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Immediate reactions to proton pump inhibitors: Clinical findings and testing outcomes

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Abstract
Background: Proton pump inhibitors (PPIs) are identified to cause immediate hypersensitivity reactions and cross-reactivity among them. In this study, we aimed to describe the clinical features of immediate-type hypersensitivity reactions caused by PPIs, the results of drug tests performed with PPIs, and the cross-reactivity between PPIs. There are immediate hypersensitivity reactions with PPIs and there may be cross-reactivity between PPIs. In this study, we aimed to describe the clinical features of immediate-type hypersensitivity reactions caused by PPIs, the results of drug tests performed with PPIs and the cross-reactivity between PPIs.
Methods: Adult patients who described an immediate hypersensitivity reaction to PPIs between March 1, 2017 and March 1, 2023 were evaluated.
Results: Of the 47 patients included in the study, 89.4% were females, and the suspected PPI in 68% of the patients was lansoprazole. Anaphylaxis accounted for 72.3% of reactions, and the most common reaction was grade 2 (42.6%) according to Ring Messmer. Those who had two or more reactions to the same or different PPI were 51.1% of patients. A positivity rate of 43.8% was observed in the skin prick test with the suspected drug, 33.3% in the intradermal test, and 100% in the provocation test. There is varying potential for cross-reactivity among five different PPIs.
Conclusions: İmmediate hypersensitivity reactions are observed among PPIs, particularly to lansoprazole, with the majority of reactions being anaphylaxis. Multiple life-threatening reactions can be prevented by increasing awareness of allergies to PPIs. Cross-reactivities among PPIs are variable, and further studies are needed to elucidate cross-reactivity with PPIs.

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Introduction

Proton pump inhibitors (PPIs) are potent drugs that inhibit gastric acid secretion. The mechanism of action is inhibition of hydrogen–potassium adenosine triphosphatase (H+/K+-ATPase). These are widely used in the treatment of gastrointestinal diseases, such as gastroesophageal reflux and peptic ulcers, and are also often used in conjunction with other drugs to prevent gastric damage.[1] The risk of moderate adverse reactions with PPIs is considered around 1–3%.[1] Although PPIs are one of the most commonly prescribed group of drugs globally and are considered safe and effective, immediate or non-immediate/delayed hypersensitivity reactions to them may range from mild symptoms to life-threatening situations. Type 1 (immediate-type) hypersensitivity symptoms, such as urticaria, angioedema, and even life-threatening anaphylaxis, can occur with PPIs.[2,3] Limited data are available in literature regarding PPI hypersensitivity reactions, diagnostic test results, and cross-reactivity among PPIs.[4] This study aimed to evaluate the clinical features, and skin and provocation test results of immediate-type hypersensitivity reactions to PPIs and to determine their cross-reactivity.

Materials and Methods

Study population and design

Patients aged more than 18 years who had applied to the adult immunology and allergy outpatient clinic between March 1, 2017 and March 1, 2023 because of sudden hypersensitivity reactions after intake of PPI drug were included in the study. Patients who reported symptoms related to known side effects or non-immediate reactions or reactions while taking concomitant medications were excluded from the study. The study was approved by the Adana city training and research hospital, ethics committe Adana, Turkey). Demographic data of the patients (gender, age, allergic diseases, triggering drug, onset time of reaction, affected organ/system findings, and state of consciousness) were noted. Patients' reactions were graded from 1 to 4 according to the Ring-Messmer grading scale for immediate-type hypersensitivity reactions.[5] Diagnostic tests with suspected drugs and alternative drug tests were performed on those who gave informed consent. Drug skin tests were performed at least 6 weeks after the development of reactions. Patients were advised to discontinue antihistamine and antidepressant medications at least 7 days prior to skin testing and oral provocation test (OPT). To avoid affecting skin testing and OPT results, H2 receptor blockers (H2RBs), leukotriene receptor antagonists, or anti- immunoglobulin E (IgE) medications (e.g., omalizumab) were discontinued 4 weeks prior to skin testing and OPT.

