

Occupational Airborne Contact Dermatitis From Proton Pump Inhibitors

Ashley M. Yu, BHSc[‡] and Joel G. DeKoven, MD, MHSc, FRCPC^{*†}

Few published reports have described occupational contact dermatitis from proton pump inhibitor (PPI) exposure in the literature. We present an additional case of a 58-year-old male pharmaceutical worker with an occupational airborne allergic contact dermatitis to PPIs confirmed by patch testing. This is a novel report of workplace exposure to dexlansoprazole and esomeprazole PPIs with resultant clinical contact allergy and relevant positive patch test results to these 2 agents. A literature review of all previously reported cases of occupational contact dermatitis to PPI is summarized. The case also emphasizes the importance of even minute exposures when considering workplace accommodation.

Proton pump inhibitors (PPIs) are members of the benzimidazole family and are potent inhibitors of gastric acid secretion.¹ Proton pump inhibitors are frequently used to treat acid-related disorders such as gastroesophageal reflux and peptic ulcer disease in humans and horses.¹ Pharmaceutical workers involved in the manufacturing of drugs, such as PPIs, can be exposed to active pharmaceutical ingredients that cause adverse health effects.² Although occupational contact dermatitis in the pharmaceutical industry is not uncommon,³ to date, only 10 reports of PPI exposure causing occupational contact dermatitis and cross reactions to PPIs have been described.^{4–13} We report an additional case of occupational contact dermatitis from PPI exposure.

CASE REPORT

A 58-year-old nonatopic male pharmaceutical worker presented with erythematous eruptions involving the neck, posterior auricular areas, and extensor forearms, with slight swelling and mild erythema of the upper eyelids, as seen in Figure 1. He had a 4-year history as a chemical operator in the production area of the plant, wearing rubber gloves and long-sleeved shirts. Proton pump inhibitors and intermediates manufactured or processed during his time of occupational airborne exposure as

a production worker included dexlansoprazole (DEA30, DEA34, DEA38, DEA50, DEA70), esomeprazole magnesium (ESO35, ESO50), lansoprazole, omeprazole magnesium, and pantoprazole



Figure 1. The initial presentations of occupational airborne allergic contact dermatitis to PPIs. Note the eczematous appearance (A) of the skin on the neck and (B) of the upper eyelids.

From the *Division of Dermatology, University of Toronto; and †Department of Occupational and Environmental Health, St. Michael's Hospital, Toronto; and ‡Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada.

Address reprint requests to: Joel G. DeKoven, MD, MHSc, FRCPC, Division of Dermatology, 2075 Bayview Ave, M1 M736, Toronto, Ontario, Canada M4N 3M5. E-mail: ashley.yu@uottawa.ca.

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sodium (PTS30, PTS40). Esomeprazole was formulated in the largest quantity in the plant.

On diagnosis of possible occupational airborne contact dermatitis, the patient was removed from the production plant setting to working in an office at a distant site in the same building of the pharmaceutical company. Subsequently, although he had been working for 6 years in the office setting with no direct exposure to the handling of PPIs, he described his condition as ongoing and would experience flares from even mild and indirect airborne exposures. One distinct eruption of note occurred after receipt of paperwork from another pharmaceutical plant, where the patient reacted immediately with the same erythematous eruption on his eyelids, posterior neck, and auricular areas. As a result, he was referred for further evaluation.

Patch testing was performed with the NACDG (North American Contact Dermatitis Group) standard series. In addition, custom allergens of all of the PPIs formulated by the pharmaceutical manufacturer were tested using the active pure powdered PPIs involved in the production process. A range of concentrations was chosen based on a review of the literature. The patches were applied to the patient's back with Finn Chambers (SmartPractice, Phoenix, Ariz) on Scanpor tape (Norgesplaster A/S, Vennesla, Norway) and read at D2 and D7 according to the International Contact Dermatitis Research Group criteria. Positive patch test results, seen in Figure 2 and Table 1, confirmed his contact allergy to PPIs. There were no reactions to the NACDG Standard Series.

