

Anaphylaxis to proton pump inhibitors

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SUMMARY

Proton pump inhibitors (PPI) are widely used for the treatment of peptic ulcer, but cases of anaphylactic reactions have rarely been described. We present a patient who experienced an episode of urticaria 30 minutes after oral intake of an omeprazole capsule.

Skin prick tests to omeprazole, pantoprazole and lansoprazole were positive. Challenge test with lansoprazole was carried out and within 45 minutes the patient developed urticaria, facial edema, vomiting, and hypotension. Oral challenge with other imidazole derivatives (ketoconazole, cimetidine, metronidazole) were carried out with good tolerance.

Serum tryptase levels determined 3 hours after the adverse reaction to lansoprazole were elevated. Specific IgE to PPI were not detected by an enzyme-linked immunosorbent assay technique.

The clinical findings, positive skin prick test to PPI and elevated serum tryptase levels suggest that an IgE-mediated mechanism was implicated in the reactions to both omeprazole and lansoprazole. Skin prick tests may be a useful tool for detecting patients sensitized to PPI.

An experimental protocol was used to detect specific IgE antibodies against PPI, which may explain RAST negativity.

The previous findings suggest that cross-reactivity between PPI exists, but not with other imidazoles.

Key words: Anaphylaxis. Proton pump inhibitors. Omeprazole. Lansoprazole. Pantoprazole. Cross reactivity. Imidazoles.

peptic ulcer. Both these drugs are benzimidazole derivatives and are structurally and pharmacologically related (1).

A 40-year-old woman was referred to our unit because she had experienced an episode of urticaria and facial edema, 30 minutes after oral intake of omeprazole (40 mg) for dyspepsia one year previously. She had previously taken lansoprazole with good tolerance. The patient had no personal or family history of atopic disease, or other drug sensitivity. At the time of the reactions, she was not taking any concomitant therapy.

ALLERGOLOGIC STUDY

Skin prick tests with common inhalant, food, latex, and *Anisakis simple* × were negative. Skin prick tests with omeprazole (4 mg/ml), pantoprazole (4 mg/ml) and lansoprazole (3 mg/ml) diluted in saline serum were positive (wheal 8 × 10 mm and 7 × 6 mm respectively with erythema). The lansoprazole wheal was 3 × 3 mm. Skin prick tests with the previous drugs were negative in 10 healthy controls. Total IgE was 53 UI/ml. No specific IgE antibodies to PPI were detected using an enzyme-linked immunosorbent assay technique.

The patient's written informed consent was obtained and challenge tests with other imidazole derivatives was carried out: cimetidine, metronidazole, and ketoconazole were administered in increasing amounts until therapeutic dose, with good tolerance. Challenge with lansoprazole was carried out and 30 minutes after oral intake of 15 mg the patient developed generalized itching, facial edema, vomiting and hypotension. The clinical picture resolved within 90 minutes after treatment with adrenaline, methylprednisolone, chlorpheniramine and ringer's lactate. Serum tryptase levels were determined 3 hours later and again 15 days after the adverse re-

The proton pump inhibitors (PPI) omeprazole and lansoprazole are extensively used in the treatment of

action to lansoprazole by radioimmunoassay (tryptase RIACT Pharmacia) and measured 4 and 0.8 U/l respectively.

DISCUSSION

We present a patient who experienced an episode of urticaria and angioedema after oral intake of omeprazole and an episode of anaphylactic shock to lansoprazole.

The clinical findings, positive skin prick test to PPI and elevated serum tryptase levels suggest that an IgE-mediated mechanism was involved in both reactions. An experimental protocol was used to detect specific IgE antibodies against PPI, which could explain RAST negativity.

To date anaphylaxis to PPI has rarely been described. Galindo et al (2). and Ottenwanger (3) reported patients who developed anaphylaxis to omeprazole. In both patients, skin prick tests with PPI were positive. Natch (4) reported two patients with anaphylactic reactions to omeprazole, lansoprazole and pantoprazole.

The adverse reactions to omeprazole and lansoprazole experienced by our patient, and the positivity of skin prick tests with PPI suggests cross-reactivity between these drugs, as others authors have suggested (4). Skin prick tests may be a useful tool for detecting patients sensitized to PPI.

Cross-reactivity among imidazoles has previously been postulated. Marren and Powell (5) found 34 reports of cross reactions between imidazoles. The nature of cross reactions, especially of contact dermatitis reactions, seems to be unpredictable.

Our patient tolerated other imidazoles (cimetidine, ketoconazole, metronidazole). Thus, in this case, cross-reactivity was restricted to PPI, although further studies are needed to provide more precise information.

PPIs are extensively used and reported experience indicates that they are well tolerated. However, anaphylactic reactions can sometimes be observed, and cross-reactivity between the different molecules exists.

RESUMEN

Los inhibidores de la bomba de protones (IBP) se utilizan habitualmente para el tratamiento de la úlcera péptica, pero rara vez se han descrito casos de reacciones anafilácticas. Presentamos a una paciente que experimentó un episodio de urticaria 30 min

después de la ingestión oral de una cápsula de omeprazol.

Las pruebas cutáneas con omeprazol, pantoprazol y lansoprazol fueron positivas. Se realizó una prueba de provocación con lansoprazol y la paciente presentó urticaria, edema facial, vómitos e hipotensión en un plazo de 45 min. Se efectuó una provocación oral con otros derivados imidazólicos (ketoconazol, cimetidina, metronidazol), que fueron bien tolerados. Las concentraciones séricas de triptasa, obtenidas 3 h después de la reacción adversa al lansoprazol, presentaban valores elevados. No se detectó IgE específica frente IBP mediante una técnica de ELISA.

Los datos clínicos, la positividad de la prueba cutánea con IBP y la elevación de las concentraciones séricas de triptasa indican que estaba implicado un mecanismo mediado por IgE a las reacciones al omeprazol y lansoprazol. Las pruebas de punción cutánea fueron un instrumento útil para detectar pacientes sensibilizados a los IBP. El hecho de que se utilizase un protocolo experimental para detectar anticuerpos IgE específicos contra la bomba de protones podría explicar la negatividad de RAST.

Estos resultados indican que existe reactividad cruzada entre los IBP, pero no con otros imidazoles.

Palabras clave: Anafilaxia. Inhibidores de la bomba de protones. Omeprazol. Lansoprazol. Pantoprazol. Reactividad cruzada. Imidazoles.

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