

Excipients in Oral Antihistamines Can Perpetuate Allergic Contact Dermatitis

Elizabeth M. Tocci, B.A.,* Amanda Robinson, M.D.,† Leah Belazarian, M.D.,†,‡ Elizabeth Foley, M.D.,† Karen Wiss, M.D.,†,‡ and Dianne L. Silvestri, M.D.,†,§

**University of Massachusetts Medical School, Worcester, Massachusetts, †Division of Dermatology and ‡Department of Pediatrics, University of Massachusetts Medical School, Worcester, Massachusetts, §Contact Dermatitis Referral Clinic, Worcester, Massachusetts*

Abstract: Propylene glycol is a well-documented causative agent of allergic contact dermatitis (ACD). It is also reported to cause systemic dermatitis after ingestion of foods or medicines containing it and after intravenous injection of a medicine with propylene glycol in its base. We describe two adolescents with sensitivity to propylene glycol confirmed by patch testing whose dermatitis improved dramatically after cessation of oral antihistamines containing propylene glycol. We report these cases to alert providers to the potential for worsening of ACD due to systemic exposure to propylene glycol in patients with a cutaneous sensitivity to the allergen.

Propylene glycol is a well-documented causative agent of allergic contact dermatitis (ACD). In children, the clinically relevant prevalence of ACD due to propylene glycol is difficult to determine, but it has been shown to be one of the top 15 contact allergens in children (1). Because of propylene glycol's versatile chemical properties and low toxicity, it is a common component of topical and oral medications, personal care products, and foods. There are reports of patients with ACD to propylene glycol who developed systemic dermatitis after ingestion of propylene glycol in foods or oral solutions (2,3). A systemic reaction in a patient previously sensitized to propylene glycol has been linked to exposure from intravenous valium containing it in its base (4). We describe two adolescents with sensitivity to propylene glycol confirmed by

patch testing in whom complete improvement of dermatitis seemed to depend on cessation of oral antihistamines containing propylene glycol.

CASE REPORTS

Patient 1

A healthy 13-year-old boy had a 2-year history of a diffuse eczematous eruption. He tried oral antihistamines and various topical corticosteroids, achieving temporary improvement. On examination, he had lichenified papules and vesicles symmetrically distributed over his extremities, shoulders, and lower back. He underwent patch testing with the North American Series 65 plus 15 additional allergens

Address correspondence to Karen Wiss, M.D., Division of Dermatology, UMMHC, 281 Lincoln Street, Worcester, MA 01605, or e-mail: Karen.Wiss@umassmemorial.org.

(Chemotechnique Diagnostics, Vellinge, Sweden) using Finn Chambers (Epitest, Tuusula, Finland) on Scanpor Tape (Norgesplaster, Vennesla, Norway). Patch tests were removed at 48 hours and read at 48 and 96 hours using standard scoring that requires erythema and induration for positivity. At both intervals, there were + or ++ reactions to nickel, cobalt, and propylene glycol (30% aq) and + to benzyl alcohol at 96 hours. His dermatitis improved dramatically after eliminating propylene glycol-containing and fragranced personal care products, switching to propylene glycol-free topical betamethasone dipropionate ointment, and implementing a nickel-free diet. To control an id reaction, it was necessary to substitute ceramic for metal orthodontia. Flare of his rash twice during seasonal use of oral cetirizine syrup led to the discovery that his formulation of antihistamine contained propylene glycol. Substituting an alternative propylene glycol-free antihistamine led to dramatic improvement.

Patient 2

A 14-year-old girl had a lifelong history of atopic dermatitis that had worsened in the past 2 years. She was treated with topical steroids, emollients, bleach baths, narrowband ultraviolet light B, and oral antihistamines, with minimal improvement. Her itch affected her sleep and school performance. On examination, erythematous scaly eczematous plaques covered 95% of her cutaneous surface. Patch tests performed by an outside dermatologist with the North American Standard Series 70 (AllergEAZE, Smart Practice, Calgary, Alberta, Canada) using Finn Chambers on Scanpor tape were removed and interpreted at 48 hours, with the only reaction being a + to propylene glycol (30% aq) that persisted at 96 hours. She experienced some improvement with discontinuation of topical preparations containing propylene glycol and had complete resolution after switching to propylene glycol-free hydroxyzine syrup. When rechallenged with oral hydroxyzine containing propylene glycol, she once again experienced generalized dermatitis.

