, a commonly used low-potency topical corticosteroid, and hydrocortisone acetate (0.5% or 1%) have been approved by USFDA in over-the-counter (OTC) formulations. It is often combined with lignocaine, hydroquinone, antifungal/anticandidal or antimicrobial agents to be used for relief of minor skin irritations (itching/rashes caused by eczema, insect bites, soaps, detergents, cosmetics, jewelry, etc.), and itching of scalp/anogenital area or to relieve the discomfort of oral sores. Hydrocortisone perhaps remains the most studied and several cases of ACD from it have been reported.[5,10,39,40] Alani and Alani[5] observed positive patch test reaction with hydrocortisone in 91.3% of 23 patients of suspected hydrocortisone sensitivity whereas the observed prevalence was 4.8% in patients suspected of ACD in a later report.[39] Such a high prevalence of contact sensitivity has been attributed to its easy OTC availability.[40] Hydrocortisone aceponate has also caused widespread ACD.[41]

Budesonide is a locally acting corticosteroid with less systemic adverse effects. It exhibits potent glucocorticoid activity and weak mineralocorticoid activity. It is available as a nasal spray to treat allergic rhinitis, inhaler for the long-term management of asthma and chronic obstructive pulmonary disease, and delayed release oral and rectal formulations to treat inflammatory bowel diseases. It is a frequent contact sensitizer and along with tixocortol pivalate appears to be the best patch test marker for hydrocortisone contact sensitivity.[42,43] Although a positive patch test to tixocortol pivalate usually indicates sensitivity to hydrocortisone, one-third of patients will be allergic to hydrocortisone-17-butyrate or other corticosteroid molecules which could also be because of cross-reactions due to similar structure.[7,40]

Bircher *et al*.[44] describe a 27-year-old female patient who developed aggravation of her cosmetics contact dermatitis following topical prednisolone-21-acetate and betamethasone valerate used sequentially. She developed a severe exanthematous rash after oral prednisolone 40 mg/d. Patch testing showed positive reactions from multiple corticosteroids including hydrocortisone, prednisolone, tixocortol pivalate, desoximetasone, diflucortolone-21-valerate, betamethasone-17-valerate, hydrocortisone-17-butyrate, and hexacorton but not to triamcinolone. Relevant positive patch test reactions from prednisolone were also obtained by Davis *et al*.[16] in 0.51% of 1187 patients with suspected corticosteroid ACD. Methylprednisolone aceponate is another emerging contact sensitizer. A health worker having a recurrent history of multifactorial hand dermatitis not responding to treatment showed strong patch test reactions with the commercial preparation that she was using as well as its active ingredient, methylprednisolone aceponate.[45]

Mometasone furoate and fluticasone propionate have but low risk of contact sensitization and are less likely to cross-react with other corticosteroids.[46,47] Clobetasol propionate is more sensitizing than betamethasone dipropionate and contact sensitivity to clobetasol propionate is not uncommon and a prevalence rate between 0.004% and 0.08% has been reported.[16,48,49] The contact sensitivity from desonide has been described sporadically but is a more frequent contact sensitizer than budesonide.[42,43,50] Contact allergy to beclomethasone dipropionate has also been described.[51]

PATHOMECHANISM OF CORTICOSTEROID CONTACT ALLERGY

The exact pathomechanism of corticosteroid contact allergy remains obscure. Based on observed cross-reaction patterns, it has been suggested that haptenization of corticosteroid after skin penetration and oxidized C_{21} position, the proposed site for fixation to skin proteins, plays an important role in the corticosteroid allergenicity.[2,52] It has been also suggested that the key factor in the degree of immunogenicity of the corticosteroid molecule perhaps depends on the ability of the steroid glyoxal breakdown products to bind arginine.[53] This is evident from the reduction of this ability from halogenation of the steroid molecule explaining why halogenated steroids such as betamethasone are less allergenic despite their extensive

use.[54] However, it is also possible that aldehyde formation plays a role in both ethanol and corticosteroid contact hypersensitivity given that positive patch testing from ethanol, which is also degraded through aldehydes is more frequent in corticosteroid-sensitive patients.[2,55] These variations in immunogenicity of the corticosteroid molecule also reflect why some corticosteroids are more allergenic than others.

CLINICAL PRESENTATIONS

The clinical features of corticosteroid allergy are often difficult to discern and depend on the route of exposure and site of application.[10] After topical application of an offending corticosteroid, the contact dermatitis may get modified due to its anti-inflammatory effect wherein a more intense reaction is seen at the edge of the lesion than in the center of the treated area in the presence of other signs of prolonged corticosteroid use.[56] The preexisting dermatitis may deteriorate or evolve into a resistant-to-treat chronic skin lesion.[57-59] However, manifestation as hand eczema was infrequent in a series of 315 patients.[12] Acute generalized exanthematous pustulosis-like eruptions from topical hydrocortisone-17-butyrate, erythema multiforme-like contact dermatitis, and a severe angio-edematous facial swelling with an acute eczematous reaction from topical budesonide and desoximethasone have occurred.[60-62] Distant ipsilateral exacerbation of toxicoderma-like eruption over the trunk was observed due to budesonide following repeated usage study of budesonide-allergic patients.[63] Prednicarbate reportedly had caused genital edema with erythema and vesicles.[64] An eczematous reaction may also occur at the injection site from injected corticosteroids.[23] Similarly, periorificial eczematous eruptions with occasional involvement of the adjacent mucosae, trunk, and flexures have occurred mainly from budesonide in nasal spray or inhalers for asthmatic patients.[33,65-71] Airborne contact dermatitis from budesonide inhaler has been described.[37,38,72,73] Hydrocortisone has been also implicated in photocontact dermatitis in a patient, who had a delayed positive patch test to hydrocortisone and on multiple testing proved to be due to photoallergy in the ultraviolet-A action spectrum.[74] A flare-up of old budesonide patch test sites and distant skin lesions has been observed in budesonide-sensitive patients after budesonide inhalation.[75]

