Hypersensitivity reaction to omeprazole in a patient treated for *Helicobacter pylori*

Sarah Anderson and Sarah Christensen

Ther Adv Gastroenterol

2015, Vol. 8(2) 101–104

DOI: 10.1177/
1756283X14564314

© The Author(s), 2015.

Reprints and permissions:
[http://www.sagepub.co.uk/
journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)

Introduction

Helicobacter pylori infection remains one of the most common bacterial infections in humans [Pounder and Ng, 1995; Cave, 1996]. These infections can cause gastritis, peptic ulcer disease, and gastric adenocarcinoma [Peterson *et al.* 2000]. Standard eradication regimens include combinations of antibiotics and antisecretory agents such as proton-pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RAs) [Chey and Wong, 2007]. PPIs have been used more commonly over H2RAs due to more effective acid suppression and antibacterial effects [Stoschus *et al.* 1996; McGowan *et al.* 1994; Gisbert *et al.* 2003]. We report the case of a *H. pylori*-positive patient who developed a hypersensitivity reaction to omeprazole therapy. The patient was subsequently treated with a triple therapy regimen that included pantoprazole without incident.

Case report

A 37-year-old woman with a medical history significant for alcoholic hepatitis presented with a chief complaint of ongoing nausea for several weeks. The patient had stopped drinking alcohol 12 weeks prior. Her medication regimen included furosemide 20 mg PO twice daily, spironolactone 50 mg PO daily, and tramadol 50 mg PO every 6 hours as needed. The patient also had six rods of retained levonorgestrel hormonal contraceptive. On the day of presentation, her liver function tests were within normal limits (total bilirubin 1.2 mg/dl, alkaline phosphatase 123 U/l, aspartate aminotransferase 34 U/l, alanine aminotransferase 26 U/l), as were her lipase (169 pg/ml) and serum creatinine (0.6 mg/dl) levels.

A serum *H. pylori* antibody test was ordered and the patient was treated with omeprazole 20 mg PO twice daily for the nausea and high pretest probability of *H. pylori* infection. The next day, serology testing confirmed a positive *H. pylori* test. Five days later, the patient reported an

all-over urticarial rash. The patient confirmed taking the omeprazole twice daily for 3 days, discontinuing the drug on day 4, and on day 6 the rash had resolved. The precise day of therapy on which the rash appeared is unknown.

The patient was challenged with pantoprazole 40 mg PO twice daily (in addition to amoxicillin and clarithromycin) for 14 days. The patient completed her 14 day course of triple therapy and was continued on pantoprazole for ongoing gastroesophageal reflux disease (GERD) symptoms with no adverse reactions.

Based on the Naranjo Adverse Drug Reaction Probability Scale, the hypersensitivity to omeprazole was probable (score = 6; Table 1) [Naranjo *et al.* 1981].

Discussion

Treatment of *H. pylori* involves bacterial eradication and gastric ulcer healing with antibiotics and a PPI [Chey and Wong, 2007]. While PPIs are generally well-tolerated, PPI-induced hypersensitivity reactions can occur. These include urticaria, angioedema, anaphylaxis, cytopenia, vasculitis, acute allergic interstitial nephritis, contact dermatitis, drug rash with eosinophilia and systemic symptoms, Stevens–Johnson syndrome, and toxic epidermal necrolysis [Bose *et al.* 2013; Chang, 2012; Sobrevia Elfau *et al.* 2010].

Patients with PPI-related hypersensitivity fit into one of three categories: (1) hypersensitive to all PPIs; (2) selectively hypersensitive to PPIs, or (3) hypersensitive to one PPI and tolerant of all others (Table 2) [Sobrevia Elfau *et al.* 2010]. Category 1 may be explained by structural similarities as all commercially available PPIs are modified benzimidazoles with a shared pyridine ring. In category 2, selective hypersensitivity may occur based on the presence of side chain substitution on the PPI.

Correspondence to:
Sarah Anderson, PharmD
University of Colorado
Skaggs School
of Pharmacy and
Pharmaceutical Sciences
- Clinical Pharmacy, Mail
Stop C238 12850 East
Montview Boulevard,
Room V20-2129, Aurora,
CO 80045, USA
[sarah.anderson@
ucdenver.edu](mailto:sarah.anderson@ucdenver.edu)

Sarah Christensen, MD
Denver Health Medical
Center - Community
Health Services, Denver,
CO, USA

Table 1. Naranjo Adverse Drug Reaction Probability Scale results.

