

LETTER TO THE EDITOR

Anaphylactic Reaction to Omeprazole

TO THE EDITOR: Omeprazole is a proton pump inhibitor (PPI) with an excellent therapeutic index. Adverse events are uncommon, and anaphylactic reactions have rarely been described (1). We present a patient with anaphylaxis to omeprazole. A 38-yr-old woman was referred to our department with itching of the palms, facial angioedema, edema of eyelids and nose, nausea, generalized urticaria, bronchospasm, and dizziness and collapse 15 min after having taken an omeprazole capsule (Losec, 20 mg; AstraZeneca, Sweden) for peptic ulcer. No other drugs had been administered during the previous 12 h. She received epinephrine, dimetindene, hydrocortisone, and salbutamol nebulizers. In the past, she had had several courses of omeprazole, with the last one being 6 months before. She had no history of atopy.

Three months later, specific allergy tests were performed. Skin prick tests (SPTs) with common inhalant, food allergens, and other imidazole derivatives (ketoconazole, metronidazole) were negative. The skin prick and intradermal tests with proton inhibitor pumps (PPIs) were positive only to omeprazole and negative to others (Table 1). Five normal controls were tested negative to all substances.

The serum samples were sent to the laboratory of Phadia (Uppsala, Sweden) and tested for immunoglobulin E (IgE) antibodies against omeprazole with experimental prototype reagents. Two couplings were made (2-benzimidazolepropionic acid and 4-methoxy-3,5-dimethyl-2-pyridinemethanol). The tests did not confirm the presence of IgE antibodies.

The challenge test with omeprazole was not carried out for ethical reasons. Subsequently, a single-blind challenge with lansoprazole and rabeprazole showed no reactions.

Our patient experienced an anaphylactic reaction to omeprazole, as suggested by the history and the positive skin tests. We did not detect other possible causes of anaphylaxis such as food, drugs, insect sting, or capsule shell (2).

SPTs with PPIs proved to be the only accurate method to confirm IgE-mediated hypersensitivity. The literature has shown that SPT with PPIs seems to be a simple, accurate, and uneventful method of identification of offending agents and is quite helpful with the problems of cross-reactivity among PPIs (1, 3, 4), except for cases reported by Pimiento and Kamann (5, 6).

The serum-specific IgE levels could not be measured *in vitro* by radioallergosorbent test. Only Camboa *et al.* (7) reported a case confirming the existence of specific IgE to omeprazole using an *in vitro* method of basophil activation test (flow cytometric cellular allergic stimulation tests [FAST]).

The majority of the reports of anaphylactic reactions demonstrate the presence of cross-reactivity for the whole group, based on skin test sensitivity (Table 2) (1, 3, 5, 8–10). In our case, the patient was sensitized only to omeprazole according to skin test reactivity and had negative oral challenge test to lansoprazole and rabeprazole. Our results are in accordance with some studies in the literature. (4, 11, 12)

The desensitization to omeprazole may be an option only for patients with positive SPT to all commercially available PPI forms, but is not the treatment of choice, as suggested by Confin-Cohen *et al.* (1). In the literature, there are several case reports on anaphylaxis to PPIs, but they lack data on cross-reactivity (13–19).

In cases of suspected PPI hypersensitivity, challenge tests are not usually recommended to confirm the diagnosis because SPTs proved to be an effective tool for the identification of the offending agent in all cases but two (5, 6). In our

Table 1. Skin Tests Results With Proton Pump Inhibitors

Agent	Skin Prick Test	Intradermal Test	Intradermal Test
Omeprazole (IV)	4 mg/mL	0.004 mg/mL	0.04 mg/mL
• Losec	8 × 10 mm	6 × 5 mm	8 × 9 mm
• Lordin	7 × 9 mm	7 × 4 mm	6 × 8 mm
• Penrazol	8 × 9 mm	5 × 6 mm	7 × 8 mm
Omeprazole (caps)	20 mg/mL	ND	ND
• Losec	6 × 8 mm		
• Lordin	7 × 7 mm		
• Penrazol	8 × 5 mm		
Lansoprazole (caps 30 mg/mL)	Negative	ND	ND
Pantoprazole (tab 40 mg/mL)	Negative	ND	ND
Rabeprazole (tab 10 mg/mL)	Negative	ND	ND
Esomeprazole (tab 20 mg/mL)	Negative	ND	ND
Histamine 1 mg/mL	4 × 5 mm	ND	ND
Histamine 0.1 mg/mL	ND	ND	8 × 10 mm

NR = not reacted; ND = not been done.