Mucosal contact sensitivity from topically applied corticosteroids is not uncommon and contact stomatitis from tixocortol pivalate lozenges has been reported.[76] Mucosal symptoms such as worsening of rhinitis, nasal congestion, nasal burning and pruritus, soreness in the nostrils, and perforation of the nasal septum have been reported infrequently from budesonide or tixocortol pivalate in nasal formulations.[66-68,77-79] Corticosteroid inhalers for respiratory use have caused pruritus, dryness, erythema and edema of the mouth, dry cough, and odynophagia.[67,79,80] Corticosteroids in ophthalmic formulations can cause periocular dermatitis and/or edema, conjunctival congestion, itching, burning, pain, and smarting of eyes.[34]

SYSTEMIC CONTACT DERMATITIS FROM CORTICOSTEROIDS

Systemic contact-type dermatitis is not uncommon after systemic administration of corticosteroids in pre-sensitized patients.[81,82] Occurrence and deterioration of dermatitis with spread to previously unaffected skin and development of severe exanthematous rash after oral administration of prednisolone has been reported, although patients could tolerate betamethasone and triamcinolone.[44] A flare-up of past contact dermatitis and old patch test sites can happen after provocations with hydrocortisone.[83] Pruritus, pain, and facial edema without any other skin changes were reported from chewing tixocortol pivalate tablets.[84] Systemic contact dermatitis from hydrocortisone has been aptly demonstrated by positive patch tests in patients pre-sensitized to hydrocortisone and hydrocortisone-17-butyrate (four patients) and to hydrocortisone-17-butyrate but not to hydrocortisone (two patients).[85,86] The patients also developed dermatitis at the sites of previous contact dermatitis after oral provocation with 100 or 250 mg hydrocortisone reflecting that systemic contact dermatitis from prednisolone in a patient sensitive to hydrocortisone is possible. A patient allergic to hydrocortisone developed systemic contact dermatitis when given prednisolone, a cross-reacting corticosteroid, and the dermatitis cleared when betamethasone, a non-cross-reacting corticosteroid, was administered.[87] Bianchi *et al*.[88] describe a case of systemic contact dermatitis developed three days after oral administration of dexamethasone-21-disodium phosphate initially and then with oral deflazacort in a patient sensitized to hydrocortisone-17-butyrate, budesonide, and desoximetasone used for lichen planus.

Generalized maculopapular rash, papulovesicular rash, pustular lesions-, erythematous or urticarial rashes have been reported from corticosteroids injected into the skin intra-articularly and intravascular.[11]

DIAGNOSIS

Not many diagnostic tools are available. The availability of lymphocyte transformation test, the *in vitro* test for delayed hypersensitivity, needs expertise and remains limited to experimental laboratories. Intradermal testing is not preferred due to the associated risk of skin atrophy whereas detailed clinical history and examination along with patch testing using a corticosteroid series [Table 1] and a standard series remains the diagnostic approach of choice. A high index of clinical suspicion is imperative for early diagnosis and common clues to corticosteroid contact dermatitis include worsening of dermatitis, uncommon and/or changing clinical pattern, or when there is no improvement of existing dermatitis despite continuous treatment in an individual with strong predisposing factors (*vide supra*).

Table 1: International corticosteroid series (updated in January 2018)*.

S. No.	Patch test antigens	Conc. (w/w)	Veh.
1.	Budesonide	0.01%	pet
2.	Betamethasone-17-valerate	1.0%	pet
3.	Triamcinolone acetonide	1.0%	pet
4.	Tixocortol-21-pivalate	0.1%	pet
5.	Aclomethasone-17,21-dipropionate	1.0%	aq
6.	Clobetasol-17- dipropionate	1.0%	pet
7.	Dexamethasone-21-phosphate disodium salt	1.0%	pet
8.	Hydrocortisone-17-butyrate	1.0%	pet
9.	Desoximetasone	1.0%	pet
10.	Betamethasone-17,21-dipropionate	1.0%	pet
11.	Methylprednisolone aceponate	1.0%	pet
12.	Corticosteroid mix 1. Budesonide (0.1%) 2. Hydrocortisone-17 butyrate (1.0%) 3. Tixocortol-21-pivalate (1.0%)	2.1%	pet
13.	Hydrocortisone-21-acetate	1.0%	pet

*This series is a selection of haptens found in topical corticosteroid creams and ointments and authorized by the International Contact Dermatitis Research Group (ICDRG) and marketed by Chemotechnique MB Diagnostics AB, Vellinge, Sweden (www.chemotechnique.se), Veh.: Vehicle. pet: Petrolatum

PATCH TESTING IN CORTICOSTEROIDS CONTACT SENSITIVITY

Contact dermatitis from the topical corticosteroids may be from hypersensitivity to the corticosteroid itself or to one of the ingredients in the vehicle or base.[89] In a retrospective study of 1188 patients patch tested with corticosteroids, 10.7% had allergic reactions to at least one corticosteroid while multiple corticosteroid sensitivity was seen in 4.7% of patients reflecting that patients may be allergic to single or multiple corticosteroids.[16] Sensitivity to 21-diol acetate, a chemical impurity in hydrocortisone acetate, is another possible reason for contact dermatitis in such patients.[90] Emulsifying agents, propylene glycol, chlorocresol, parabens, benzyl alcohol, ethylenediamine hydrochloride, isopropyl palmitate, polysorbate 60, stearyl alcohol, sodium dioctyl sulfosuccinate, sodium metabisulfite, 1,2,6-hexanetriol, sorbic acid, cetostearyl alcohol, sodium lauryl sulfate, lanolin, chlorocresol, miconazole, neomycin, lignocaine, fragrances, or menthol in topical corticosteroid formulations may cause contact dermatitis in some patients.[11,91,92] However, most corticosteroid ointments do not contain preservatives and are unlikely to cause contact sensitivity.