DISCUSSION

Our cases illustrate two adolescents with positive patch tests to propylene glycol who had dramatic improvement of dermatitis after elimination of propylene glycol exposure, achievable only with a change in topical and oral medications. Although propylene glycol is a known irritant, our patients were tested

with the concentration recommended by the American Contact Dermatitis Society. Persistence of response at the late reading in both cases favors a true allergic response rather than a typically decrescendo reaction of irritation. Both patients patch-tested negative to all classes of topical steroids but were tested neither for their personal formulations nor their antihistamines. The second patient was rechallenged with an oral antihistamine containing propylene glycol and experienced a recurrence of her generalized dermatitis.

Propylene glycol is a common excipient, and its presence is often overlooked (5). Flared, generalized, or refractory dermatitis may represent a systemic contact dermatitis provoked by ingestion, injection, inhalation, or other systemic exposure to a previously identified cutaneous contact allergen. We report these cases to alert providers to the potential for worsening of ACD due to ingested propylene glycol in patients with cutaneous sensitivity to the allergen.

Because propylene glycol is ubiquitous in food, medications, and personal care products, elimination of exposure can be difficult. Propylene glycol is added to processed foods to thicken or moisten them. It is a common ingredient in store-bought salad dressings, packaged baked goods, dry ingredient mixes, and even fast food items. Scheman et al (6) recently published data using foodfacts.com to illustrate common foods containing propylene glycol. The website is a useful resource for patients since it details the ingredients of 75,000 foods.

For dermatologists, identifying propylene glycol-free therapies can be a challenge. The inactive ingredients in the tablets, capsules, and syrups of antihistamines vary greatly. Some formulations of each vehicle contain propylene glycol and other formulations do not. For instance, hydroxyzine oral suspensions (syrups) may or may not contain propylene glycol, depending on the manufacturer. The generic hydroxyzine syrup produced by Silarx Pharmaceuticals (Carmel, NY) and hydroxyzine syrup with the trade name Atarax do not contain propylene glycol. Children's Benadryl Allergy Cherry Flavored Liquid (diphenhydramine hydrochloride solution), Children's Zyrtec Allergy Dissolve Tabs (cetirizine hydrochloride), and Children's Claritin Allergy Grape Flavored Chewables (loratadine) also do not contain propylene glycol.

Similar to oral antihistamines, there are propylene glycol-free topical corticosteroids available in a variety of classes and vehicles, but finding one may take some research on behalf of the prescriber. In the United States, formulations of desoximetasone

ointment usually contain only white petrolatum and oil such as mineral or coconut as inactive ingredients, making desoximetasone potentially a good choice for propylene glycol-allergic patients, but the inactive ingredients in drugs can change, so it is always prudent to verify the ingredients of a medication before prescribing it. An online source for accessing the most current U.S. Food and Drug Administration label information is DailyMed (<http://www.dailymed.nlm.nih.gov>), a website sponsored by the National Library of Health. This resource is useful for prescribers and patients for finding propylene glycol-free prescription and over-the-counter medications. Providers should also keep in mind that there are other oral antihistamine excipients that can provoke systemic dermatitis in patients with a cutaneous sensitivity to that excipient. These additives include chemicals in the sorbitan group (e.g., sorbitol), azo dyes (e.g., RD&C Red 40), and aspartame, among others (5). The best approach may be to educate

patients to review active and inactive ingredients before using any topical or oral medications and to collaborate with a pharmacist.

REFERENCES

1. Jacob S, Brod B, Crawford G. Clinically relevant patch test reactions in children—a United States based study. *Pediatr Dermatol* 2008;25:520–527.
2. Lowther A, McCormick T, Nedorost S. Systemic contact dermatitis from propylene glycol. *Dermatitis* 2008;19: 105–108.
3. Hannuksela M, Förström L. Reactions to peroral propylene glycol. *Contact Dermatitis* 1978;4:41–45.
4. Fisher AA. Systemic contact dermatitis to intravenous Valium in a person sensitive to propylene glycol. *Cutis* 1995;55:327–328.
5. McEnery-Stonelake M, Silvestri DL. Contact allergens in oral antihistamines. *Dermatitis* 2014;25:83–88.
6. Scheman A, Cha C, Jacob SE et al Food avoidance diets for systemic, lip, and oral contact allergy: an American contact alternatives group article. *Dermatitis* 2012;23: 248–257.