Criterion	Yes	No	Do not know or not applicable
Are there previous conclusive reports on this reaction?	+1	0	0
Did the adverse event occur after the suspected drug was administered?	+2	-1	0
Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0
Did the adverse reaction reappear when the drug was readministered?	+2	-1	0
Are there alternative causes (other than the drug) that could have on their own caused the reaction?	-1	+2	0
Did the reaction reappear when a placebo was given?	-1	+1	0
Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0
Was the adverse event confirmed by any objective evidence?	+1	0	0
Total Score: 6			
Note: Bold text indicates the score applicable to the case described. Information from Naranjo et al. [1981].			

The third category describes patients who exhibit hypersensitivity to a single PPI and are tolerant of all others [Sobrevia Elfau *et al.* 2010; Garrido Fernández *et al.* 2008; Özdemir *et al.* 2013].

In this case, the patient developed a hypersensitivity to omeprazole and tolerated pantoprazole. It is unknown whether the patient is intolerant of any other PPIs and therefore fits either category 2 or 3 (Table 2). Omeprazole and pantoprazole both contain substitutions in their benzimidazole rings but have slightly different pyridine rings (Figure 1) [AstraZeneca, 2013; Wyeth, 2013]. Omeprazole has a methoxy chain and pantoprazole a difluoromethoxy chain in their respective benzimidazole rings and omeprazole has two methyl and one methoxy groups in its pyridine ring while pantoprazole has two methoxy groups in this ring [Sobrevia Elfau *et al.* 2010; Garrido Fernández *et al.* 2008; Özdemir *et al.* 2013; AstraZeneca, 2013; Wyeth, 2013]. These variations in ring substitutions may explain why our patient reacted to omeprazole but not to pantoprazole despite both having predominantly substituted benzimidazole rings.

Alternative eradication regimens involve the use of quadruple therapy containing an H2RA [Chey and Wong, 2007]. One first-line regimen for *H. pylori* eradication includes bismuth subsalicylate

525 mg PO 4 times daily, metronidazole 250 mg PO 4 times daily, and tetracycline 500 mg PO 4 times daily for 2 weeks plus ranitidine 150 mg PO BID for 4 weeks. This regimen has a 75–90% eradication success rate, which is similar to clarithromycin-based triple therapy [Chey and Wong, 2007]. However, this regimen has several potential disadvantages, including decreased efficacy due to use of an H2RA, large pill burden with frequent dosing, and perceived increase in adverse effects [Chey and Wong, 2007; Fischbach *et al.* 2004].

In patients with a severe PPI allergy who require a PPI for treatment, PPI desensitization can be performed. One case report describes a 44-year-old male with symptomatic *H. pylori* gastritis who failed triple therapy twice and manifested an anaphylactic reaction to omeprazole during the third round. He underwent oral omeprazole desensitization in the inpatient setting, starting with 0.001 mg of omeprazole with a doubling of each dose given at 20-minute intervals. The final dose of 16 mg occurred after 5.6 hours of therapy, with a cumulative exposure of 32.6 mg. The patient was successfully treated with omeprazole 20 mg PO BID following the desensitization [Confino-Cohen and Goldberg, 2006]. Based on the cost and complexity of inpatient PPI desensitization, this

Table 2. Proton-pump inhibitor (PPI) cross-reactivity patterns.

Pattern	Description
1	Allergy to a single PPI with cross-reactivity to all PPIs
2	Allergy to two PPIs with tolerance of two alternative PPIs
3	Allergy to a single PPI with tolerance of all alternative PPIs

Information from Sobrevia Elfau *et al.* [2010].

Figure 1. Omeprazole and pantoprazole structural formulas with highlighted differences.
[Information from AstraZeneca, 2013; Wyeth, 2013].

option may be less desirable than treating a PPI-allergic patient with an H2RA instead.

Conclusion

A patient with *H. pylori* experienced a hypersensitivity reaction to omeprazole and was successfully treated with triple therapy that included amoxicillin, clarithromycin, and pantoprazole without incident. Because PPI use is so prevalent, hypersensitivity reactions to PPIs are not uncommon and yet cross-reactivity among members of the drug class is not clear. A patient may tolerate an alternative PPI or may be allergic to the entire drug class, in which case a different antisecretory agent would be warranted.

