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CASE REPORT

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Successful Oral Desensitization to Rabeprazole: A Case Report of a Patient with Duodenal Ulcer

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ABSTRACT

We report a 26-year-old female patient who developed anaphylaxis after the use of pantoprazole and esomeprazole and was successfully desensitized with rabeprazole.

The patient, who was diagnosed with duodenal ulcer by gastroscopy, was prescribed pantoprazole 40 mg tablet for treatment. Thirty minutes after taking the first dose of pantoprazole, generalized urticaria, angioedema of the lips, abdominal pain, diarrhea, shortness of breath and hypotension (blood pressure: 80/40 mmHg) developed. No loss of consciousness developed. Since dyspeptic complaints continued, esomeprazole 40 mg tablet was prescribed to the patient 1 month later. Generalized urticaria, abdominal pain, diarrhea and dyspnea developed 40 minutes after taking the first dose of esomeprazole.

As hypersensitivity to PPIs was considered, skin tests were performed with all PPIs to detect alternative PPIs, as skin tests are safe and specific. A positive reaction was detected to all PPIs in the skin tests, so no oral provocation was performed with PPIs. Desensitization was planned because treatment with PPI was necessary and there was no alternative treatment. This patient who developed anaphylaxis with pantoprazole and esomeprazole was successfully desensitized with rabeprazole.

In conclusion, in cases of hypersensitivity to PPIs, the possibility of cross-reactivity should be kept in mind and skin tests with PPIs should be performed before performing oral provocation testing. If no alternative is found, a PPI desensitization protocol can be applied.

Keywords: Proton pump inhibitors, anaphylaxis, skin tests, cross-reactivity, desensitization

INTRODUCTION

Proton pump inhibitors (PPIs) are widely used in the treatment of gastrointestinal diseases, such as gastroesophageal reflux or peptic ulcer. PPIs are generally well tolerated medications with a low risk of side-effects (1). Hypersensitivity reactions are rarely observed, but anaphylaxis, urticaria or dyspnea have been identified in some of the reports (2,3).

Although medication is avoided in most cases when a hypersensitivity reaction develops, it may be necessary in some cases to use the drug for optimal treatment. In these cases, drug desensitization is recommended (4). Drug desensitization is defined as the induction of a temporary state of tolerance of a compound responsible for a hypersensitivity reaction. After a successful procedure, temporary tolerance develops to the drug responsible for the hypersensitivity reaction (4).

Although the frequency of hypersensitivity reactions with PPIs is gradually increasing, there is only one case in the literature in which successful desensitization with PPI (omeprazole) was performed (5). We wanted to present a patient who developed anaphylaxis after the use of pantoprazole and esomeprazole and was successfully desensitized with rabeprazole. This case can be considered important as it is only the second reported case in which desensitization was successfully performed with PPI.

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CASE PRESENTATION

A 26-year-old female patient underwent gastroscopy due to dyspeptic complaints ongoing for many years. On the diagnosis of duodenal ulcer after gastroscopy, pantoprazole 40 mg tablet was prescribed. Thirty minutes after taking the first dose of pantoprazole, the patient developed widespread urticaria and pruritus throughout the body, angioedema on the lips, abdominal pain, diarrhea, shortness of breath, and hypotension (blood pressure: 80/40 mmHg). There was no loss of consciousness. From the clinical findings, anaphylaxis was diagnosed, and intramuscular epinephrine, intravenous methylprednisolone and phenyramine were administered and a 0.9% isotonic sodium chloride infusion was initiated. After about 3 hours, the clinical picture improved.

Since dyspeptic complaints continued, esomeprazole 40 mg tablet was prescribed to the patient 1 month later. Forty minutes after taking the first dose, widespread urticaria and pruritus, abdominal pain, diarrhea, and shortness of breath were observed. Blood pressure was measured as 100/60 mmHg, but no loss of consciousness was reported. Intravenous methylprednisolone and phenyramine were applied and a 0.9% isotonic sodium chloride infusion was initiated. Adrenaline was not administered. The clinical picture improved after 2 hours.

Skin Tests

Hypersensitivity reaction with both pantoprazole and esomeprazole suggested cross-reactivity, and skin tests with all PPIs were planned.

Skin prick tests (SPT) were performed with undiluted commercial oral preparations of esomeprazole tablet (40 mg), rabeprazole tablet (20 mg), pantoprazole tablet (40 mg), lansoprazole capsule (30 mg), and omeprazole capsule (20 mg). Histamine (10 mg/mL) and saline 0.9% were used for positive and negative controls, respectively. For SPT, after grinding the capsules and tablets of the medications in commercial form, the solution was prepared by adding 1 mL of 0.9% NaCl. SPTs were performed on the forearm and read after 20 minutes. The result was considered positive if there was a reaction of swelling approximately 3 mm larger than the negative control and surrounded by erythema. A positive reaction was observed against all PPIs in the skin tests (Table I).

A control group of 10 healthy volunteers underwent skin prick testing with the same protocol to confirm the positive response and exclude an irritant response, and the results were negative in all the control subjects.

Table I: Skin test results with proton pump inhibitors.

