Austin Journal of Allergy

Austin Publishing Group

Open Access Full Text Article

Case Report

Non Immediate-type Hypersensitivity Reactions to Proton Pump Inhibitors

Giuliana Zisa[1]*, Luisa Bommarito[1], Francesca Riccobono[1], Joseph Scibilia[2] and Maurizio Galimberti[3]

[1]Allergology and Immunology Unit, Novara Hospital, Italy
[2]Allergy and Immunology, Ospedale Niguarda, Milan, Italy
[3]Allergy consultant Fleming Research, Novara, Italy

***Corresponding author:** Giuliana Zisa, Allergology and Immunology Unit, Novara Hospital, Italy

Received: July 28, 2014; **Accepted:** August 16, 2014; **Published:** August 18, 2014

Keywords

Hypersensitivity; Proton pump inhibitors; Skin tests

Proton pump inhibitors (PPIs), commonly used for gastrointestinal diseases, are associated with a low incidence of adverse reactions [1-5].

We present two patients with non immediate reactions to such drugs diagnosed in our allergy clinic during 2011 to 2012.

Written informed consent was obtained from each patient before the performance of skin and provocation tests. Cutaneous sensitivity to esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole was evaluated by skin tests (prick and intradermal tests) for esomeprazole, omeprazole and pantoprazole at a concentration of 40 mg/ml, for rabeprazole 20 mg/ml, lansoprazole 15 mg/ml (at 1:1 for prick test and at 1:1000, 1:100 and 1:10 dilutions for intradermal tests). Histamine and saline were used as positive and negative controls, respectively. Skin tests with tested drugs were negative in five control subjects. A safe alternative drug was found for both patients after a negative single-blind, placebo-controlled oral provocation test with a proton pump inhibitor that displayed negative results in skin tests.

Oral provocation test started with a single dose of talc as placebo and then increasing doses (one-quarter and three-quarter of a therapeutic dose) of PPI in identical opaque capsules were given at 1-hour intervals. Patients were kept under observation for 2 hours after the last provocation dose.

Characteristics of reactions and results of skin tests and provocation test are described in table 1.

The first patient is a 49 years old non atopic man with ulcerative proctitis, gastroesophageal reflux disease and atrophic gastritis with intestinal metaplasia. He was in treatment with ranitidine 300 mg/die and mesalazine 800 mg twice a day. In june 2008 and in january 2009 he developed generalized pruritus and urticaria with tightness in the throat and difficulty in swallowing during five days treatment with esomeprazole 40 mg once daily. After the first reaction he was treated with methylprednisolone and dexchlorpheniramine. In the second episode his symptoms spontaneously resolved within 24 hours after interruption of the treatment. In august 2011 cutaneous sensitivity to esomeprazole, lansoprazole, omeprazole, pantoprazole and rabeprazole was evaluated by skin tests (prick and intradermal tests). The patient presented a negative response to all PPIs tested at 20 minutes reading while presented a positive response to pantoprazole at 48 hours reading. A single-blind, placebo-controlled oral provocation test with lansoprazole 30 mg, resulted negative at skin tests, showed tolerance to the drug.

The second patient is a 51 years old atopic man with allergic rhinitis to ragweed. In January 2010 he complained eyelid angioedema after 12 hours from intake of one tablet of pantoprazole and subsequently 12 hours after the assumption of one tablet of lansoprazole. In March 2012 he was evaluated in our centre and skin prick and intradermal tests were performed with PPIs: he presented a negative response to all PPIs tested at 20 minutes reading while presented a positive response to esomeprazole and lansoprazole at 48 hours reading. He tolerated oral provocation test with rabeprazole 20 mg (skin tests were negative).

We describe two non immediate reactions to PPIs with positive response to intradermal test at 48 hours reading performed > 24 months from the reaction.

Skin tests showed the cross-reactivity with other PPIs tested and allowed to choose a safe alternative drug for both patients; the

Table 1: Characteristics of patients and results of skin tests and provocation test.

