



Case Report

Lessons from two cases of anaphylaxis to proton pump inhibitors

S.-W. Choi* MD, J.-M. Han* MD, Y.-J. Bae† MD, Y. S. Lee† MD, Y. S. Cho† MD PhD, H.-B. Moon† MD PhD and T.-B. Kim† MD PhD

*Department of Internal Medicine, and †Division of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

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SUMMARY

What is known and Objective: Proton pump inhibitors (PPIs), which are widely used for the treatment of peptic ulcers and gastroesophageal diseases, reduce both basal and stimulated gastric acid secretion by inhibiting the parietal cell enzyme H(+)-K(+)-adenosine triphosphatase. There have been several reports of hypersensitivity reactions to PPIs but anaphylaxis is very rare. We report on two cases of anaphylaxis to PPIs.

Case summary: Our two interesting and instructive cases of anaphylaxis to PPIs relate to the orally disintegrating form of lansoprazole and omeprazole. The first patient had taken esomeprazole 20 mg/day for 1 month without any side effects before experiencing anaphylaxis to lansoprazole. To our knowledge, this is the first report of anaphylaxis to the orally disintegrating form of lansoprazole. In the second case, the patient was misdiagnosed with penicillin allergy which she suffered from earlier.

What is new and Conclusion: Physicians need to be more aware of the possibility of hypersensitivity to PPIs.

WHAT IS KNOWN AND OBJECTIVE

Proton pump inhibitors (PPIs), which are widely used for the treatment of peptic ulcers and gastroesophageal diseases, reduce both basal and stimulated gastric acid secretion by inhibiting the parietal cell enzyme H(+)-K(+)-adenosine triphosphatase. Combinations of PPIs and antibiotics are often prescribed to eradicate *Helicobacter pylori* and to prevent gastropathy induced by non-steroidal anti-inflammatory drugs. To date, there have been several reports of type I hypersensitivity reactions to PPIs, which were urticaria, angioedema and anaphylaxis.^{1–4} Here, we present two patients with anaphylaxis to PPIs, one each to lansoprazole and omeprazole.

DETAILS OF THE CASES

Case 1: A 74-year-old woman visited the emergency room (ER) complaining of dizziness, dyspnoea and generalized skin rash after taking the orally disintegrating form of lansoprazole. She

had a history of diabetes and liver cirrhosis caused by hepatitis B virus. Beginning 1 month earlier, she had taken esomeprazole and mosapride for gastroesophageal reflux disease without any side effects. Because her symptoms persisted, however, her physician switched her from esomeprazole to the orally disintegrating form of lansoprazole. Immediately after taking a lansoprazole tablet, she developed a tingling sensation on her tongue, lips and mouth, followed 10 min later by shortness of breath, tightness in her throat and dizziness. When she arrived at the ER, her blood pressure was 78/41 mmHg and skin rash and swelling were apparent on her face, neck and chest. She recovered after the administration of two injections of intramuscular epinephrine and intravenous pheniramine and hydrocortisone.

Case 2: A 49-year-old woman was referred to the allergy clinic for the evaluation of her previous anaphylactic reactions. Two years earlier, she experienced anaphylaxis after taking clarithromycin, amoxicillin and omeprazole for *H. pylori* eradication. At that time, she developed generalized urticaria, facial angioedema and dyspnoea. A physician informed her that those reactions might be induced by penicillin. She experienced a second anaphylactic reaction after taking an aluminium-based antacid, itopride and omeprazole for dyspepsia. The results of skin prick and intradermal tests for allergy to penicillin at our allergy clinic were negative. We suspected that omeprazole was the culprit drug and performed an oral provocation test with this agent. Thirty minutes after taking 10 mg omeprazole, she developed urticaria with an itching sensation over both lower extremities, periorbital swelling, facial flushing, sweating and dizziness. Her blood pressure decreased to 90/60 mmHg, and her pulse rate was 100 beats/min. She recovered after the administration of systemic methylprednisolone and antihistamine (Table 1).