DISCUSSION

A literature review indicated a total of 10 published reports of occupational contact dermatitis caused by PPIs.^{4–13} Cases of contact dermatitis from PPI exposure were identified using MEDLINE via OVID (from 1946). Subject heading and key word searches for contact dermatitis, contact allergy, allergic contact dermatitis, cutaneous adverse drug reactions, proton pump inhibitor, dexlansoprazole, esomeprazole, ilaprazole, lansoprazole, omeprazole, pantoprazole,

TABLE 1. The Results of Custom PPI Patch Testing on Day 7

Patch Test	Result
Omeprazole 10% pet	++
Omeprazole 1% pet	++
Omeprazole 1% alcohol	++
Omeprazole 0.1% pet	++
Esomeprazole 50 1% pet	++
Esomeprazole 1% pet	++
Pantoprazole 10% pet	++
Pantoprazole 1% pet	++
Dexlansoprazole 10% pet	++
Dexlansoprazole 1% pet	+

Pet indicates petroleum.

and rabeprazole were used. Citations of each article identified were reviewed to ascertain additional relevant reports. Including the present case, a review of all cases reported in the literature is summarized in Table 2.

All reported cases were described in workers of the pharmaceutical or horse industry, who presented with eczematous lesions in areas ranging from the face, eyelids, neck, and arms. Cases were described as occurring after direct contact with the skin or airborne exposure, highlighting the importance of the use of protective equipment such as masks, gloves, and full-coverage clothing by pharmaceutical workers handling PPI-containing products and intermediates² and horse workers handling GastroGard.^{11,12} Effective treatments include removal from workplace exposure,^{4,8,9} oral antihistamines,⁵ topical corticosteroids,^{5,7} or oral corticosteroids.¹⁰ Many cases also demonstrated that exposure to 1 type of PPI can yield positive patch test results to the offending drug as well as additional classes of PPIs,^{5,8,11} not only confirming the risk of sensitization but also the phenomenon of cross reactions with PPIs.

Omeprazole, pantoprazole, and rabeprazole have been described as having a strong sensitization capacity as contact allergens, requiring concentrations as little as 0.03 moles to induce a response in sensitized guinea pigs.^{13,14} The presentation of paroxysmal sudden-onset contact dermatitis from minimal and indirect airborne PPI exposure further underscores the low elicitation threshold of these agents. In addition, our case seems to be the first known report with exposure to dexlansoprazole and esomeprazole PPIs resulting in clinical contact allergy and relevant positive patch test results rather than arising solely from cross reactivity to other PPI exposures. This demonstrates the direct potential for dexlansoprazole and esomeprazole to act as possible sensitizing agents. Even on removal from the manufacturing environment where our patient was exposed to these PPIs, he remained highly sensitive. The need for total avoidance of exposure is illustrated.

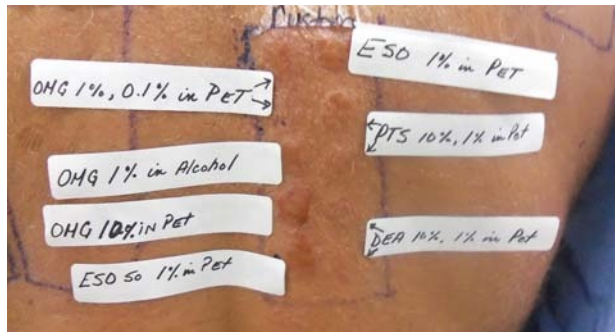


Figure 2. An image of custom patch testing on day 7.