Table 2. Literature on Allergy to PPIs

Author	Offending Drug	Cross-Reactivity	Age	Sex	SPT	ID	Challenge
Galindo (9)	Omeprazole	Lansoprazole	35	Male	Omeprazole (–)	Omeprazole (+) Lansoprazole (+)	ND
Kaatz (13)	Pantoprazole (no allergy)	No detected	45	Female	Pantoprazole (–)	ND	Pantoprazole (+)
Richardi (14)	Pantoprazole	ND	41	Female	ND	ND	ND
Richardi (14)	Pantoprazole	ND	38	Male	ND	ND	ND
Cohen (1)	Omeprazole	Pantoprazole	44	Male	Omeprazole (+) Pantoprazole (+)	Omeprazole (+) Pantoprazole (+)	ND but desensitization
Ottervanger (15)	Omeprazole	ND	47	Male	Omeprazole (+)	ND	ND
Haeney (2)	Omeprazole capsule shell	ND	44	Male	ND	ND	ND
Gonzalez (3)	Omeprazole	Lansoprazole, Pantoprazole	40	Female	Omeprazole (+) Pantoprazole (+) Lansoprazole (+)	ND	Lansoprazole (+)
Gamboa (7)	Omeprazole- fast test positive	ND	75	Male	Omeprazole (+)	ND	ND
Zallo (10)	Omeprazole	Pantoprazole Lansoprazole	24	Female	Omeprazole (–) Pantoprazole (–) Lansoprazole (–)	Omeprazole (+) Pantoprazole (+) Lansoprazole (+)	ND
Pimiento (5)	Lansoprazole	Rabeprazole	24	Female	Lansoprazole (+) Rabeprazole (–) Omeprazole (–) Pantoprazole (–)	Omeprazole (–) Pantoprazole (–)	Lansoprazole (+) Rabeprazole (+) Omeprazole (–) Pantoprazole (–)
Roldan (16)	Lansoprazole	ND	34	Male	ND	ND	ND
Porcel (4)	Lansoprazole	None	42	Female	Lansoprazole (+) Rabeprazole (–) Omeprazole (–) Pantoprazole (–)	Lansoprazole (+) Rabeprazole (–) Omeprazole (–) Pantoprazole (–)	Omeprazole (–) Pantoprazole (–) Esoprazole (–)
Natsch (8, 14)	Omeprazole Lansoprazole	ND	54	Female	ND	ND	ND
Natsch (8)	Pantoprazole	ND	61	Male	ND	ND	ND
Fardet (11)	Pantoprazole	ND	42	Male	ND	ND	Pantoprazole (+) Lansoprazole (–)
Kollmeier (17)	Pantoprazole	ND	47	Male	ND	Pantoprazole (+)	ND
Bowlby (18)	Omeprazole	ND	34	Female	ND	ND	Omeprazole (+)
Dermikan (12)	Lansoprazole	None	54	Female	Lansoprazole (+) Rabeprazole (–) Omeprazole (–) Pantoprazole (–)	ND	Omeprazole (–)
Kamann (6)	Omeprazole	ND	53	Female	Omeprazole (–)	ND	Omeprazole (+)
Gratacos (19)	Pantoprazole	ND	70	Male	ND	ND	ND

ND = not been done.

case, a provocation test was performed for both lansoprazole and rabeprazole in order to detect an alternative drug and assess the sensitivity of SPT with these drugs. PPIs are a rare cause of anaphylaxis, but health-care professionals need to be aware of this possibility. The cross-reactivity of the whole group should not be assumed and a complete study should be carried out.

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