Our two patients developed anaphylaxis to lansoprazole and omeprazole, respectively. These reactions were likely due to IgE-mediated hypersensitivity because they occurred immediately after the ingestion of the culprit drug. The first patient had taken esomeprazole 20 mg/day for 1 month without any side effects before experiencing anaphylaxis to orally disintegrating lansoprazole. Orally disintegrating drugs are likely absorbed more rapidly than drugs absorbed in the intestine. It is unusual, however, for individuals to have an anaphylactic reaction to lansoprazole, but not to esomeprazole. Several patients with hypersensitivity reactions to lansoprazole have been described,^{3,5,6} as well as those with cross-reactivity to rabeprazole.^{5,7} However, patients hypersensitive to lansoprazole showed no cross-reactivity to omeprazole or pantoprazole. The results of

Correspondence: T.-B. Kim, MD, PhD, Division of Allergy and Clinical Immunology, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Pungnap-2dong, Songpa-gu, Seoul 138-736, Korea. Tel.: 82-2-3010-3280; fax: 82-2-3010-6969; e-mail: allergy@medimail.co.kr

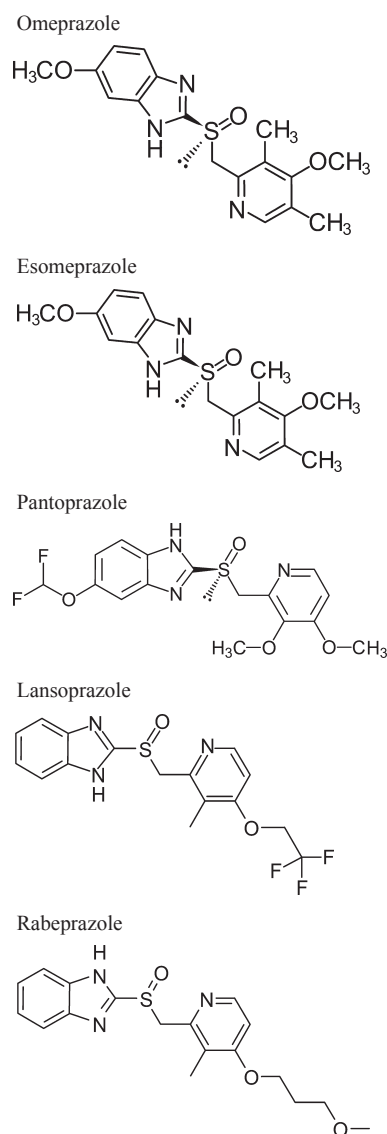
Table 1. Results of omeprazole oral provocation tests

Dosage of drug	Time	Blood pressure (mmHg)	Heart rate (beats/min)	Physical findings
Baseline		106/59	82	
10 mg	30 min	126/79	94	Itching sense on both legs
20 mg	30 min	114/62	79	Urticaria on both hands and legs, eyelid mild swelling and facial flushing
	1 h	90/60	100	Whole-body urticaria and facial swelling, sweating and dizziness
	2 h	120/80	80	Improved after the administration of antihistamine and corticosteroid

skin prick tests and oral challenge tests have suggested cross-reactivities among different PPIs.^{3,7,8} These cross-reactivities may be associated with the subtle differences in the molecular structure of the PPIs. PPIs are modified benzimidazoles with a pyridine ring, which differ in substitutions on both rings. Omeprazole, esomeprazole and pantoprazole are structurally similar, in that their benzimidazole rings have a methoxy and a difluoromethoxy chain. In contrast, lansoprazole and rabeprazole are structurally similar in that neither has a substitution in that ring (Fig. 1).^{2,7}

However, our first case showed that despite the molecular differences, physicians should be cautious and not assume that there is no cross-reactivity between omeprazole and lansoprazole. In addition, because our first patient was tolerant to esomeprazole and had not previously taken lansoprazole, she may have become sensitized to esomeprazole, followed by a severe reaction to lansoprazole. Unfortunately, we were unable to determine the cross-reactivity among the other PPIs because she refused to undergo skin prick or oral challenge tests. We were interested in determining whether this patient is still tolerant to esomeprazole after the development of anaphylaxis to lansoprazole.

Our second patient was confirmed as having omeprazole-induced anaphylaxis by an oral provocation test. Indeed, the physician who treated her first anaphylaxis episode suspected penicillin as the culprit drug instead of omeprazole. Although anaphylaxis to penicillin is more common, physicians should consider the possibility of anaphylaxis to PPIs, despite their low incidence.

**Fig. 1.** The structures of various proton pump inhibitors.

WHAT IS NEW AND CONCLUSION

Physicians need to be more aware of the possibility of hypersensitivity to PPIs and should explain the risk of anaphylaxis to their patients. Nevertheless, physicians do not need to hesitate to prescribe PPIs, because the reactions described are serious but very rare.

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