National Journal of Physiology, Pharmacy and Pharmacology

CASE REPORT

A rare case of adverse drug reaction to pantoprazole 3 times in the same patient: A case report

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Received: June 16, 2019; **Accepted:** July 13, 2019

ABSTRACT

Pantoprazole is one of the most widely used proton-pump inhibitors for gastric acid suppression. Its better adverse effect profile has resulted in its overprescription and large over-the-counter use. Anaphylactic reaction to pantoprazole is relatively rare. We present a case report of a 38-year-old male who presented with anaphylactic reaction to pantoprazole ranging from a mild rash to potentially life-threatening anaphylactic shock on three different occasions. This case report highlights the importance of proper patient education, their awareness regarding adverse drug reactions to drugs, their role in informing the treating doctors regarding the same, and the need for careful history taking by doctors regarding drug allergies and cautious use of even the most commonly used drugs and those with low incidence of adverse effects.

KEY WORDS: Anaphylactic Reactions; Pantoprazole; Proton-pump Inhibitor; Adverse Drug Reaction

INTRODUCTION

Pantoprazole is one of the most widely used proton-pump inhibitors (PPIs) for the treatment of gastroesophageal reflux disease (GERD), peptic ulcers, Zollinger–Ellison syndrome, and other related diseases. PPIs cause very few adverse effects.[1] The incidence of anaphylactic reaction to PPIs and H2 receptor antagonists together has been reported as 0.3–0.7% only.[2] This has contributed to their overprescription and large-scale over-the-counter sales. Their use may not be recorded in medical history resulting in adverse reactions caused by them going unnoticed and hence not reported.

Elaborating here, a case report with the same patient in three different case scenarios involving the same drug that is pantoprazole and its adverse reactions ranging from a mild rash to anaphylactic shock. This case report highlights the importance of history taking regarding known allergies in patients before prescribing any drug, patients awareness of informing doctors of prior drug exposures and its allergies and to increase awareness that most widely used drugs like PPIs can also cause potentially severe allergic reactions.

Access this article online	
Website: www.njppp.com	Quick Response code
DOI:10.5455/njppp.2019.9.0724613072019	

CASE REPORT

Case Scenario 1

A 38-year-old male patient, with sedentary lifestyle, presented to the outpatient department (OPD) with symptoms suggestive of gastritis. After thorough history taking and examination, the patient was prescribed tablet pantoprazole 40 mg OD on empty stomach early morning, for a week and advised diet, and lifestyle modification.

The patient came back the next day to OPD with facial flushing, erythematous macular skin rash, and itching all over the body. All this appeared around 1 h after intake of one tablet pantoprazole 40 mg on empty stomach in the

morning. There was no angioedema, difficulty in breathing, or change in voice. Vitals were stable (blood pressure was 130/80, pulse 82 beats per minute regular), systemic examination was normal.

The patient was given injection pheniramine 22.75 mg intravenous and kept under observation. His symptoms subsided in some time. As the patient confirmed that he had not taken any other drug with pantoprazole, a note was given to the patient saying that he had possibly suffered an allergic reaction to pantoprazole and asked to inform any doctors of the same, before treatment in the future. The patient was discharged on syrup antacid as he tolerated it well.

Case Scenario 2

Around 2 months later, the same patient presented in emergency department with similar complaints of flushed face, erythematous skin rash, and itching all over body after taking one tablet of pantoprazole 40 mg orally. On inquiry, the patient said that he was prescribed tablet pantoprazole 40 mg OD and tablet ibuprofen 400 mg BD by another general practitioner in view of muscular pain in back. The trade name of tablet pantoprazole was different from the one prescribed 2 months ago; therefore, he did not realize that it was pantoprazole nor did he mention his drug allergy to the doctor. As a result, of which the patient took tablet pantoprazole 40 mg oral (different brand) and developed allergic reaction. He did not take tablet ibuprofen 400 mg. The patient also complained of recurrent epigastric and the left-sided chest pain.

The patient was treated with pheniramine 22.75 mg intravenous and this time was investigated thoroughly for possible causes of gastritis and the left-sided chest pain.

Investigations

Routine blood reports of complete hemogram, liver function tests, renal function tests, serum lipids, blood sugar, thyroid function test, and urine analysis were within normal limits. Electrocardiogram (ECG) and treadmill test were normal, ultrasound and computed tomography scan abdomen were normal. Endoscopy revealed antral gastritis.

To find alternatives for the treatment of gastritis, an oral challenge test was done with tablet ranitidine 150 mg. The patient developed similar allergic reaction with ranitidine as well. He and his wife were clearly cautioned regarding allergy to tablet pantoprazole and tablet ranitidine and were given another note to produce before doctors whenever he approached one. He was discharged with syrup antacid, which he tolerated well, diet, and lifestyle modifications.

Case Scenario 3

The same patient presented to the emergency department again, after around 3 months of his last visit, with severe gastritis, burning epigastric pain, and multiple episodes of vomiting. His vitals were stable (blood pressure 130/80, pulse 72 beats per minute regular), ECG was within normal limits. Systemic examination was normal.

The doctor on duty in the emergency department was different, and neither the patient nor his wife produced the note regarding his drug allergy to pantoprazole and ranitidine. Furthermore, they did not inform the doctor verbally regarding his drug allergy.

He was given injection pantoprazole 40 mg intravenously and syrup antacid 20 ml orally. Within 10 min of injection, the patient started feeling dizzy, had flushed face, profuse sweating, palpitations, difficulty in breathing, and cold and clammy extremities.

On examination, the patient was afebrile, blood pressure 80 mmHg systolic, pulse 120 beats per minute, feeble, respiratory rate 33/min, SpO_2 – 84%, and RBSL – 138 mg%. Systemic examination was normal.