Skin prick test (SPT)

Drug skin prick tests (SPTs) were performed with titrations prepared at nonirritant doses according to the recommendations of the European Network on Drug Allergy (ENDA) and the European Academy of Allergy and Clinical Immunology (EAACI) drug hypersensitivity group.[6] Histamine dihydrochloride, 10 mg/mL, was used as a positive control, and 0.9% saline was used as a negative control. SPT was applied directly using undiluted intravenous forms of pantoprazole (40 mg/mL), esomeprazole (40 mg/mL), and omeprazole (40 mg/mL). SPT was performed by crushing either capsule or tablet form of PPI, which had no injectable form, with a mortar and dissolving it in 1 mL of 0.9% NaCl. Such dilutions were prepared with rabeprazole 20-mg tablet and lansoprazole 30-mg capsule.[4] SPTs were applied to the volar forearm to be read after 20 min. A mean wheal diameter of ≥3 mm greater than the negative control at 15 min was considered positive.

Intradermal test (IDT)

Intradermal tests were performed only with injectable forms of omeprazole (40 mg/mL), esomeprazole (40 mg/mL), and pantoprazole (40 mg/mL). IDT was performed with the maximum nonirritating concentration of 4 mg/mL as mentioned in the literature.[4,7] A bleb/induration of 2–3 mm was created on the skin with 0.02–0.05 mL of injection. Wheal diameter of ≥3 mm demonstrated IDT positivity; avoid erythematous induration. IDT test was considered positive and was terminated if erythematous induration of ≥3 mm occurred in the evaluation made 15 min after the application of the test with diluted concentrations. General clinical manifestations and vital signs were monitored for up to 6 h after the test.

Drug provocation test

Drug provocation testing (DPT) was performed if SPTs for the suspected drug were negative. A single-blind, placebo-controlled OPT with a suspected PPI was performed in patients who provided informed consent after SPT. Placebo was given on day 1. On day 2, omeprazole 40 mg, pantoprazole 40 mg, and esomeprazole 40 mg were given in divided doses of 5 mg, 5 mg, 10 mg, and 20 mg; rabeprazole 5 mg, 5 mg, and 10 mg, and lansoprazole 30 mg, were given in divided doses at 30-min intervals.[8] Blood pressure, heart rate, and oxygen saturation were recorded before initiation and prior to each dose (with dose increments at every 30 min). The test result was considered positive if clinical symptoms (urticaria, angioedema, and rashes) appeared, there was a 20% increase in heart rate, compared to the patient's baseline value, or oxygen saturation decreased below 90%.

Statistical analyses

Data processing and statistical analyses were performed using Statistical Package for the Social Sciences (SPSS), version 22 (IBM Corp., Chicago, IL). Categorical variables were summarized as frequencies (n) and percentages (%), while the distribution of continuous variables was evaluated for normality using the Kolmogorov–Smirnov test. Variables that do not show a normal distribution were presented as median (min–max).

Results

The median age of 47 patients was 50 years (range 21–82 years), and 89.4% of the patients were females. A history of allergic disease was present in 31.9% of the patients. The most common reaction occurred with lansoprazole (68%), followed by pantoprazole (19.1%) and rabeprazole (10.7%). Two different PPIs that caused reactions were experienced by 12.7% of patients. PPIs that caused reactions are shown in Figure 1. In all, 72.3% of the patients described anaphylaxis, followed by urticaria (23.4%) and urticaria and angioedema (4.3%). Patients' reactions classified according to the severity of Ring–Messmer scale as grade 4, grade 3, grade 2, and grade 1 were 6.4%, 23.4%, 42.6%, and 27.7%, respectively. In all, 24 patients (51.1%) had experienced reactions with the same or different PPI for two or more times. Demographic and clinical characteristics of the patients are shown in Table 1.

In the tests performed with the suspected drug, 46.9% positivity was observed in SPT, 33.3% in IDT, and 100% in OPT. The number of patients tested with reactive drugs and who tested positive are shown in Figure 2. OPT with lansoprazole, pantoprazole, and esomeprazole yielded 100% positivity. Also, SPT with omeprazole yielded 100% positivity. Diagnostic tests and test positivity for PPIs are shown in Figure 3. No positivity was detected in SPT, IDT, and OPT performed with ranitidine and famotidine as alternative drugs.

