

Occupational contact allergy to omeprazole and fluoxetine

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Occupational exposure to active pharmaceutical ingredients can cause adverse health effects, particularly in personnel working with potent compounds such as steroids or those with the capacity to cause cumulative damage, such as antineoplastic drugs and antibiotics (1).

Although omeprazole and other proton pump inhibitors are potentially sensitizing, occupationally acquired cases are rare (2, 3). In the case of fluoxetine,

a commonly prescribed antidepressant, no cases stemming from occupational exposure have previously been reported.

Case Report

A 60-year-old man, with no pre-existing history of atopy or lifestyle risk factors, presented with a 4-year history of sporadic episodes of a rash involving the face and neck, together with swelling of the eyelids that responded to symptomatic treatment. For 12 years he had worked in the synthesis of active ingredients for a pharmaceutical company, primarily omeprazole and fluoxetine. In recent months, his skin rash and facial oedema had worsened

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to the point of requiring treatment with corticosteroids. These symptoms would improve at weekends and recur within a few minutes of him returning to his job.

Omeprazole and fluoxetine were the active pharmaceutical principles to which the patient was regularly exposed.

Prick tests were performed at non-irritant concentrations – 40 mg/ml for omeprazole and 20 mg/ml for fluoxetine – in the patient as well as in 6 healthy controls. Histamine hydrochloride and saline were used as positive and negative controls, respectively. A wheal diameter 3 mm greater than the negative control was considered to be positive response.

Prick tests gave positive responses to both active compounds, with 6×6 mm and 5×6 mm wheal diameters for omeprazole and fluoxetine, respectively. Prick tests gave negative results in all 6 healthy controls.

In vitro laboratory studies, consisting of a histamine release test by radioimmunoassay, were also performed to support the results obtained on prick testing; this test showed positive results with both omeprazole (46%) and fluoxetine (>60%).

Omeprazole was patch tested in saline solution at 0.1%, 0.5%, and 1% (4), and fluoxetine was tested at both a therapeutic concentration (20 mg/ml) and a 1:10 dilution. Readings at D2 and D4 showed positive results with omeprazole (+++ at 1%, ++ at 0.5%, and ++ at 0.1%). Fluoxetine patch testing gave negative results at both test concentrations. Control patch tests with omeprazole and fluoxetine gave negative results in all 6 healthy controls.

On the basis of the patient's clinical presentation, together with the *in vivo* and *in vitro* test results, the patient left his job, with full resolution of all symptoms.

Discussion

Omeprazole is a proton pump inhibitor. It is administered orally or intravenously, and is widely used in the treatment of gastro-oesophageal reflux disease, peptic ulcer disease, and Zollinger–Ellison syndrome. Meding (2) reported two occupational cases of allergic contact dermatitis caused by omeprazole in pharmaceutical workers, and Conde-Salazar et al. (3) described another two

cases in pharmaceutical industrial workers. In addition, Confino-Cohen and Golberg (5) proposed a desensitization protocol for omeprazole anaphylaxis.

Fluoxetine is a commonly prescribed antidepressant. Beer et al. (6) described the first case of hypersensitivity caused by fluoxetine associated with a rash, eosinophilia and arthralgia during treatment with fluoxetine; however, no occupationally acquired cases have been published. Moreover, cases involving simultaneous dual reactions to active pharmaceutical compounds are unusual.

When testing for type I hypersensitivity, prick tests provide rapid supportive evidence for diagnosis or exclusion of IgE-mediated reactions, with high specificity and good sensitivity. *In vitro* studies are usually performed to support and quantify data obtained with prick tests, to control the evolution in time to sensitization, and to determine the clinical immunological response to immunotherapy. The histamine release test is an *in vitro* assay that is useful for further discrimination between individuals who are sensitized or not sensitized by IgE. It measures the release of histamine by peripheral blood basophils following the interaction of haptens with IgE antibodies bound to cellular membrane receptors (7).

In this particular case, our *in vivo* and *in vitro* data confirmed the presence of IgE-mediated hypersensitivity to both omeprazole and fluoxetine. The two compounds are not structurally related, so it is unlikely that the concomitant allergy resulted from a cross-reaction. Patch testing also confirmed the existence of type IV hypersensitivity to omeprazole in this patient.

The patient's clinical course, with the disappearance of skin symptoms following avoidance of further exposure to both allergens, confirmed the role of occupational exposures in his disease. This is the first reported case of occupational sensitivity to fluoxetine, as well as the first of concomitant occupational allergy to both omeprazole and fluoxetine. Our data indicate the importance of carefully analysing the occupational exposure histories of patients with suspected type I or type IV hypersensitivity to allergens, to determine whether work exposure plays a causal role.

References

- 1 Heron R J L, Pickering F C. Health effects of exposure to active pharmaceutical ingredients (APIs). *Occup Med (Lond)* 2003; **53**: 357–362.
- 2 Meding B. Contact allergy to omeprazole. *Contact Dermatitis* 1986; **15**: 36–37.
- 3 Conde-Salazar L, Blancas Espinosa R, Pérez Hortet C. Occupational airborne contact dermatitis from omeprazole. *Contact Dermatitis* 2007; **56**: 44–46.
- 4 Conde-Salazar L, Vargas E, Valks R. Dermatitis alérgica aerotransportada en la industria químico-farmacéutica. *Actas Dermosifiliogr* 2004; **95**: 429–35.
- 5 Confino-Cohen R, Goldberg A. Anaphylaxis to omeprazole: diagnosis and desensitization protocol. *Ann Allergy Asthma Immunol* 2006; **96**: 33–36.
- 6 Beer K, Albertini J, Medenica M, Busbey S. Fluoxetine-induced hypersensitivity. *Arch Dermatol* 1994; **130**: 803–804.
- 7 Mayorga C, Sanz M L, Gamboa P M et al. *In vitro* diagnosis of immediate allergic reactions to drugs: an update. *J Investig Allergol Clin Immunol* 2010; **20**: 103–109.