Tixocortol pivalate, budesonide, and hydrocortisone-17-butyrate in petrolatum can detect most cases allergic to corticosteroids and are recommended to be included in standard series as screening markers despite no consensus for optimal patch test concentrations and a good number of false-positive results.[54] Petrolatum remains the vehicle of choice for tixocortol pivalate and budesonide but not for hydrocortisone-17-butyrate, whereas ethyl alcohol appears better dilutant for most corticosteroids and concentrations from 0.02% to 0.002% are usually recommended for use.[54,93] It is also recommended to include ethanol, propylene glycol, and isopropanol or higher concentrations of corticosteroids for patch testing.[10,16,94,95] However, higher concentrations tend to suppress the reaction and produce late reactions while lower concentrations produce reactions on day two but may not be adequate to elicit a positive response. However, a 48-h occlusion time is considered best as whitening of the skin at the patch test site from vasoconstriction may be noted after 48 h. Corticosteroids in early reading can produce an "edge effect" consisting of a reaction at the edges of the patch and not in the central area due to the higher concentration of test material and the resultant anti-inflammatory effect. Since corticosteroids can suppress and delay erythema, early negative reactions are not uncommon and up to 30% of corticosteroid reactions can be missed if late reading at day 7, 10 or even beyond is not performed.[54,93,96] Tixocortol pivalate in ethanol or hydrocortisone in a 1:1 mixture of ethanol and dimethylsulfoxide (improves penetration through the epidermis) is as sensitive and specific marker for hydrocortisone allergy as intradermal skin tests with hydrocortisone.[23,97]

A combination of tixocortol pivalate (0.1%) and budesonide (0.01%) present in the European and Spanish standard series and hydrocortisone-17-butyrate in the TRUE test and North American Contact Dermatitis Group standard series remain the best choice for screening corticosteroid-allergic subjects.[98] Indian standard series does not have any corticosteroid marker for screening of suspected cases. Tixocortol pivalate and budesonide could detect more than 90% cases of corticosteroid contact sensitivity in a study of 2123 patients patch tested to evaluate tixocortol pivalate, hydrocortisone butyrate, budesonide, betamethasone valerate, clobetasone butyrate, and clobetasol propionate for their ability to detect these cases.[99] However, the best way to screen for corticosteroid allergy is to patch test commercial corticosteroid preparations used/brought by the patient in view of the unavailability of tixocortol pivalate in most countries and for the possibility of contact sensitivity from an excipient or the commercial corticosteroid formulation itself.[23,100] The "usage" or repeated open application test (ROAT) also provides a simple and useful diagnostic tool.[63]

CROSS-REACTION PATTERNS AND CLASSIFICATION

Cross-reactivity patterns have not been observed for immediate hypersensitivity reactions as they have been for ACD. Although

Table 2: Four classes of corticosteroids based on frequency of cross-reactivity.

	Structure and Corticosteroid marker for patch test screening	Cross reactivity
Class A-Hydrocortisone-type		
• Hydrocortisone with C17 and/or C21-acetate ester type • Tixocortol pivalate • Prednisone • Prednisone±acetate • Methylprednisolone±acetate/aceponate • Clopredinol, Fludrocortisone acetate	***Structure*** • C_{21}-Shortchain ester or thioester ***Corticosteroids patch test marker*** • Tixocortol-21-pivalate	1. Within the group 2. With group D2 corticosteroids 3. With budesonide-(S)-isomer
Class B-Triamcinolone Acetonide-type		
• Triamcinolone acetonide or alcohol • Amcinonide type • Flucinolone acetonide • Budesonide • Halcinonide • Flucinonide acetonide • Desonide • Flunisolide, procinonide, Flucloronide	***Structure*** • C_{16}, C_{17}-cisketal or -diol ***Corticosteroids patch test marker*** • Budesonide	1. Within the group 2. Budesonide-(S)-isomer corticosteroids 3. With group A and D2 corticosteroids
Class C- Betamethasone dipropionate (not Valerate)-type		
• Betamethasone dipropionate 0.0125% and disodium phosphate type • Dexamethasone and disodium phosphate type • Desoximetasone • Diflucortolone valerate • Flucortolone pivalate • Clocortolone pivalate	***Structure*** • C_{16}-methyl substitution • Halogen substitution • Non-esterified • C_{16}-methyl substitution • Halogen substitution • Stable esters (-valrate, pivalate)	1. Betamethasone and/or dexamethasone and group B corticosteroids 2. No significant cross reactions observed
Class D- Hydrocortsoe-17-Butyrate-type		
Class D1 (Less labile)- • Betamethasone valerate 0.1%, Betamethasone dipropionate 0.05% • Clobetasol propionate and butyrate type • Mometasone furate • Flucortolone hexanoate and pivalate • Aclometasone dipropionate • Diflorasone diacetate • Beclomethasone dipropionate	***Structure*** • C_{16}-methyl substitution • Halogen substitution • C_{17}-long chain • C^{21}-possible side chain ***Corticosteroids patch test marker*** • Clobetasol-17-propionate	1. Rare cross-reaction between aclomethasone dipropionate and group A budesonide 2. Group D2 corticosteroids
Class D 2 (More labile)* • Hydrocortisone-17-butyrate, aceponate, and buteprate type • Prednicarbate	***Structure*** • C_{16}-no methyl substitution • No halogen substitution • C_{17}-long chain ester • C_{21}-possible side chain ***Corticosteroids patch test marker*** • Hydrocortisone-17-butyrate	1. Within the group 2. With group A corticosteroids 3. With budesonide-(S)-isomer