A probable diagnosis of "drug-induced anaphylactic shock" was made and treatment started immediately. A large-bore intravenous cannula was secured. The patient was given injection adrenaline 0.5 mg of 1:1000 intramuscularly, 100 mg of injection hydrocortisone, and 22.75 mg of injection pheniramine intravenously. Inhalational oxygen at 4 L/min through oxygen mask and normal saline pints was started (30 ml/kg). The patient responded well to treatment and did not require ventilatory support.

The patient's condition improved slowly and after 3 h, he completely recovered. His blood pressure was 130/80 mmHg, pulse 78 beats per minute regular, respiratory rate 16/min, and SpO_2 99%, and systemic examination was normal. Subsequent blood investigations were within normal limits. He was kept under observation for 2 more days, which were uneventful, and later discharged. The patient was strictly advised not to take pantoprazole and ranitidine and cautioned about the consequences if he did so and also explained the need to inform the doctors regarding his allergic response. A clear note of pantoprazole and ranitidine allergy was made on all his medical papers.

The patient was referred to a gastroenterologist in view of his recurrent gastritis and GERD where he has now been prescribed tablet acotiamide 100 mg TDS for 3 weeks which he tolerates well and is free from symptoms of gastritis.

DISCUSSION

PPIs are the most potent suppressors of gastric acid secretion. They exert their action by irreversibly inactivating the H^+, K^+-ATPase (proton pump) present at the canaliculi of the parietal cells of stomach, such that acid secretion is inhibited

till new pump molecules are synthesized. This provides a prolonged gastric acid suppression of up to 24–48 h. They are used for the treatment of GERD, peptic ulcers, Zollinger–Ellison syndrome, and other related diseases. They have very low incidence of adverse effects; the most common side effects are nausea, abdominal pain, constipation, diarrhea, headaches, and skin rashes. Anaphylactic shock is a rare adverse effect of PPIs.[1] This better side effect profile has resulted in their overprescription and large-scale over-the-counter sale. Their use may not be recorded in medical history resulting in adverse reactions caused by them going unnoticed and unreported.

In this case series, we have a 38-year-old male with allergic reactions to the same drug that is pantoprazole, on three different occasions. Temporal relationship was observed between the drug administration and appearance of symptoms. Allergic reactions to both oral and intravenous routes have manifested. With oral intake of tablet pantoprazole, the allergic reaction was mild. Causality assessment of these adverse drug reactions was done by the WHO-UMC and Naranjo's algorithm for causality assessment, which indicated "probable," and according to Modified Hartwig and Siegel severity assessment scale, was level 3. While with intravenous injection of pantoprazole, the patient developed anaphylactic shock which according to causality assessment by the WHO-UMC and Naranjo's algorithm indicated "definite" and according to Modified Hartwig and Siegel severity assessment scale, was level 5. Cross-sensitivity of pantoprazole with ranitidine has been observed in this patient. A case of ranitidine and pantoprazole cross-sensitivity has been recorded in 2017.[3]

Although pantoprazole is a widely used drug with comparatively less adverse drug reactions, anaphylactic reactions to pantoprazole have been reported in literature. The incidence of anaphylactic reaction to PPIs and H2 receptor antagonists together has been reported as 0.3–0.7% only.[2] The reason for under-reporting of adverse drug reactions to PPIs or H2 receptor antagonist may be because they are frequently used without prescription, and hence, their use may not be recorded in medical history and anaphylaxis caused by them may seem to be idiopathic.

A case with anaphylaxis to oral pantoprazole 40 mg with Kounis syndrome has been described.[4] A case of pantoprazole anaphylaxis with cross-reactivity to all PPIs has been reported in literature.[5] Anaphylactic shock has been reported with oral as well as intravenously administered pantoprazole.[6-8]

Drug-induced anaphylaxis is an unanticipated and severe allergic reaction. To avoid this, the patient, who has had an allergic reaction to a drug, has to be educated to avoid further exposure to that drug and made aware of the consequences. Furthermore, proper documentation regarding patient's allergic reaction to a drug should be made in their medical papers. In this case, however, the patient was informed and documentation was made regarding the drug allergy, neither did he show the documentation nor did he tell the treating physician regarding his previous drug allergy. Here comes the need for careful history taking regarding drug allergies and cautious use of even the most commonly used drugs and those with low incidence of adverse effects.

Acotiamide is a new drug used for the treatment of functional dyspepsia (FD) developed by Zeria Pharmaceutical Co., Ltd. (Tokyo, Japan) and approved in Japan. It is a new prokinetic agent which performs its gastroprokinetic function by enhancing acetylcholine release by acting as an antagonist of the M1 and M2 muscarinic receptors in the enteric nervous system and inhibiting acetylcholinesterase activity.[9] A long-term safety and efficacy trial conducted in Europe (open-label Phase 3 trial) showed improvement of quality of life and work productivity in patients having postprandial distress syndrome symptoms of FD and the long-term safety of acotiamide treatment was confirmed. Treatment-related adverse events encountered were nausea, abdominal distension, and constipation.[10] It is pending approval by the United States Food and Drug Administration.

CONCLUSION

This case report highlights the importance of proper patient education, their awareness regarding adverse drug reactions to drugs, their role in informing the treating doctors regarding the same, and the need for careful history taking by doctors regarding drug allergies and cautious use of even the most commonly used drugs and those with low incidence of adverse effects.

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How to cite this article: Kakode KP, Kakode VP. A rare case of adverse drug reaction to pantoprazole 3 times in the same patient: A case report. Natl J Physiol Pharm Pharmacol 2019;9(10):1052-1055.

Source of Support: Nil, **Conflict of Interest:** None declared.