In four of the nine patients with a reaction to pantoprazole, OPT with lansoprazole, esomeprazole, rabeprazole, and omeprazole was negative. In eight patients with a reaction to lansoprazole, DPT with omeprazole, rabeprazole, esomeprazole, and pantoprazole was negative. However, one patient tested positive for rabeprazole with OPT. Two patients with a reaction to esomeprazole underwent DPT with lansoprazole, rabeprazole, pantoprazole, and omeprazole. One patient tested positive with DPT for both rabeprazole and pantoprazole as well as omeprazole. In one patient with a reaction to rabeprazole, SPT for lansoprazole was positive, and in two patients, SPT for both rabeprazole and lansoprazole was positive. In one patient with a history of reactions for both omeprazole and lansoprazole, OPT with esomeprazole was positive (Table 2).

Table 3 shows the drugs and their proportions considered to have cross-reactivity based on test results.

Discussion

This study presents 47 patients who reported immediate reactions to PPIs, and in most cases, the use of lansoprazole was suspected to be the reactive drug. Most of the patients who reported reactions were females, and most of the immediate reaction to PPIs was anaphylaxis. The most common PPIs causing anaphylaxis vary from country to country. In Italy, esomeprazole and lansoprazole are the most common PPIs, while in Spain, omeprazole is the most common cause of anaphylaxis. In our study also, lansoprazole was found to be the most common reactive agent in Italy. The most frequently suspected drug in immediate hypersensitivity reactions with PPI was lansoprazole; this result was similar to the results of previous studies conducted in Italy.[9–11] The fact that lansoprazole is the most common agent could be due to its higher usage compared to other PPIs in Italy.[12]

In our study, 42 (89.4%) patients were females, showing a clear predominance over males. A study analyzing approximately 17.5 million adverse event reports from the Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) between 1999 and 2019 described that 62.71% of drug-induced anaphylaxis patients were women.[13] The underlying reasons for the high incidence of drug-induced hypersensitivity reactions and anaphylaxis in women are not fully elucidated.[14] However, factors such as the second X chromosome in women, cyclical hormonal changes, progesterone and oestrogen, which affect the balance of T-helper-1–T-helper-2 cells and alter the immune system's response pattern, or exposure to triggering agents

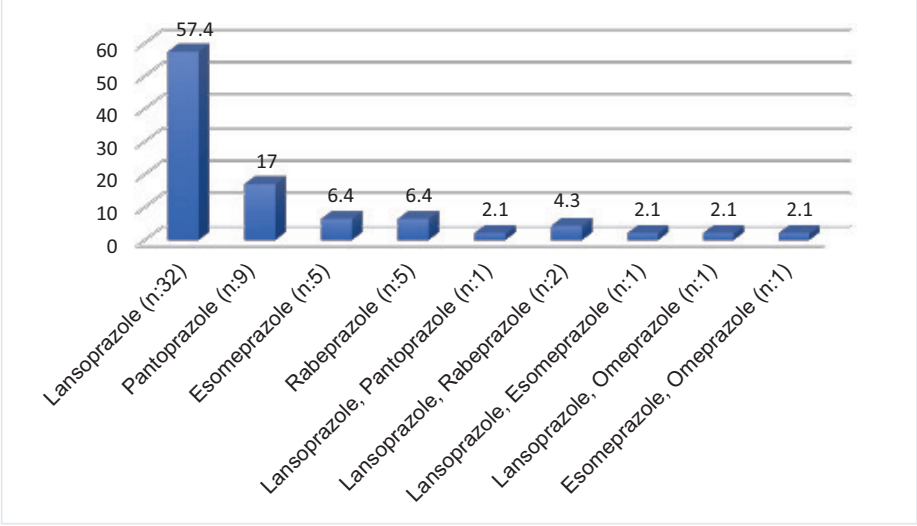

Figure 1 Proton pump inhibitors causing the reaction.

Table 1 Demographic and clinical characteristics of patients.