*Lipophilic prodrugs that penetrate skin only

the exact mechanism remains unclear, most researchers have tried to explain cross-reactions based on the similarity of the basic structural cyclopentanoperhydrophenanthrene ring and its modifications through halogenations and/or esterification to improve therapeutic efficacy. However, budesonide lacks cross-reactivity with desonide despite being closely related chemically.[101] Whereas, hydrocortisone sensitivity may be accompanied by hypersensitivity to more potent topical corticosteroids and cross-reaction is common between hydrocortisone and methylprednisolone.[5,8] Furthermore, cross-reactions have been reported uncommonly between betamethasone and triamcinolone, budesonide and

Table 3: Modified classification of corticosteroids.

Group-1	Group-2	Group-3
Non-methylated, non-halogenated molecules	Halogenated molecules with a cis-ketal or diol structure at C_{16}/C_{17}	Halogenated methylated molecules at C_{16}
Corresponds to Budesonide and Group A and D2 of the classification of Coopman *et al*.[65]	Corresponds to Group B of the classification of Coopman *et al*.[65]	Corresponds to Group C and D1 of the classification of Coopman *et al*.[65]
Budesonide*	Amcinonide	Aldometasone dipropionate
Clopredinol	Desonide**	Beclomethasone dipropionate
Cortisone acetate	Fluchloronide	Betamethasone
Dichlorisone acetate	Flumoxonide	Betamethasone-17-valerate
Difluprednate	Flunisolide*	Betamethasone dipropionate*
Fludrocortisone acetate	Fluocinolone	Betamethasone sod. phosphate*
Fluoromethaone	Fluocinonide	Clobetasol propionate
Fluprednisolone acetate	Halocinonide	Clobetasol butyrate
Hydrocortisone*	Triamcinolone	Desoximetasone
Hydrocortisone aceponate	Triamcinolone acetonide*	Desoximethasone*
Hydrocortisone acenate	Triamcinolone benetonide	Dexamethasone acetate
Hydrocortisone-17-butyrate*	Triamcinolone diacetate	Dexamethasone sod. phosphate
Hydrocortisone-21-butyrate*	Triamcinolone hexacetonide	Difludortolone valerate
Hydrocortisone hemisuccinate		Diflorasone diacetate
Isofluprednone acetate		Flumethasone pivalate
Mazipredone		Fluocortin butyl
Medrysone		Fluocortolone
Methylprednisolone acetate*		Fluocortolone caprylate
Methylprednisolone aceponate		Fluocortolone pivalate
Methylprednisolone hemisuccinate*		Fluocortolone acetate
Prednicarbate		Halometasone
Prednisolone*		Meprednisone
Prednisolone capoate		Fluticasone propionate
Prednisolone pivalate		Mometasone
Prednisolone sodium metasulfobenzoate		
Prednisolone succinate		
Prednisone		
Tixocortol pivalate		

*Corticosteroids used for patch test panel for respective group. **Desonide is a non-halogenated molecule

amcinonide or prednicarbate.[102,103] These observations reflect a vast variability of the sensitizing potential of different corticosteroids. This led Coopman *et al*.[65] to group corticosteroids into four groups, namely, A, B, C, and D based on their chemical structure and frequency of cross-reaction patterns. As cross-reactions were not consistent as predicted or expected according to this classification, group D was further divided into two subgroups, D1 and D2 [Table 2].[2,22,104,105] This classification was re-modified in 2011 and corticosteroids were divided into three groups; 1, 2, and 3 based on molecular models of corticosteroids and cross-reaction patterns on patch testing [Table 3].[22,106-108] Based on the observations that linking to proteins and consequent haptenization is easier in group-1 steroids due to lack of C_{16}-methyl substitution and non-halogenation resulting in higher chances of hypersensitivity, it is also proposed to divide patients into two profiles depending on whether they are sensitized to one or more groups of corticosteroids.[106] The profile-1 patients would react to steroids from one group only wherein cross reactions seem to be due to electrostatic fields whereas profile-2 patients would react to two or three groups of corticosteroids due to immunological recognition of the molecular structure of the steroid. Although the clinical utility of this classification in predicting reactions remains undefined, profile-2 patients seem to be at greater risk of generalized skin reactions after systemic corticosteroid administration.

MANAGEMENT

Management of these patients remains complex, as the diagnosis is rarely suspected. Although the recent classification of corticosteroids based on chemical structure and patient profiles to one or more groups depending on their allergy can be predictive, few patients during follow-up may not show any reaction following topical application of other corticosteroids from the group that

they had contact sensitivity. However, withdrawal of the offending corticosteroid formulation and avoidance of all topical corticosteroids from the offending group as per the current classification will be prudent for profile-1 patients. As cross-reaction patterns after inhaled or systemic administration are not well defined, recommendations for their use may remain confusing. It is always appropriate to do patch testing or a usage test/ROAT with the suspected drug, corticosteroid series, and a standard series to rule out sensitization for specific management recommendations. For profile-2 patients, other measures such as calcineurin inhibitors can be recommended whereas reserve corticosteroids can be used for emergency situations only, when no alternative is available.[11]