	SPT	
	Wheal / Flare Diameter, mm	
Drugs	**Before desensitization**	**After desensitization**
Omeprazole (20 mg/mL)	10x10 / 40x32	(-) / 4x3
Pantoprazole (40 mg/mL)	12x12 / 25x20	(-) / 3x2
Esomeprazole (40 mg/mL)	14x10 / 35x25	(-) / 4x4
Rabeprazole (20 mg/mL)	12x12 / 40x30	(-) / (-)
Lansoprazole (30 mg/mL)	9x8 / 20x18	(-) / 3x2
Histamine (10 mg/mL)	8x8 / 14x12	10x10 / 42x30
Negative control	(-)	(-)

SPT: Skin prick test, **(-):** Negative.

Desensitization

The desensitization protocol was carried out in the allergy unit of the hospital under the supervision of nurses and doctors, after obtaining the consent of the patient. Resuscitation equipment was made available during the process.

Rabeprazole 20 mg tablet was dissolved in 0.9% NaCl solution by creating serial 10-fold dilutions. In oral desensitization, the initial dose was 0.01 mg and the doses, which were increased twofold 12 times, were administered at 30-minutes interval (Table II). The patient tolerated the procedure with no problems.

Table II: Desensitization protocol with rabeprazole.

Step	Dilution	Time (min)	Dose, ml	Dose, mg	Cumulative dose, mg
1	1/1000	30	0.5 ml	0.01mg	0.01 mg
2	1/1000	30	1 ml	0.02mg	0.03 mg
3	1/1000	30	2 ml	0.04 mg	0.07 mg
4	1/1000	30	4 ml	0.08 mg	0.15 mg
5	1/100	30	0.5 ml	0.1 mg	0.25 mg
6	1/100	30	1 ml	0.2 mg	0.45 mg
7	1/100	30	2 ml	0.4 mg	0.85 mg
8	1/100	30	4 ml	0.8 mg	1.65 mg
9	1/10	30	0.5 ml	1 mg	2.65 mg
10	1/10	30	1.5 ml	3 mg	5.65 mg
11	1/10	30	3 ml	6 mg	11.65 mg
12	1/10	30	6 ml	12 mg	23.65 mg

In the skin tests performed with all PPIs 72 hours after the completion of desensitization, the wheal dimensions were significantly reduced (Table II). The treatment of the patient was completed without any problems in 6 weeks.

DISCUSSION

This desensitization protocol applied as described here can be applied in cases where there is a hypersensitivity reaction with PPIs and alternative treatments are not available or are less effective, taking the risk/benefit ratio into consideration.

PPIs are commonly prescribed drugs and are quite safe. However, hypersensitivity reactions may occur and anaphylaxis is the most common clinical picture in patients with immediate-type hypersensitivity reactions to PPIs (6,7). Clinicians should be aware that these medications may be responsible for the anaphylactic reaction (8).

Hypersensitivity reactions to PPIs are often diff-icult to diagnose. As PPIs are often taken with other medications and before meals, they are rarely considered as the possible triggers of the reaction, and other drugs or foods are considered more likely causes (9). In cases where hypersensitivity to PPIs is suspected, skin tests are simple, safe and highly specific (6). Skin tests have been shown to have high positive predictive value and specificity in hypersensitivity reactions with PPIs (3,10). At the same time, skin tests are very important in revealing the problem of cross-reactivity between PPIs (4,7). Cross-reactivity exists among the various PPIs, although the patterns of cross-reactivity are variable (2,11). PPIs have a benzimidazole ring and a pyridine ring. Four general patterns of cross-reactivity, which could be explained by the chemical structure of PPIs, have been identified based on the published articles: hypersensitivity to all PPIs, lansoprazole-rabeprazole hypersensitivity, omeprazole-esomeprazole-pantoprazole hypersensitivity, and hypersensitivity with a selective single PPI (2,10,12). In the current case, skin tests were applied while looking for an alternative PPI for the patient, and the result was positive with all PPIs. Positive skin tests are also important to avoid oral challenge testing (7). Based on the SPT data, confirmatory oral provocation testing is not applied to patients with skin test positivity to the PPI responsible or alternative PPIs.

PPI therapy is recommended for symptomatic patients with a history of duodenal ulcer. However, as in the current case, when there is cross-reaction within the whole group, when alternative medicine cannot be found, and in cases where the indication for treatment outweighs the risks of the procedure, a desensitization protocol with PPI is recommended (4,7). There is only one case in the literature in which desensitization was performed with PPI. That case was a patient who developed anaphylaxis with omeprazole and cross-reacted with pantoprazole, and was then successfully desensitized with omeprazole (5). In the current case, cross-reactivity was detected between all PPIs. On the recommendation of the gastroenterology clinic to treat the patient with rabeprazole, successful desensitization was performed with rabeprazole.

CONCLUSION

In case of hypersensitivity to PPIs, the possibility of cross-reactivity should be kept in mind and skin tests with PPIs should be performed before conducting oral provocation testing. If no alternative is found, a PPI desensitization protocol can be applied.

Conflict of Interest

The authors declare that there is no conflict of interest.

Authorship Contributions

Concept: **Eray Yıldız, Fatih Çölkesen, Şevket Arslan,** Design: **Gökhan Aytekin, Recep Evcen, Filiz Sadi Aykan,** Data collection or processing: **Recep Evcen, Filiz Sadi Aykan, Mehmet Kılınç,** Analysis or Interpretation: **Eray Yıldız, Gökhan Aytekin, Mehmet Kılınç, Şevket Arslan,** Literature search: **Recep Evcen, Filiz Sadi Aykan, Mehmet Kılınç,** Writing: **Eray Yıldız, Fatih Çölkesen, Gökhan Aytekin,** Approval: **Eray Yıldız, Fatih Çölkesen, Şevket Arslan.**

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