Patient	Age (Years)	Gender	PPI	Reaction	Grade	Duration (Minutes)	Number of reactions
1	45	M	P	Anaphylaxis	3	40	2
2	43	F	P	Urticaria	1	30	1
3	41	F	P, L	Anaphylaxis	3	5	2
4	46	F	E	Anaphylaxis	4	5	2
5	54	F	L	Anaphylaxis	2	15	2
6	44	F	L	Anaphylaxis	2	30	2
7	30	F	L	Anaphylaxis	2	30	2
8	55	F	L	Anaphylaxis	2	30	2
9	57	F	L	Anaphylaxis	3	15	2
10	63	F	P	Anaphylaxis	2	40	2
11	40	M	L	Anaphylaxis	2	30	1
12	36	F	R, L	Anaphylaxis	4	30	2
13	36	F	L	Anaphylaxis	2	30	1
14	50	F	R, L	Anaphylaxis	2	30-240	3
15	57	F	R	Anaphylaxis	4	20	1
16	52	F	E	Anaphylaxis	3	20	2
17	48	F	L, O	Anaphylaxis	2	60	3
18	38	F	E, O	Anaphylaxis	2	30	1
19	30	F	R	Anaphylaxis	3	60	1
20	82	F	L	Urticaria	1	360	1
21	38	F	L	Anaphylaxis	2	120	1
22	59	F	L	Urticaria	1	240	2
23	62	F	L	Anaphylaxis	2	10	1
24	52	F	L	Anaphylaxis	3	60	2
25	62	F	L	Anaphylaxis	2	60	1
26	54	F	L	Urticaria, angioedema	1	60	1
27	60	F	P	Urticaria	1	360-480	3
28	42	F	P	Anaphylaxis	2	60	1
29	30	M	L	Urticaria, angioedema	1	10	1
30	21	F	L	Urticaria	1	120	1
31	41	F	L	Anaphylaxis	2	20	2
32	48	F	L	Anaphylaxis	2	10-15	2
33	48	F	L	Urticaria	1	120	1
34	57	F	L	Anaphylaxis	2	30-240	2
35	55	F	L	Anaphylaxis	3	15	1
36	52	F	L	Anaphylaxis	3	10	1
37	25	F	L	Anaphylaxis	3	10	2
38	57	F	L	Anaphylaxis	3	10	2
39	54	F	P	Anaphylaxis	2	10	1
40	58	F	L	Anaphylaxis	3	30	1
41	60	F	P	Anaphylaxis	2	30	2
42	45	F	P	Urticaria	1	30	1
43	23	F	L	Urticaria	1	60	1
44	50	M	L	Anaphylaxis	2	60	1
45	60	M	R	Urticaria	1	60-120	2
46	50	F	L, E	Urticaria	1	60	3
47	48	F	E	Urticaria	1	20	1

M: male; F: female; P: pantoprazole; L: lansoprazole; R: rabeprazole; E: esomeprazole; O: omeprazole.

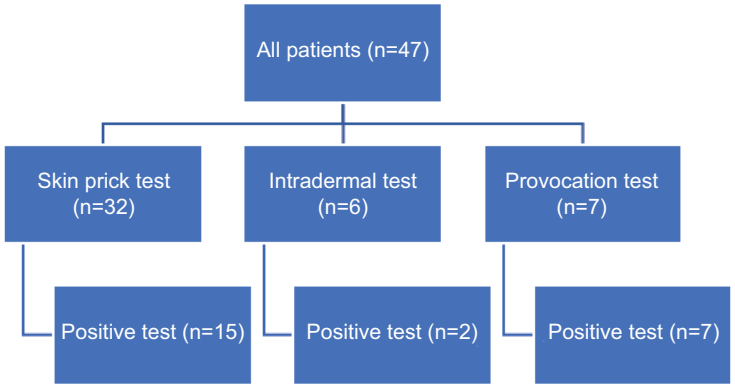

Figure 2 Number of patients tested positive with reactive drugs.