CONCLUSION

1. Contact dermatitis, a delayed hypersensitivity reaction, from corticosteroids with a prevalence of 0.5–5% across regions is being increasingly recognized and the putative allergens vary across countries. No Indian data are available for comparison.
2. Corticosteroid contact allergy is a major concern for the management of the patient and is therapeutically challenging in dermatology practice. Clinical suspicion remains paramount for an early diagnosis in view of hard-to-interpret clinical presentation(s) and diagnostic test results that require a thorough knowledge of this condition.
3. Exacerbation of primary dermatosis/dermatitis, an acute eczematous reaction, erythema multiforme-like or localized edematous reactions, or other unusual presentations should raise clinical suspicion of corticosteroid ACD in patients on topical corticosteroid therapy, especially in presence of other predisposing factors.
4. The recent classification of corticosteroids based on their chemical structure and cross-reaction patterns has led to type patients according to whether they are allergic to corticosteroids from one or more groups. This, in turn, has made it possible to select and recommend corticosteroids that can be prescribed safely.
5. Tixocortol-21-pivalate (0.1% pet), budesonide (0.01% pet), and hydrocortisone-17-butyrate (1.0% pet) can identify the majority of patients with corticosteroids ACD. However, patch testing with additional corticosteroid(s) will be required to identify remaining corticosteroid-sensitive patients. It is also important to consider sensitivity from the excipients. Thus, patch testing with commercial formulations obtained from the patient, a standard series preferably with corticosteroid screening haptens, and a corticosteroid series is important. It is also advisable to test with corticosteroids from a group other than the one a patient is allergic to for planning alternative treatment. Nevertheless, discordant results are often observed between the results of patch tests and the patient's tolerance to various commercial preparations.
6. The consideration for described cross-reactivity patterns can help in the identification of a corticosteroid that can be tolerated. Once the culprit drug has been identified, the patient should be advised about alternative corticosteroids. Betamethasone and deflazacort due to their low sensitizing potential can be recommended for emergency use. Topical calcineurin inhibitors can be other options in additional cases.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Baeck M, Nicolas JF, Pilette C, Tennstedt D, Goossens A. Allergic hypersensitivity to topical and systemic corticosteroids: A review. Allergy 2009;64:978-94.
2. Matura G. Contact allergy to corticosteroids. Allergy 2000;55:698-704.
3. Skoet R, Zachariae R, Agner T. Contact dermatitis and quality of life: A structured review of the literature. Br J Dermatol 2003;149:452-6.
4. Isaksson M, Bruze M. Contact allergen of the year. Corticosteroids. Dermatitis 2005;16:3-5.
5. Alani MD, Alani SD. Allergic contact dermatitis to corticosteroids. Ann Allergy 1972;30:181-5.
6. Dooms-Goossens AE, Anderson KE, Burrows D, Camarasa JG, Ducombs G, Frosch PJ, *et al*. A survey of the results of patch

