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Propylene Glycol: An Often Unrecognized Cause of Allergic Contact Dermatitis in Patients Using Topical Corticosteroids

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ABSTRACT

Propylene glycol (PG) is considered to be a ubiquitous formulary ingredient used in many personal care products and pharmaceutical preparations. It is an organic compound commonly found in topical corticosteroids (CS). Cutaneous reactions to PG are mostly irritant, but allergic contact dermatitis to PG is well-documented. Cosensitization to PG and topical CS can occur, making it challenging to choose the appropriate topical CS in a PG-allergic patient. This review is aimed at guiding clinicians in the selection of a suitable topical corticosteroid when presented with patients allergic to PG.

Key Words: *allergic contact dermatitis, corticosteroids, propylene glycol, topical*

Propylene glycol (PG) is a colorless, viscous, nearly odorless liquid that is used as an intermediate for the synthesis of other chemicals.^{1,2} It is a multifunctional excipient that is used in many products as a solvent, vehicle, humectant, or emulsifier.³ The annual PG production and global demand are rapidly increasing.³ Vehicles for topical corticosteroid preparations commonly include PG for enhancing stratum corneum penetration. In addition to topical steroids, PG can also be found in other topical pharmacologic preparations, including antibacterials, antifungals, benzoyl peroxide, and emollients.¹ Cutaneous reactions to PG have been recognized since 1952.¹

Sources of PG

Approximately half of the PG produced is used in the synthesis of other chemicals.² The other half is utilized in the manufacturing of many industrial and personal care products. PG is used as a plasticizer, solvent (in lacquers and varnishes), and as a component in antifreeze products, lubricants, cutting-fluids, and inks. It is found in many cosmetic and pharmaceutical preparations, food (for coloring, thickening, and flavoring), and household cleansers. In a recent study by the North American Contact Dermatitis Group (NACDG), personal care products were found to be the most common sources of exposure to PG (53.8%), followed by topical steroids, and other topical medicaments.³

Allergic Contact Dermatitis to PG

Cutaneous reactions to PG are classified into four groups: irritant contact dermatitis, allergic contact dermatitis (ACD), non-immunologic contact urticaria, and subjective or sensory irritation.⁴ The incidence of true ACD to PG is unknown. This is primarily attributed to the difficulty in determining the ideal concentration for patch testing that would be nonirritating, but high enough to elicit an allergic response. The majority of skin reactions to PG are irritant in nature, however, true allergic sensitization does occur. The most convincing evidence of allergic sensitization to PG is the development of systemic contact dermatitis after giving PG orally to PG-allergic patients.⁵ The overall prevalence of allergic reactions to PG was found to be relatively low (3.5%) by the NACDG.³ The NACDG currently recommends using a 30% aqueous PG solution for patch testing.³ In our experience at the University of British Columbia Contact Dermatitis Clinic, the prevalence of positive patch test reactions to PG over a 2 year period was 1.57% (13/828 patients). It was presumed that an increased individual susceptibility to irritation may also be associated with allergic reactivity through reduction of the skin's barrier function and the release of cytokines.² To confirm an allergy to PG, it has been recommended that positive patch test reactions should be followed by serial dilution patch tests, repeat open application tests or oral challenge tests, or all three of these assessments.⁴

PG and ACD to Topical Corticosteroids

The prevalence of ACD from topical corticosteroids (CS) is unknown. ACD to topical CS should be suspected if the dermatitis worsens or does not improve during treatment. ACD can result from an allergy to the steroid molecule or to a component of the vehicle. CS are divided into four classes on the basis of structure and cross-reactivity pattern: classes A (hydrocortisone type), B (triamcinolone acetonide type), C (betamethasone type), and D.⁶ Class D is further divided into D1 (betamethasone dipropionate type) and D2 (methylprednisolone aceponate type). There are different screening markers that are used for patch testing to the corticosteroid classes. The screening markers used on the NACDG screening series are as follows: tixocortol-21-pivalate (class A), budesonide and triamcinolone acetonide (class B), clobetasol-17-propionate (class D1), and hydrocortisone-17-butyrate (class D2).⁶ Patch test reactions to class A steroids are the most common.⁷ Reactions to classes B and D steroids are less common, whereas reactions to class C steroids are extremely rare.⁷ The most common cross-reactions are between steroids in classes A and D2, followed by classes B and D2, and classes A and B.⁸

An investigation by the NACDG demonstrated that topical CS were responsible for 18.3% of the positive patch test reactions to PG.³ In a recent study, PG was found to be the most common allergen in topical CS, being present in 64% of the steroidal products.⁷ It was especially common in branded ointments and gels. Moreover, studies have reported a significant number of patients have a concomitant reaction to both topical CS and PG, which suggests the possibility of cosensitization.^{3,8}

Case Report

A 55-year-old female presented to our clinic with a history of severe recurrent eyelid dermatitis resulting in multiple visits to the emergency room and treatment with systemic steroids. Her left leg dermatitis also recently worsened. The patient's past