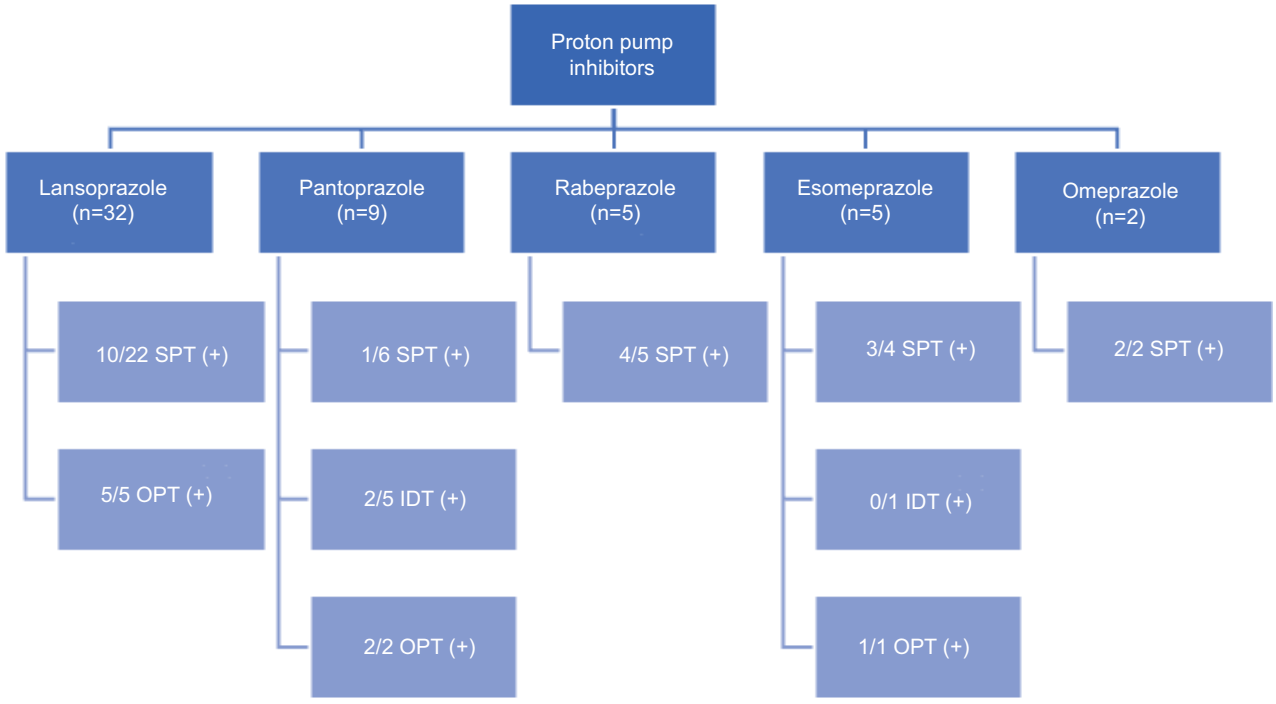

Figure 3 Diagnostic tests and test positivity for proton pump inhibitors.

Table 2 Skin test and oral provocation test (OPT) results based on the suspected drug.

Suspected drug	N	Negative SPT/OPT	Positive OPT	Positive SPT
P	9	4 patients L, E, R, O negative OPT	-	-
L	8	8 patients O, R, E, P negative OPT	1 patient R	-
E	2	-	1 patient R, P, O	-
R	3	-	-	1 patient L 2 patients R+L
O + L	1	-	1 patient E	-

P: pantoprazole; L: lansoprazole; R: rabeprazole; E: esomeprazole; O: omeprazole; SPT: skin prick test; OPT: oral provocation test.

Table 3 Possible cross-reactivity proportions according to test results.

Suspected drug	N	Number of cross-reactions	Proportion
Pantoprazole	9	0	0%
Lansoprazole	8	1	12.5%
Esomeprazole	2	1	50%
Rabeprazole	3	3	100%
Omeprazole + lansoprazole	1	1	100%

before the development of anaphylaxis and during childbirth because of use of medications may contribute to the higher incidence of drug reactions in women.[15–17] Although progesterone suppresses histamine release, it is stated that it may induce IgE-mediated reactions or increase sensitivity to inflammatory mediators.[17,18]

Most hypersensitivity reactions to PPIs are immediate-type reactions, and approximately half of all reactions are considered severe enough to be classified as anaphylaxis.[10,19] In our study, patients who reported anaphylaxis with PPIs accounted for nearly three-quarters of patients with immediate hypersensitivity to PPIs. Additionally, anaphylaxis was observed in 72.3% of patients, urticaria in 23.4%, and both urticaria and angioedema in 4.3% of patients. In a recent review of case reports and small case series describing hypersensitivity reactions to PPIs, most of these reactions were acute (309 out of 443; 69%), and anaphylaxis was observed in 53.6% of patients, while angioedema or urticaria was observed in 44.1% of patients.[12] In a study comprising 2,119 patients in the French pharmacovigilance database, PPIs caused urticaria or angioedema in six patients and anaphylaxis in 14 patients (70%).[20] When the reactions were evaluated in terms of grading, grade 2 reactions occurred in 42.6% patients, grade 1 reactions in 27.7% patients, grade 3 in 23.4% patients, and grade 4 in 6.4% patients. Nearly half of the patients had experienced more than one reaction with similar or different PPIs. Patients may not be able to relate and may retake similar or different PPIs and experience reactions to the group.