tests with tixocortol pivalate. Contact Dermatitis 1989;20:158.
7. Wilkinson SM, English JS. Hydrocortisone sensitivity: An investigation into the nature of the allergen. Contact Dermatitis 1991;25:171-81.
8. Dooms-Goossens A, Andersen KE, Brandäo FM, Bruynzeel D, Burrows D, Camarasa J, *et al*. Corticosteroid contact allergy: An EECDRG multicentre study. Contact Dermatitis 1996;35:40-4.
9. Wattanakrai P, Temnithikul B, Pootongkam S. Pattern of corticosteroid allergy in Thailand. Dermatitis 2010;21:203-6.
10. Dooms-Goosens A, Morren M. Results of routine patch testing with corticosteroid series in 2073 patients. Contact Dermatitis 1992;26:182-91.
11. Berbegal L, DeLeon FJ, Silvestre JF. Hypersensitivity reactions to corticosteroids. Actas Dermosifiliogr 2016;107:107-15.
12. Bircher AJ, Thürlimann W, Hunziker T, Pasche-Koo F, Hunziker N, Perrenoud D, *et al*. Contact hypersensitivity to corticosteroids in routine patch patients. A multicenter study of the Swiss Contact Dermatitis Research Group. Dermatology 1995;191:109-14.
13. Svendsen SV, Bach RO, Mortz CG. Prevalence of contact allergy to corticosteroids in a Danish patient population. Contact Dermatitis 2022;87:273-9.
14. Jacob SE, Steele T. Corticosteroid classes: A quick reference guide including patch test substances and cross-reactivity. J Am Acad Dermatol 2006;54:723-7.
15. Pérez-Crespo M, Silvestre JF, Lucas A, Mataix J, Ballester I. Allergic contact dermatitis due to corticosteroids: A 3-year retrospective study in a hospital skin allergy unit. Actas Dermosifiliogr 2009;100:291-7.
16. Davis MD, El-Azhary RA, Farmer SA. Results of patch testing to a corticosteroid series: A retrospective review of 1188 patients during 6 years at Mayo Clinic. J Am Acad Dermatol 2007;56:921-7.
17. Vind-Kezunovic D, Johansen JD, Carlsen BC. Prevalence of and factors influencing sensitization to corticosteroids in a Danish patch test population. Contact Dermatitis 2011;64:325-9.
18. Keegel T, Saunders H, Milne R, Sajjachareonpong P, Fletcher A, Nixon R. Topical corticosteroid allergy in an urban Australian centre. Contact Dermatitis 2004;50:6-14.
19. Gönül M, Gül U. Detection of contact hypersensitivity to corticosteroids in allergic contact dermatitis patients who do not respond to topical corticosteroids. Contact Dermatitis 2005;53:67-70.
20. Reduta T, Laudanska H. Contact hypersensitivity to topical corticosteroids- frequency of positive reactions in patch tested patients with allergic contact dermatitis. Contact Dermatitis 2005;52:109-10.
21. Pratt MD, Mufti A, Lipson J, Warshaw EM, Maibach HI, Taylor JS, *et al*. Patch test reactions to corticosteroids: Retrospective analysis from the North American Contact Dermatitis Group 2007-2014. Deramtitis 2017;28:58-63.
22. Baeck M, Drieghe J, Chemelle JA, Terreux R, Goossens A. Delayed hypersensitivity to corticosteroids in a series of 315 patients: Clinical data and patch-test results. Contact Dermatitis 2009;61:163-75.
23. Isaksson M. Corticosteroids. Dermatol Ther 2004;17:314-20.
24. Burden AD, Beck MH. Contact hypersensitivity to topical corticosteroids. Br J Dermatol 1992;127:497-500.
25. Wilkinson SM, English JS. Hydrocortisone sensitivity: Clinical features of 59 cases. J Am Acad Dermatol 1992;27:683-7.
26. Lutz ME, El-Azhary RA, Gibson LE, Fransway AF. Contact hypersensitivity to tixocortol pivalate. J Am Acad Dermatol 1998;38:691-5.
27. Foti C, Bonifazi E, Casulli C, Bonamonte D, Conserva A, Angelini G. Contact allergy to corticosteroids in children with atopic dermatitis. Contact Dermatitis 2005;52:162-3.
28. Kot M, Bogaczewicz J, Kręcisz B, Woźniacka A. Contact hypersensitivity to haptens of the European Standard Series and corticosteroid series in the population of adolescents and adults with atopic dermatitis. Dermatitis 2014;25:72-6.
29. Kot M, Bogaczewicz J, Kręcisz B, Woźniacka A. Contact allergy in the population of patients with chronic inflammatory dermatoses and contact hypersensitivity to corticosteroids. Adv Dermatol Allergol 2017;34:253-9.
30. Wilkinson SM, Morrey K, Hollowood K, Heagerty AH, English JS. HLA-A B and DR antigens in hydrocortisone contact hypersensitivity. Contact Dermatitis 1993;28:295-7.
31. Schoenmakers A, Vermorken A, Degreef H, Dooms-Goossens A. Corticosteroid or steroid allergy? Contact Dermatitis 1992;26:159.
32. Lamb SR, Wilkinson SM. Contact allergy to progesterone and estradiol in a patient with multiple corticosteroid allergies. Dermatitis 2004;15:78-81.
33. Baeck M, Pilette C, Drieghe J, Goossens A. Allergic contact dermatitis to inhalation corticosteroids. Eur J Dermatol 2010;20:102-8.
34. Baeck M, de Potter P, Goossens A. Allergic contact dermatitis following ocular use of corticosteroids. J Ocul Pharmacol Ther 2011;27:83-92.
35. Malik M, Tobin AM, Shanahan F, O'Morain C, Kirby B, Bourke J. Steroid allergy in patients with inflammatory bowel disease. Br J Dermatol 2007;157:967-9.
36. Bianchi AJ, Pelloni F, Messmer SL, Muller D. Delayed hypersensitivity reactions to corticosteroids applied to mucous membranes. Br J Dermatol 1996;135:310-3.
37. Baeck M, Goossens A. Patients with airborne sensitization/ contact dermatitis from budesonide-containing aerosols 'by proxy'. Contact Dermatitis 2009;1:1-8.
38. Raison-Peyron N, Co Minh HB, Vidal-Mazuy A, Guilhou JJ, Guillot B. Connubial contact dermatitis to an inhaled corticosteroid. Ann Dermatol Venereol 2005;132:143-6.
39. Wilkinson SM, Cartwright PH, English JS. Hydrocortisone: An important cutaneous allergen. Lancet 1991;337:761-2.
40. Watsky KL, Warshaw EM. Allergic contact dermatitis: Another adverse effect of over-the counter hydrocortisone. Arch Dermatol 2007;143:1217-8.
41. El Sayed F, Ammoury A, Launais F, Bazex J. Contact dermatitis to hydrocortisone aceponate in Efficort cream inducing widespread reaction. Contact Dermatitis 2005;53:242-3.
42. O'Hagan AH, Corbett JR. Contact allergy to budesonide in a breath-actuated inhaler. Contact Dermatitis 1999;41:53.
43. Auricchio L, Nino M, Suppa F. Contact sensitivity to budesonide in a child. Contact Dermatitis 2000;42:359.
44. Bircher AJ, Levy F, Langauer S, Lepoittevin JP. Contact allergy to topical corticosteroids and systemic contact dermatitis from prednisolone with tolerance of triamcinolone. Acta Derm