	Patient 1	Patient 2
Sex	M	M
Age	49	51
Atopy	No	Yes
Drug involved in reaction	Eso	Lanso, Panto
Ome SPT/ID*	-	-
Ome ID**	-	-
Panto SPT/ID*	-	-
Panto ID**	1:10 +; 1:100 +	-
Eso SPT/ID*	-	-
Eso ID**	-	1:10 +
Rabe SPT/ID*	-	-
Rabe ID**	-	-
Lanso SPT/ID*	-	-
Lanso ID**	-	1:10 +;1:100 +
Provocation Test	Negative with Lanso 30 mg	Negative with Rabe 20 mg

Ome: Omeprazole; Panto: Pantoprazole; Eso: Esomeprazole; Rabe: rabeprazolo; Lanso: Lansoprazole; SPT: skin prick test; ID: intradermal skin test; *SPT/ID with reading at 20 minutes; **ID with reading at 48 hours.

Citation: Zisa G, Bommarito L, Riccobono F, Scibilia J and Galimberti M. Non Immediate-type Hypersensitivity Reactions to Proton Pump Inhibitors. Austin J Allergy. 2014;1(2): 2.

alternative drug was determined after a negative single-blind, placebo-controlled oral provocation test with a negative drug skin test.

The clinical features of the reactions to PPIs described in most reports suggest an IgE-mediated mechanism, as demonstrated by immediate positive reaction to skin test [1,2,4-6]. To our knowledge this is the first report of documented intradermal test positivity at 48 hours for PPIs which may suggest a cellular-mediated mechanism. The cross-reaction pattern observed was not very clear (reaction with esomeprazole and skin test positivity for pantoprazole in the first case; reaction with pantoprazole and lansoprazole with skin test positivity for lansoprazole and esomeprazole in the second case). We did not perform patch skin testing, which has been reported to result positive in some cases of fixed drug eruption and DRESS, both induced by esomeprazole [7,8].

In consideration of the different patterns of cross-reaction within PPIs class [2,4-6], it may prove useful to evaluate the cross-reactivity of the whole group by a complete study on a large group of patients with a history of hypersensitivity reactions to at least one of these drugs.

In accordance with other reports [1,2,4-6] we emphasize the importance of skin tests and its usefulness to establish cross-reactivity between PPIs also in the diagnosis of non immediate-type hypersensitivity reactions to them.

Skin tests and oral provocation tests with PPIs are intended to find a safe alternative drug for the treatment of gastrointestinal diseases.

References

1. Bose S, Guyer A, Long A, Banerji A. Evaluation and management of hypersensitivity to proton pump inhibitors. Ann Allergy Asthma Immunol. 2013; 111: 452-457.
2. Kepil Özdemir S, Yılmaz I, Aydin Ö, Büyüköztürk S, Gelincik A, et al. Immediate-type hypersensitivity reactions to proton pump inhibitors: usefulness of skin tests in the diagnosis and assessment of cross-reactivity. Allergy 2013; 68: 1008-1014.
3. Chang Y-S. Hypersensitivity reactions to proton pump inhibitors. Curr Opin Allergy Clin Immunol 2012; 12: 348-353.
4. Demirkan K, Bozkurt B, Karakaya G, Kalyoncu AF. Anaphylactic reaction to drugs commonly used for gastrointestinal system diseases: 3 case reports and review of the literature. J Investig Allergol Clin Immunol 2006; 16: 203-209.
5. Sobrevia Elfau MT, Garcés Sotillos M, Ferrer Clavería L, Segura Arazuri N, Monzón Ballarin S, et al. Study of cross-reactivity between proton pump inhibitors. J Investig Allergol Clin Immunol 2010; 20: 157-161.
6. Garrido Fernández S, Cumplido JA, Rábano A, Martínez D, Blanco C, et al. Allergy to proton pump inhibitors: diagnosis and assessment of cross-reactivity. J investing Allergol Clin Immunol 2008; 18: 140-141.
7. Morais P, Baudrier T, Mota A, Cunha AP, Cadinha S, et al. Nonpigmented fixed drug eruption induced by esomeprazole. Cutan Ocul Toxicol 2010; 29: 217-220.
8. Caboni S, Gunera-Saad N, Ktiouet-Abassi S, Berard F, Nicolas JF. Esomeprazole-induced DRESS syndrome. Studies of cross-reactivity among proton-pump inhibitor drugs. Allergy 2007; 62: 1342-1343.

Austin J Allergy - Volume 1 Issue 2 - 2014
Submit your Manuscript | www.austinpublishinggroup.com

Citation: Zisa G, Bommarito L, Riccobono F, Scibilia J and Galimberti M. Non Immediate-type Hypersensitivity Reactions to Proton Pump Inhibitors. Austin J Allergy. 2014;1(2): 2.