TABLE 2. Occupational Contact Dermatitis Caused by PPIs: A Summarized Literature Review

Reference	Sex	Age, y	Occupation	Atopic Status	Offending Drug	Prior Exposure, y	Reaction	Patch Test	Concentration (%) and Route	Result
Meding ⁴	F	25	Pharmaceutical chemist	N/R	Omeprazole	N/R	Eczema on eyelids	Omeprazole	0.25, 0.5, 1% pet	+++
Meding ⁴	F	59	Pharmaceutical animal worker	N/R	Omeprazole	N/R	Eczema on eyelids with redness, edema, and itching	Omeprazole	0.1, 0.5, 1% alcohol	+
Vilaplana and Romaguera ⁵	M	58	Pharmaceutical worker	–	Lansoprazole	3.5	Pruritic papules on face, neck, upper arms, and forearms	Lansoprazole	10, 50% pet	++
Akan and Moss ⁶	F	41	Pharmacy technician	+	Lansoprazole	N/R	Pruritic facial rash associated with eyelid edema and mild urticaria	Lansoprazole	10, 50% pet	++
Conde-Salazar et al ⁷	M	25	Pharmaceutical worker	+	Omeprazole	5	Eczematous pruritic plaques on face, eyelids, neck, and hands	Omeprazole	N/R%, powder, diluent, NaHCO ₃	+
Conde-Salazar et al ⁷	M	35	Pharmaceutical supervisor	N/R	Omeprazole	N/R	Pruritic dermatitis on eyelids, nose, and perioral area	Omeprazole	0.1, 0.5% alcohol	++
Neumark et al ⁸	M	33	Pharmaceutical operator	+	Pantoprazole	6	Dermatitis on face and eyelids	Omeprazole Pantoprazole	5, 10% diluent 1, 5, 10% pet	+
Sanz-Gallén et al ⁹	M	60	Pharmaceutical worker	–	Omeprazole	8	Rashes on face and neck with facial edema	Omeprazole	0.1, 0.5, 1% sal	++
Alarcón et al ¹⁰	M	33	Pharmaceutical worker	–	Pantoprazole	7	Rash on face, neck, and hands	Pantoprazole	1, 5, 10% route N/R	++
Alarcón et al ¹⁰	M	41	Pharmaceutical maintenance worker	–	Lansoprazole	7	Rash on face and eyelid edema	Lansoprazole	10, 50% route N/R	++
Alarcón et al ¹⁰	M	49	Pharmaceutical worker	–	Lansoprazole Omeprazole Pantoprazole	21	Rash on face, neck, and arms	Lansoprazole Omeprazole Pantoprazole	10, 50% sal 0.1, 0.5, 1% sal 1, 5, 10% sal	+++ + +++
Al-Falah et al ¹¹	F	44	Horse trainer	N/R	GastroGard	N/R	Pruritic dermatitis involving the eyelids, face, neck, and forearms	GastroGard Dexlansoprazole Esomeprazole Lansoprazole Omeprazole Pantoprazole Rabeprazole GastroGard	25, 50, 100% pet 1, 10% pet 1, 10% pet 1, 10% pet 1, 10% pet 1, 10% pet 1, 10% pet 5% aq	+ ++ ++ –/+ + ++ + ++
Alwan et al ¹²	M	49	Racehorse worker	N/R	GastroGard	N/R	Eczematous rash on left thumb, scrotum, upper thigh, eyelids	GastroGard	5% aq	++
Ghatan et al ¹³	N/R	N/R	Pharmaceutical workers	N/R	Omeprazole	N/R	N/R	Omeprazole	0.1, 0.5, 1% sal	N/R
Current case	M	58	Pharmaceutical company worker	–	Dexlansoprazole Esomeprazole Lansoprazole Omeprazole Pantoprazole	4	Erythematous rash on the face, eyelids, neck, and forearms	Dexlansoprazole Esomeprazole 50 Esomeprazole	1, 10% pet 1% pet 1% pet	+ ++ ++ ++ ++
								Omeprazole Omeprazole Pantoprazole	0.1, 1, 10% pet 1% alcohol 1, 10% pet	++ ++ ++

N/R indicates not recorded; GastroGard, a 37% omeprazole-containing paste¹¹; pet, petroleum; sal, saline; aq, aqueous.

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