Venereol (Stockh) 1995;75:490-5.
45. Cahill J, Nixon R. Allergic contact dermatitis to methylprednisolone aceponate in a topical corticosteroid. Australas J Dermatol 2004;45:192-3.
46. Wilkinson SM, Beck MH. Fluticasone propionate and mometasone furoate have a low risk of contact sensitization. Contact Dermatitis 1996;34:365-6.
47. Goossens A, Huygens S, Matura M, Degreef H. Fluticasone propionate: A rare contact sensitizer. Eur J Dermatol 2001;11:29-34.
48. Butler D, Afshar M, Calame A, Jacob SE. Allergic contact dermatitis to clobetasol used for stasis dermatitis. Austin J Clin Case Rep 2014;1:1002.
49. Sommer S, Wilkinson SM, English JS, Gawkrodger DJ, Green C, King CM, *et al*. Type-IV hypersensitivity to betamethasone valerate and clobetasol propionate: Results of a multicentre study. Br J Dermatol 2002;147:266-9.
50. Garner LA, Cruz PD Jr. Contact puzzle: Worsening of a recurrent facial eruption despite treatment. Diagnosis: Allergic contact dermatitis caused by desonide. Am J Contact Dermatitis 1999;10;81-2.
51. Cooper SM, Shaw S. Contact allergy to beclomethasone dipropionate. Contact Dermatitis 1998;39:271.
52. Lepoittevin JP, Drieghe J, Dooms-Goossens A. Studies in patients with corticosteroid contact allergy. Understanding cross-reactivity among different steroids. Arch Dermatol 1995;131:31-7.
53. Wilkinson SM, Jones MF. Corticosteroid usage and binding to arginine: Determinants of corticosteroid hypersensitivity. Br J Dermatol 1996;135:225-30.
54. English JS. Corticosteroid-induced contact dermatitis: A pragmatic approach. Clin Exp Dermatol 2000;25:261-4.
55. Matura M, Lepoittevin JP, Arbez Gindre C, Goossens A. Testing with corticosteroid aldehydes in corticosteroid sensitive patients (preliminary results). Contact Dermatitis 1998;38:106-8.
56. Reitamo S, Lauerma AI, Stubb S, Käyhko K, Visa K, Förström L. Delayed hypersensitivity to topical corticosteroids. J Am Acad Dermatol 1986;14:582-9.
57. Venning VA. Fluticasone propionate sensitivity in a patient with contact allergy to multiple corticosteroids. Contact Dermatitis 1995;33:48-9.
58. Hayakawa R, Suzuki M, Ukei C, Ogino Y, Arisu K, Hiramoto K, *et al*. A case of budesonide contact allergy. Contact Dermatitis 1992;26:128-9.
59. Hayakawa R, Matsunaga K, Suzuki M, Ogino Y, Arisu K, Arima Y, *et al*. Allergic contact dermatitis due to amcinonide. Contact Dermatitis 1990;23:49-50.
60. Broesby-Olsen S, Clemmensen O, Andersen KE. Allergic contact dermatitis from a topical corticosteroid mimicking acute generalized exanthematous pustulosis. Acta Derm Venereol 2005;85:444-61.
61. Stingeni L, Caraffini S, Assalve D, Lapomarda V, Lisi P. Erythemamultiforme-like contact dermatitis from budesonide. Contact Dermatitis 1996;34:154-5.
62. Stingeni L, Hansel K, Lisi P. Morbiliform erythema multiforme-like eruption from desoxymethasone. Contact Dermatitis 1996;35:363-4.
63. Isaksson M, Bruze M. Repetitive usage testing with budesonide in experimental nickel-allergic contact dermatitis in individuals hypersensitive to budesonide. Br J Dermatol 2001;145:38-44.
64. Miranda-Romero A, Sánchez-Sambucety P, Bajo C, Martinez M, Garcia-Munoz M. Genital edema from contact allergy to prednicarbate. Contact Dermatitis 1994;30:41-4.
65. Coopman S, Degreef H, Dooms-Goossens A. Identification of cross-reaction patterns in allergic contact dermatitis from topical corticosteroids. Br J Dermatol 1989;121:27-34.
66. Jorro G, Rochina A, Morales C, Burches E, Pelaez A. Contact allergy to topical budesonide in nasal spray. Contact Dermatitis 1993;28:254.
67. Garijo MA, Gonzalez PB. Cutaneous-mucosal allergic contact reaction due to topical corticosteroids. Allergy 1995;50:833-6.
68. Bircher AJ. Short induction phase of contact allergy to tixocortol pivalate in a nasal spray. Contact Dermatitis 1990;22:237-8.
69. Bircher AJ, Pelloni F, Messmer SL, Muller D. Delayed hypersensitivity reactions to corticosteroids applied to mucous membranes. Br J Dermatol 1996;135:310-3.
70. Faria A, Marote J, de Freitas C. Contact allergy to budesonide in a nasal spray. Contact Dermatitis 1992;27:57.
71. Lauerma AI, Kiistala R, Mäkinen-Kiljunen S, Haahtela T. Allergic skin reaction after inhalation of budesonide. Clin Exp Allergy 1993;23:232-3.
72. Pontén A. Airborne occupational contact dermatitis caused by extremely low concentrations of budesonide. Contact Dermatitis 2006;55:121-4.
73. Corazza M, Baldo F, Osti F, Virgili A. Airborne allergic contact dermatitis due to budesonide from professional exposure. Contact Dermatitis 2008;59:318-9.
74. Reitschel RL. Photocontact dermatitis to hydrocortisone. Contact Dermatitis 1978;4:334-7.
75. Isaksson M, Bruze M. Allergic contact dermatitis in response to budesonide reactivated by inhalation of the allergen. J Am Acad Dermatol 2002;46:880-5.
76. Callens A, Vaillant L, Machet L, Pelucio-Lopez C, de CalanS, Lorette G. Contact stomatitis from tixocortol pivalate. Contact Dermatitis 1993;29:161.
77. Iglesias-Cadarso A, Diaz C, Laguna JJ, Hernandez-Weigand P. Allergic contact dermatomucositis to budesonide. J Allergy Clin Immunol 1994;94:559-60.
78. Isaksson M, Bruze M, Wihl JA. Contact allergy to budesonide and perforation of the nasal septum. Contact Dermatitis 1997;37:133.
79. Bircher AJ, Pelloni F, Langauer Messmer S, Muller D. Delayed hypersensitivity reactions to corticosteroids applied to mucous membranes. Br J Dermatol 1996;135:310-3.
80. Garcia-Abujeta JL, Fernandez L, Maquiera E, Picans I, Rodriguez F, Jerez J. Contact allergy to budesonide in an oral spray. Contact Dermatitis 1995;32:253.
81. Isaksson M. Systemic contact allergy to corticosteroids revisited. Contact Dermatitis 2007;57;386-8.
82. Chew AL, Maibach HI. Multiple corticosteroids orally elicited allergic contact dermatitis in a patient with multiple topical corticosteroid allergic contact dermatitis. Cutis 2000;65:307-11.
83. Soria A, Baeck M, Goossens A, Marot L, Duveille V,

