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Occupational Contact Allergy to Proton Pump Inhibitors and Ranitidine

Case Report

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Abstract

Proton pump inhibitors [PPIs] are members of the benzimidazole family and are commonly used in the treatment of acid disorders, such as gastro-oesophageal reflux disease, peptic ulcer disease, associated Helicobacter pylori infection, and Zollinger-Ellison syndrome, as they are potent inhibitors of gastric acid secretion.

Ranitidine is a histamine H2 receptor antagonist, used in the treatment of duodenal ulcers and gastric hypersecretory states.

We present four cases of occupational contact allergy to PPIs [lansoprazole, omeprazole, and pantoprazole] and ranitidine. All four patients worked in the pharmaceutical industry and underwent skin prick testing and patch testing with the active ingredients that they handle at work, in addition to the standard battery of allergens.

All skin prick tests were negative; patch tests were positive for PPIs [lansoprazole, omeprazole and pantoprazole] and ranitidine.

In any individual with occupational exposure to these substances, a complete medical history should be taken, and their health should be monitored; working conditions should be optimised to avoid or minimize this type of occupational risk.

Key words: Contact dermatitis, Allergy, Occupational Diseases, Proton Pump Inhibitions, Ranitidine.

Introduction

Occupational exposure to active pharmaceutical ingredients can cause adverse health effects [1]. Depending on the type of substance and exposure, several occupational dermatoses have been described among workers in the pharmaceutical industry, including irritation, contact allergy, photosensitivity, urticaria, acne venerate, and less frequently, fixed drug eruptions, steroid-induced rosacea, and even toxic epidermal necrolysis [2].

Although proton pump inhibitors [PPIs] and ranitidine are potentially sensitizing, occupationally acquired cases in the pharmaceutical industry are uncommon [3-10].

We present four cases of occupational contact allergy to PPIs [lansoprazole, omeprazole and pantoprazole] and ranitidine.

Case reports

The four cases were men working in the pharmaceutical industry, aged between 35 and 59 years old, with an exposure time of between 4 and 19 months. The time between onset of symptoms and diagnosis was between 1 and 3 months. None of the patients had a history of atopy. All were production workers. Signs and symptoms

occurred when they were in contact with PPIs or ranitidine and reduced or disappeared when they were not in contact.

The clinical features in these patients consisted of a rash on the face, neck, dorsal hands, and/or forearms, and eyelid swelling. All had itching, and one had conjunctival hyperaemia.

[30 mg/mL and 3 mg/mL saline]. In all four cases, the results of skin prick testing were negative.

Patch testing was performed according to the Spanish Contact Dermatitis Research Group [GEIDC] standard patch test series, and with lansoprazole [10%, 50%], omeprazole [0.1%, 0.5%, 1%] and pantoprazole [1%, 5%, 10%], all

Table 1: Main features of the four cases of occupational contact dermatitis caused by proton pump inhibitors and ranitidine.

Case	Sex	Age [years]	Workplace exposure [months]	Offending drug	Clinical features
Case 1	M	35	18	Lansoprazole Omeprazole Pantoprazole	Pruritic rash on face and neck, bilateral palpebral oedema and conjunctival hyperaemia.
Case 2	M	46	4	Ranitidine	Pruritic rash on face, neck, dorsum of hands and forearms.
Case 3	M	48	19	Omeprazole Ranitidine	Pruritic rash on face and dorsum of hands.
Case 4	M	59	8	Omeprazole Pantoprazole Ranitidine	Pruritic rash on face and neck.

Table 2: Patch testing results

Patch testing results	Case 1 [D2]	Case 1 [D4]	Case 2 [D2]	Case 2 [D4]	Case 3 [D2]	Case 3 [D4]	Case 4 [D2]	Case 4 [D4]
Omeprazole [0.1%]	+	++	-	-	+++	+++	+	+
Omeprazole [0.5%]	+	++	-	-	+++	+++	+	+
Omeprazole [1%]	+	++	-	-	+++	+++	+	+
Lansoprazole [10%]	+	+	-	-	-	-	-	-
Lansoprazole [50%]	+	+	-	-	-	-	-	-
Pantoprazole [1%]	+	+	-	-	-	-	++	++
Pantoprazole [5%]	+	+	-	-	-	-	++	++
Pantoprazole [10%]	+	+	-	-	-	-	++	++
Ranitidine base [0.5%]	-	-	+++	+++	++	++	++	++
Ranitidine hydrochloride [0.1%]	-	-	+++	+++	++	++	++	++
Ranitidine hydrochloride [0.5%]	-	-	+++	+++	++	++	++	++
GEIDC standard patch test series	-	-	-	-	-	-	-	-

All four patients responded to symptomatic treatment with oral antihistamines and corticosteroids. The main clinical features of the four patients are described in Table 1, including sex, age, duration of exposure before onset of symptoms, occupational activity, drugs involved, and clinical features.

Skin prick testing and patch testing were carried out. Skin prick testingwas performed at sub-irritant concentrations: lansoprazole [15 mg/mL saline], omeprazole [40 mg/mL saline], pantoprazole [20 mg/mL saline] and ranitidine in saline, as well as ranitidine base [5% pet], ranitidine hydrochloride [1% pet] and ranitidine hydrochloride [5% pet]. The results read at 48 hours [day 2] and 96 hours [day 4] are presented in Table 2.

Positive patch test results occurred in the first patient for lansoprazole, omeprazole and pantoprazole; in the second, for omeprazole, pantoprazole and ranitidine; in the third, for omeprazole and ranitidine; and in the fourth, for ranitidine. The results are described in Table 2.

Skin prick tests and patch tests were negative in the 12 healthy controls.

Discussion

Proton pump inhibitors are members of the benzimidazole family and are commonly used in the treatment of acid disorders, including gastro-oesophageal reflux disease, peptic ulcer disease, associated Helicobacter pylori infection, and Zollinger-Ellison syndrome, as they are potent inhibitors of gastric acid secretion [6,10].

Ghatan et al performed a study in 2014 [11] in an occupational setting with 97 workers. Theyreported 31 positive LTTs [lymphocyte transformation tests] and 28 positive patch tests, demonstrating the high risk of sensitisation to omeprazole through occupational exposure.

Use of omeprazole by horse breeders and trainers has been reported to cause contact dermatitis [12,13].

Confino-Cohen& Golberg, 2006 [14] proposed a desensitization protocol for anaphylaxis to omeprazole.

Yu AM & DeKoven JG, 2015 [15] reported the first case of occupational contact dermatitis due to the newer generation PPIs dexlansoprazole and esomeprazole.

Ranitidine is ahistamine H2 receptor antagonist, used in the treatment of duodenal ulcers and gastric hypersecretory states. Exposure to ranitidine compounds is an occupational risk in the pharmaceutical industry, and reactions during the production process of medicines have been described [16,17]. Contact dermatitis has also been described with ranitidine in horse trainers [18].

In our series, all four cases had a typeIV hypersensitivity reaction, predominantly to omeprazole and ranitidine, although in some cases to lansoprazole and pantoprazole.

Conclusions

These cases show the risk of sensitization through occupational exposure to PPIs and ranitidine.

In any individual with occupational exposure to these substances, a complete medical history should be taken, and their health should be monitored; working conditions should be optimised to avoid or minimize this type of occupational risk.

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