Conflict of interest statement

The authors declare that they do not have anything to disclose regarding conflicts of interest with respect to this manuscript.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

- AstraZeneca (2013) *Product information. Prilosec (omeprazole)*. Wilmington, DE: AstraZeneca.
- Bose, S., Guyer, A., Long, A. and Banerji, A. (2013) Evaluation and management of hypersensitivity to proton pump inhibitors. *Ann Allergy Asthma Immunol* 111: 452–457.
- Cave, D. (1996) Transmission and epidemiology of *Helicobacter pylori*. *Am J Med* 100(5A): 12S–17S.
- Chang, Y. (2012) Hypersensitivity reactions to proton pump inhibitors. *Curr Opin Allergy Clin Immunol* 12: 348–353.
- Chey, W. and Wong, B. for the Practice Parameters Committee of the American College of Gastroenterology (2007) American College of Gastroenterology guideline on the management of *Helicobacter pylori* infection. *Am J Gastroenterol* 102: 1808–1825.
- Confino-Cohen, R. and Goldberg, A. (2006) Anaphylaxis to omeprazole: diagnosis and desensitization protocol. *Ann Allergy Asthma Immunol* 96: 33–36.
- Fischbach, L., van Zanten, S. and Dickason, J. (2004) Meta-analysis: the efficacy, adverse events, and adherence related to first-line anti-*Helicobacter pylori* quadruple therapies. *Ailment Pharmacol Ther* 20: 1071–1082.
- Garrido Fernández, S., Cumplido, J., Rábano, A., Martínez, D., Blanco, C. and Carillo, T. (2008) Allergy to proton pump inhibitors: diagnosis and assessment of cross-reactivity. *J Invest Allergol Clin Immunol* 18: 140–141.
- Gisbert, J., Khorrami, S., Calvet, X., Gabriel, R., Carballo, F. and Pajares, J. (2003) Meta-analysis: proton pump inhibitors vs. H2-receptor antagonists - their efficacy with antibiotics in *Helicobacter pylori* eradication. *Ailment Pharmacol Ther* 18: 757–766.
- McGowan, C., Cover, T. and Blaser, M. (1994) The proton pump inhibitor omeprazole inhibits acid survival of *Helicobacter pylori* by a urease-independent mechanism. *Gastroenterology* 107: 1573–1578.
- Naranjo, C., Busto, U., Sellers, E., Sandor, P., Ruiz, I., Roberts, E., *et al.* A method for estimating the probability of adverse drug reactions (1981) *Clin Pharmacol Ther* 30: 239–45.
- Özdemir, S., Yilmaz, I., Aydın, Ö. Büyükoztürk, S., Gelincik, A., Demirtürk, M. *et al.* (2013)

Immediate-type hypersensitivity reactions to proton pump inhibitors: usefulness of skin tests in the diagnosis and assessment of cross-reactivity. *Allergy* 68: 1008–1014.

Peterson, W., Fendrick, A., Cave, D. Peura, D., Garabedian-Ruffalo, S., Laine, L. *et al.* (2000) *Helicobacter pylori*-related disease: Guidelines for testing and treatment. *Arch Intern Med* 160: 1285–1291.

Pounder, R. and Ng, D. (1995) The prevalence of *Helicobacter pylori* infection in different countries. *Ailment Pharmacol Ther* 9(Suppl. 2): 33–39.

Sobrevia Elfau, M., Garcés Sotillos, M., Ferrer Clavería, L., Segura Arazuri, N., Monzón Ballarín, S. and Colás Sanz, C. (2010) Study of cross-reactivity between proton pump inhibitors. *J Investig Allergol Clin Immunol* 20: 157–161.

Stoschus, B., Dominguez-Munoz, J., Kalhori, N., Sauerbruch, T. and Malfertheiner, P. (1996) Effect of omeprazole on *Helicobacter pylori* urease activity *in vivo*. *Eur J Gastroenterol Hepatol* 8: 811–813.

Wyeth (2013) *Product information. Protonix (pantoprazole sodium)*. Philadelphia, PA: Wyeth Pharmaceuticals Inc., a subsidiary of Pfizer Inc.