Derouaux AS, *et al*. Patch, prick or intradermal tests to detect delayed hypersensitivity to corticosteroids? Contact Dermatitis 2011;64:313-24.
84. Quirce S, Alvarez MJ, Olaguibel JM, Tabar AI. Systemic contact dermatitis from oral prednisone. Contact Dermatitis 1994;30:53.
85. Torres V, Tavares-Bello R, Melo H, Pinto Soares A. Systemic contact dermatitis from hydrocortisone. Contact Dermatitis 1993;29:106.
86. Lauerma AI, Reitamo S, Maibach HI. Systemic hydrocortisone/cortisol induces allergic skin reactions in pre-sensitized subjects. J Am Acad Dermatol 1991;24(2 Pt 1):182-5.
87. Isaksson M, Persson LM. Contact allergy to hydrocortisone and systemic contact dermatitis from prednisolone with tolerance of betamethasone. Am J Contact Dermatitis 1998;9:136-8.
88. Bianchi L, Hansel K, Antonelli E, Bellini V, Rigano L, Stingeni L. Deflazacort hypersensitivity: A difficult-to-manage case of systemic allergic dermatitis and literature review. Contact Dermatitis 2016;75:48-65.
89. Archer CB, MacDonald DM. Chlorocresol sensitivity induced by treatment of allergic contact dermatitis with steroid creams. Contact Dermatitis 1984;11:144-5.
90. Dooms-Goossens A. Sensitisation to corticosteroids. Consequences for anti-inflammatory therapy. Drug Saf 1995;13:123-9.
91. Marston S. Contact dermatitis from cetostearyl alcohol in hydrocortisone butyrate lipocream, and from lanolin. Contact Dermatitis 1991;24:372.
92. Eubanks SW, Patterson JW. Dermatitis from sodium lauryl sulfate in hydrocortisone cream. Contact Dermatitis 1984;11:250-1.
93. Isaksson M, Andersen KE, Brandão FM, Bruynzeel DP, Bruze M, Diepgen T, *et al*. Patch testing with budesonide in serial dilutions. A multi-centre study of the EECDRG. Contact Dermatitis 2000;42:352-4.
94. Kalavala M, Statham BN, Green CM, King C, Ormerod AD, Sansom J, *et al*. Tixocortol pivalate: What is the right concentration? Contact Dermatitis 2007;57:44-6.
95. Isaksson M, Bruze M, Matura M, Goossens A. Patch testing with low concentrations of budesonide detects contact allergy. Contact Dermatitis 1997;37:241-2.
96. Subramanian S, Jerajani HR, Chowkekar S, Karkhanis A. Delayed patch test positivity to corticosteroids in chronic eczema. Contact Dermatitis 2006;54:227-8.
97. Wilkinson SM, English JS. Hydrocortisone sensitivity: A prospective study of the value of tixocortol pivalate and hydrocortisone acetate as patch test markers. Contact Dermatitis 1991;25:132-3.
98. Isaksson M, Brandao FM, Bruze M, Goossens A. Recommendation to include budesonide and tixocortol pivalate in the European standard series. Contact Dermatitis 2000;43:41-63.
99. Boffa MJ, Wilkinson SM, Beck MH. Screening for corticosteroid contact hypersensitivity. Contact Dermatitis 1995;33:149-51.
100. Isaksson M. Corticosteroid contact allergy- the importance of late readings and testing with corticosteroid used by the patients. Contact Dermatitis 2007;56:56-7.
101. Foti C, Cassano N, Vena GA. Evaluation of cross reactivity between budesonide and desonide. Contact Dermatitis 2002;47:109-10.
102. Gamboa PM, Jáuregui I, Antépara I. Contact dermatitis from budesonide in a nasal spray without cross-reactivity to amcinonide. Contact Dermatitis 1991;24:227-8.
103. Dundel FG, Elsner P, Burg G. Allergic contact dermatitis from prednicarbate. Contact Dermatitis 1991;24:59-60.
104. Wilkinson SM. Corticosteroid cross-reactions: An alternative view. Contact Dermatitis 2000;42:59-63.
105. Otani IM, Banerji A. Immediate and delayed hypersensitivity reactions to corticosteroids: Evaluation and management. Curr Allergy Asthma Rep 2016;16:18.
106. Baeck M, Chamelle JA, Goossens A, Nicolas JF, Terreux R. Corticosteroid cross reactivity: Clinical and molecular modeling tools. Allergy 2011;66:1367-74.
107. Baeck M, Goossens A. Immediate, delayed allergic hypersensitivity to corticosteroids: Practical guidelines. Contact Dermatitis 2011;66:38-45.
108. Voltolini S, Fumagalli F. Delayed corticosteroid hypersensitivity: A clinical management proposal. Eur Ann Allergy Clin Immunol 2021;53:171-6.

How to cite this article: Mahajan VK, Sharma V, Sharma N, Chandel M, Verma R. Allergic contact dermatitis caused by topical corticosteroids: A review for clinicoepidemiological presentation, evaluation, and management aspects. CosmoDerma. 2024:4:14. doi: 10.25259/CSDM_233_2023