Studies containing different results regarding cross-reactivity are available in the literature.[9,11,21–24] In a series of 11 patients, patients with positive SPTs with omeprazole also had positive SPTs with lansaprazole, rabeprazole, pantaprazole, and esomeprazole, and cross-reactivity was thought to exist between them.[22] In 2015, four different cross-reactivity patterns among PPIs were considered. The first was allergy to all PPIs. The second was a group that was allergic to omeprazole, esomeprazole, and pantoprazole but tolerant to lansoprazole and rabeprazole. The third group comprised patients who were allergic to lansoprazole and rabeprazole but tolerant to omeprazole, esomeprazole, and pantoprazole. The last group included patients who showed selective sensitivity to a single PPI and tolerance to other PPIs.[1] In our study, no cross-reactivity was observed between pantoprazole and other drugs in patients evaluated with SPTs and/or OPT, while cross-reactivity between lansoprazole and rabeprazole was demonstrated with OPT. Additionally, patients with cross-reactivity between esomeprazole and rabeprazole, omeprazole, and lansoprazole were observed. This does not align with the previously mentioned cross-classification. As can be seen, we observed cross-reactivities other than the four groups produced in 2015.[1] However, despite their molecular differences, cross-reactivities between lansoprazole and pantoprazole were considered to be common.[11] Cross-reactivity was detected between omeprazole and pantaprazole in a series of nine patients.[21] Additionally, as seen in our patients, cross-reactivity between lansoprazole–pantoprazole, lansoprazole–omeprazole, lansoprazole–esomeprazole, lansoprazole–pantoprazole–esomeprazole, and omeprazole–pantoprazole–rabeprazole–esomeprazole, which did not conform to these four groups, was reported in the literature.[9,21,25] A position paper published in 2024 showed that there was approximately 94% cross-reactivity between omeprazole and pantoprazole, 24% between lansoprazole and pantoprazole, 50% between rabeprazole and esomeprazole, and 80% between esomeprazole and omeprazole.[4] In our study, unlike previous classifications, esomeprazole showed cross-reactivity with omeprazole and rabeprazole, and in a patient allergic to omeprazole and lansoprazole, esomeprazole also demonstrated cross-reactivity.

In 2018, three main models were identified: reaction to a single PPI, selective cross-reactivity, and cross-reactivity with all PPIs.[20] H2RBs, used in the treatment of acid-related gastrointestinal diseases, were less effective than PPIs and provided milder acid suppression. H2RB drugs are used as an alternative in patients with intolerance or reaction to PPIs.[26] In some patients, provocation testing with SPT, IDT, or alternative non-PPI gastric drugs (ranitidine or famotidine) yielded positive results. We performed alternative drug tests on all patients in our study population. These drugs included H2RBs. We confirmed that no reaction occurred to these drugs using both SPT and OPT. Based on our observations, we conclude that non-PPI gastric medications are also safe for patients allergic to PPIs.

The first limitation of our study was that IDT could not be performed with lansoprazole and rabeprazole because these PPIs are not available in injectable forms. Our other limitation was that the diagnosis and/or cross-reactivity could not be confirmed due to the severe reaction or the patient not giving consent for provocation test despite negative SPT and/or IDT. Of note is the risk that enteric coatings in delayed-release formulations of PPIs may contain gelatin[27] and that this could be a possible triggering agent. There have been reports of anaphylaxis induced by gelatin in enteric coatings in gelatin-sensitive individuals.[28] Therefore, it is recommended to perform SPT and provocation test for both gelatin and drug in patients who developed a reaction after taking enteric-coated drugs

containing gelatin.[29] We were unable to test for gelatin in our study, which was a significant limitation. It is important to focus on the adverse events attributed to PPI usage. PPIs may be a cause of sudden hypersensitivity reactions. Anaphylaxis is the most common reaction, followed by urticaria and/or angioedema. Physicians should consider PPIs as potential causes of hypersensitivity reactions and be aware of cross-reactions within the PPI family.

Conclusion

Serious immediate-type hypersensitivity reactions to lansoprazole were observed, most commonly presenting as anaphylaxis. Careful drug allergy assessment is essential to identify safe alternatives, with attention to possible cross-reactivity between PPIs. Increasing awareness among patients and physicians may substantially reduce the risk, and PPI use should be restricted to well-defined indications with consideration of treatment tapering when feasible.