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medical history was significant for a previously treated venous ulcer of the left leg and chronic venous insufficiency dermatitis. There was a positive family history of atopy, but she denied any personal history of atopy. She had been applying amcinonide 0.1% (Cyclocort®) and fusidic acid 2% (Fucidin®) ointments on the leg dermatitis for many years with only intermittent improvement. Patch testing was done with the 2010 NACDG screening series (Table 1). She was found to be allergic to PG, budesonide, lanolin alcohol, balsam of Peru, and glyceryl thioglycolate. We could not identify the source of PG (amcinonide 0.1% and fusidic acid 2% ointments are both PG-free), but this patient could have been sensitized to PG from her personal care products. She was most likely sensitized to budesonide from prolonged application of amcinonide 1% ointment (a class B corticosteroid). Fusidic acid 2% ointment contains lanolin, which was an additional factor for the persistence of her dermatitis. Given that she was allergic to both PG and budesonide, it would have been helpful to know which topical CS were PG-free. Ideally, we would have prescribed her a PG-free class C or D1 topical CS. Consequently, we switched her to tacrolimus 0.1% ointment (PG- and corticosteroid-free) for treating both the eyelid and leg dermatitis. Subsequently, the eyelid dermatitis cleared. Her leg dermatitis occasionally recurs secondary to underlying venous insufficiency, for which she continues compression stocking therapy.

Ingredient	Day 3 (48 hours)	Day 7
Propylene glycol	++	++
Budesonide	++	++
Lanolin alcohol	++	++
Balsam of Peru	+	+
Glyceryl thioglycolate	-	+

Table 1: Patch test results to the 2010 North American Contact Dermatitis Group screening series

Reactions were graded using a scoring system recommended by the International Contact Dermatitis Research Group: + = erythema and papules, ++ = edema or vesicles, +++ = bullae and/or erosions, – = no reaction.

The Choice of a Topical CS in a PG-allergic Patient

Given that PG is the most common allergen in topical CS, it is important to know which topical corticosteroid to prescribe to a PG-allergic patient. We have conducted a search of all topical CS available in Canada. We have excluded topical CS that contain other active ingredients (e.g., salicylic acid). We then searched carefully for preparations that are PG-free. Ingredients of the different topical CS were checked using the *Compendium of Pharmaceuticals and Specialties* (CPS) 2010 drug reference guide in addition to pharmaceutical company website searches. We have created a chart containing all PG-free topical CS available in Canada sorted on the basis of potency and structural class (Table 2 on page 7).

Conclusion

PG is found in many products. The sensitizing potential of PG is well documented, but the true incidence of its role in ACD is unknown. PG is the most common allergen in topical CS. Cosensitization to PG and topical CS is possible. If patch testing is unavailable and the physician is highly suspecting PG allergy, we recommend prescribing any PG-free topical corticosteroid. Another option is to consider tacrolimus ointment, which is a PG-free steroid-sparing agent (pimecrolimus 1% cream contains PG). Empirically, one can prescribe a PG-free class C topical corticosteroid given the rarity of ACD to class C topical CS. Ideally, patch testing should be done if the clinical picture is suggestive of allergy to PG and/or topical CS. It is important to note that the steroid formulations discussed in this paper pertain only to topical CS products available in Canada, as products from other countries may contain different compositions of non-medicinal ingredients. We hope that this review will be of benefit in guiding physicians when choosing the appropriate topical corticosteroid in patients allergic to PG.

Structural class	Class A: Hydrocortisone type	Class B: Triamcinolone acetonide type	Class C: Betamethasone type	Class D1: Betamethasone dipropionate type	Class D2: Methylprednisolone aceponate type
Class 7: Least potent	- Hydrocortisone 0.5%, 1% [OI] (Cortoderm®) - Hydrocortisone 1%, 2.5% [CR, LO]; 2.5% [SL] (Emo-Cort®)				
Class 6: Low potency		Desonide 0.05% [OI] (Desocort®)			
Class 5: Lower mid-strength		Fluocinolone acetonide 0.01% [OL] (Derma-Smoother/FS®)		- Betamethasone valerate 0.05% [OI] (Betaderm®) - Betamethasone valerate 0.05% [CR, LO] (ratio-Ectosone) - Betamethasone valerate 0.1% [CR] (Prevex® B, ratio-Ectosone) - Betamethasone valerate 0.1%	Prednicarbate 0.1% [CR] (Dermatop®)

				[LO] (Betaderm®, ratio-Ectosone, Valisone®)
		• Triamcinolone acetonide 0.1% [OI, CR] (Aristocort®) • Amcinonide 0.1% [CR, LO] Cyclocort®, ratio-Amcinonide)	• Desoximetasone 0.05% [CR] (Topicort®) • Diflucortolone valerate 0.1% [CR, OC, OI] (Nerisone®)	Class 3: Upper mid-strength
Class 4: Mid-strength	• Triamcinolone acetonide 0.5% [CR] (Aristocort®)		• Betamethasone valerate 0.1% [OI] (Betaderm®) • Betamethasone dipropionate 0.05% [CR] (Diprosone®) • Betamethasone dipropionate 0.05% [LO] (Diprosone®, ratio-Topisone)	
		• Amcinonide 0.1% [OI] (Cyclocort®, ratio-Amcinonide)	• Desoximetasone 0.25% [CR]; 0.05% [GL] (Topicort®)	• Betamethasone dipropionate 0.05% [OI] (Diprosone®, ratio-Topisone)
Class 2: High potency				
				• Clobetasol propionate 0.05% [OI, LO] (ratio-Clobetasol) • Clobetasol propionate 0.05% [SL] (Dermovate®) • Clobetasol propionate 0.05% [SH, SP] (Clobex®)
Class 1: Superpotent				

Table 2: Propylene glycol-free topical corticosteroids available in Canada sorted by potency and structural class CR = cream, GL = gel, LO = lotion, OL = Oil, OC = oily cream, OI = ointment, SH = shampoo, SL = solution, SP = spray

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