Competing Interests

The authors had no relevant financial interests to disclose.

Author's Contributions

All authors contributed equally to this article.

Conflicts of Interests

None.

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References

1. Lombardo C, Bonadonna P. Hypersensitivity reactions to proton pump ınhibitors. Curr Treat Options Allergy. 2015, 01 June;2(2):110–23. https://doi.org/10.1007/s40521-015-0046-0
2. Thomson AB, Sauve MD, Kassam N, Kamitakahara H. Safety of the long-term use of proton pump inhibitors. World J Gastroenterol. 2010, 21 May;16(19):2323–30. https://doi.org/10.3748/wjg.v16.i19.2323
3. Chang YS. Hypersensitivity reactions to proton pump inhibitors. Curr Opin Allergy Clin Immunol. 2012, August;12(4):348–53. https://doi.org/10.1097/ACI.0b013e328355b8d3
4. Bavbek S, Kepil Özdemir S, Bonadonna P, Atanaskovic-Markovic M, Barbaud A, Brockow K, et al. Hypersensitivity reactions to proton pump ınhibitors. An EAACI position paper. Allergy. 2024, March;79(3):552–64. https://doi.org/10.1111/all.15961
5. Ring J, Messmer K. Incidence and severity of anaphylactoid reactions to colloid volume substitutes. Lancet. 1977, 26 February;1(8009):466–9. https://doi.org/10.1016/S0140-6736(77)91953-5
6. Brockow K, Garvey LH, Aberer W, Atanaskovic-Markovic M, Barbaud A, Bilo MB, et al. Skin test concentrations for systemically administered drugs—An ENDA/EAACI Drug Allergy Interest Group position paper. Allergy. 2013, June;68(6):702–12. https://doi.org/10.1111/all.12142
7. Bose S, Guyer A, Long A, Banerji A. Evaluation and management of hypersensitivity to proton pump inhibitors. Ann Allergy Asthma Immunol. 2013, December;111(6):452–7. https://doi.org/10.1016/j.anai.2013.08.022
8. Bonadonna P, Lombardo C, Bortolami O, Bircher A, Scherer K, Barbaud A, et al. Hypersensitivity to proton pump inhibitors: Diagnostic accuracy of skin tests compared to oral provocation test. J Allergy Clin Immunol. 2012, August;130(2):547. https://doi.org/10.1016/j.jaci.2012.04.048
9. Kepil Özdemir S, Öner Erkekol F, Ünal D, Büyüköztürk S, Gelincik A, Dursun AB, et al. Management of hypersensitivity reactions to proton pump ınhibitors: A retrospective experience. Int Arch Allergy Immunol. 2016;171(1):54–60. https://doi.org/10.1159/000450952
10. Kepil Özdemir S, Gelincik A, Paksoy N, Köycü Buhari G, Öner Erkekol F, Dursun AB, et al. Analysis of the factors associated with diagnostic skin test positivity in immediate-type hypersensitivity reactions due to proton pump inhibitors. Allergy. 2019, June;74(6):1187–90. https://doi.org/10.1111/all.13715
11. Kepil Özdemir S, Yılmaz I, Aydin Ö, Büyüköztürk S, Gelincik A, Demirtürk M, et al. Immediate-type hypersensitivity reactions to proton pump inhibitors: Usefulness of skin tests in the diagnosis and assessment of cross-reactivity. Allergy. 2013, August;68(8):1008–14. https://doi.org/10.1111/all.12189
12. Kepil Özdemir S, Bavbek S. Hypersensitivity reactions to proton-pump inhibitors: Clinical presentation, diagnosis, and management. Allergy Asthma Proc. 2020, 01 March;41(2):e37–44. https://doi.org/10.2500/aap.2020.41.190033
13. Yu RJ, Krantz MS, Phillips EJ, Stone CA. Emerging causes of drug-ınduced anaphylaxis: A review of anaphylaxis-associated reports in the FDA Adverse Event Reporting System (FAERS). J Allergy Clin Immunol Pract. 2021, February;9(2):819–29.e2. https://doi.org/10.1016/j.jaip.2020.09.021
14. Regateiro FS, Marques ML, Gomes ER. Drug-Induced Anaphylaxis: An update on epidemiology and risk factors. Int Arch Allergy Immunol. 2020;181(7):481–7. https://doi.org/10.1159/000507445
15. Hsu Blatman KS, Hepner DL. Current knowledge and management of hypersensitivity to perioperative drugs and radiocontrast media. J Allergy Clin Immunol Pract. 2017;5(3):587–92. https://doi.org/10.1016/j.jaip.2017.03.016
16. Castells MC. Capturing drug-ınduced anaphylaxis through electronic health records: A step forward. J Allergy Clin Immunol Pract. 2019, January;7(1):112–3. https://doi.org/10.1016/j.jaip.2018.10.045
17. Lieberman P. Epidemiology of anaphylaxis. Curr Opin Allergy Clin Immunol. 2008, August;8(4):316–20. https://doi.org/10.1097/ACI.0b013e3283036a69
18. Chen W, Mempel M, Schober W, Behrendt H, Ring J. Gender difference, sex hormones, and immediate-type hypersensitivity reactions. Allergy. 2008, November;63(11):1418–27. https://doi.org/10.1111/j.1398-9995.2008.01880.x
19. Otani IM, Banerji A. Immediate and delayed hypersensitivity reactions to proton pump ınhibitors: Evaluation and management. Curr Allergy Asthma Rep. 2016, March;16(3):17. https://doi.org/10.1007/s11882-016-0595-8
20. Tourillon C, Mahe J, Baron A, Lambert A, Yélehé-Okouma M, Veyrac G, et al. Immediate-type hypersensitivity cross-reactions to proton pump ınhibitors: A descriptive study of data from the French National Pharmacovigilance Database. Int Arch Allergy Immunol. 2019;178(2):159–66. https://doi.org/10.1159/000493581
21. Lobera T, Navarro B, Del Pozo MD, González I, Blasco A, Escudero R, et al. Nine cases of omeprazole allergy: Cross-reactivity between proton pump inhibitors. J Investig Allergol Clin Immunol. 2009;19(1):57–60.

22. Sánchez-Morillas L, Rojas Pérez-Ezquerra P, González Mendiola R, Gómez-Tembleque Ubeda P, Santos Alvarez A, Laguna-Martínez JJ. Eleven cases of omeprazole hypersensitivity: Diagnosis and study of cross-reactivity. J Investig Allergol Clin Immunol. 2014;24(2):130–2.
23. Sobrevia Elfau MT, Garcés Sotillos M, Ferrer Clavería L, Segura Arazuri N, Monzón Ballarin S, Colás Sanz C. Study of cross-reactivity between proton pump inhibitors. J Investig Allergol Clin Immunol. 2010;20(2):157–61.
24. Li PH. Skin testing for hypersensitivity and cross-reactivity between proton pump inhibitors. Hong Kong Med J. 2020, October;26(5): 450.e1–e2. https://doi.org/10.12809/hkmj198267
25. Garmendia Zallo M, Sánchez Azkarate A, Kraemer Mbula R, Liarte Ruano I, Nuñez Hernandez A, Cid De Rivera C. Cross reactivity among proton pump inhibitors: Does it exits? Allergol Immunopathol (Madr). 2004;32(2):92–5. https://doi.org/10.1016/s0301-0546(04)79235-6
26. Shim YK, Kim N. The effect of H2 receptor antagonist in acid ınhibition and ıts clinical efficacy. Korean J Gastroenterol. 2017, 25 July;70(1):4–12. https://doi.org/10.4166/kjg.2017.70.1.4.
27. Reker D, Blum SM, Steiger C, Anger KE, Sommer JM, Fanikos J, et al. “Inactive” ingredients in oral medications. Sci Transl Med. 2019, 13 March;11(483): eaau6753. https://doi.org/10.1126/scitranslmed.aau6753
28. Land MH, Piehl MD, Burks AW. Near fatal anaphylaxis from orally administered gelatin capsule. J Allergy Clin Immunol Pract. 2013, January;1(1):99–100. https://doi.org/10.1016/j.jaip.2012.09.004
29. Natsch S, Vinks MH, Voogt AK, Mees EB, Meyboom RH. Anaphylactic reactions to proton-pump inhibitors. Ann Pharmacother. 2000, April;34(4):474–6. https://doi.org/10.1345/aph.19235