

Anaphylactic Reactions associated with Pantoprazole: A Report of Two Clinical Cases

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ABSTRACT

Adverse drug reactions are a major contributor to morbidity and mortality. Though augmented reactions are common, but bizarre ones are not infrequent. Drug-induced anaphylaxis can occur with any medication, but with pantoprazole, it is not frequently reported. Two cases of anaphylaxis with pantoprazole will be discussed in this case report. Doctors need to recognize the side effects of pantoprazole that may trigger anaphylaxis, an allergic condition. They should exercise caution and avoid prescribing it without first determining the patient's allergic status and taking a complete medical history.

KEYWORDS: ADVERSE DRUG REACTIONS, ANAPHYLACTIC REACTIONS, PANTOPRAZOLE, PROTON PUMP INHIBITORS.

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INTRODUCTION

Proton pump inhibitors (PPIs) are widely prescribed drugs across clinical practise. Though it is well tolerated in a majority of population but spurious case reports of anaphylactic reactions and hypersensitivity are reported in literature. However, immediate or cell-mediated hypersensitivity reactions have been reported more frequently with pantoprazole and omeprazole compared to other PPIs. PPIs work by blocking the proton pump, in the gastric parietal cells, thereby inhibiting the secretion of H⁺ ions and the formation of gastric acid (HCl). PPIs are extensively utilized for treating gastroesophageal conditions such as peptic ulcer disease, gastroesophageal reflux disease (GERD), and Barrett's esophagus. Beside this they are also used alongside antimicrobial medications to eliminate *Helicobacter pylori* and minimize gastric injuries caused by Non-steroidal Anti-inflammatory Drugs (NSAIDs).¹

PPIs are generally well tolerated, with only a small percentage (approximately 1 to 3%) experiencing minor side effects. The most frequently reported side effects associated with PPIs include dizziness, headache, nausea, joint pain, subacute myopathy, and skin rashes. Prolonged use of these medications may contribute to hypergastrinemia as well as the impaired absorption of iron, magnesium, and Vitamin B12.

Serious adverse drug reactions such as hypersensitivity reactions, particularly allergenic reactions like anaphylaxis, drug reaction with eosinophilia and systemic symptoms (DRESS), contact dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis (TEN) have been sparsely documented.²

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Furthermore, to worsen the scenario PPIs are mostly self-prescribed nowadays without any medical prescription and most patients take it on a long-term basis, thus safety concerns about adverse effects have risen.

Drug-induced hypersensitivity reactions, characterized by immune-mediated responses, are frequently encountered in clinical settings and can pose significant risks. Therefore, identifying these hypersensitivity reactions, determining the responsible drug, and establishing a causal relationship are crucial for enhancing treatment outcomes.

Here we review 2 case reports of anaphylaxis triggered by Pantoprazole. The objective of this report is to enhance awareness in order to rationalize the prescribing of PPIs.

CASE REPORTS

Case 1:

A 50-year-old woman who visited the Gynecology Out-patient department with a primary concern of experiencing a dull aching pain in her lower abdomen for the past year. The pain was on and off in nature, not radiating to back,

not associated with food and not associated with any physical activity. It was relieved by NSAIDs prescribed by a local doctor. After appropriate investigations patient was diagnosed as a case of endometrial polyp and was advised admission and polypectomy. Next day the patient got admitted for polypectomy and endometrial aspiration. She was hypertensive and Diabetic but her BP and sugar were under control. She also gave history of Drug allergy but could not recall the drug. Preoperative preparation was done and she was administered Inj Pantop 40 mg. After 10 mins she started developing generalized edema, pruritus, sudden fall in blood pressure and pulse rate, difficulty in breathing associated with loss of consciousness. BP decreased to 80/55 mmHg and pulse was not palpable. Temperature was 98.6F. Immediately CPR (Cardio Pulmonary Resuscitation) was started following which the pulse became palpable. Inj Avil and Hydrocortisone were started immediately, i.v line secured and fluids started. To maintain airway and breathing suction was done and patient intubated after taking consent from attendants and then shifted to ICU (Intensive care unit). After an hour, on ventilatory support absence of fever, the blood pressure of patient became 136/74 mm Hg, while oxygen saturation at 99%, respiratory rate of 20/min and heart rate of 102 beats/min; Patient was extubated and after 4-5 hrs she became conscious and oriented to time place and person.

This was reported as an adverse drug reaction by i.v. Pantoprazole. On causality assessment, the ADR was characterized as probable, and notified on Vigiflow. She was monitored for a period of 12 hours. On discharge she was advised not to take pantoprazole in future and the same documented in her discharge card.

Case 2

A 38-year-old woman reported at the outpatient department with a concern of epigastric pain that began two days ago. The pain was localized, not radiating, and somewhat alleviated by eating. She did not report vomiting or melena. Her bowel movements were normal, but she experienced intermittent pain. Vital signs recorded were: blood pressure 126/80 mmHg, heart rate 76 beats/minute, respiratory rate 14 breaths/minute, and arterial oxygen saturation was 94% on room air. Following a thorough history and clinical examination, the patient received a diagnosis of gastritis and was prescribed 40 mg of oral Pantoprazole. The patient took the drug and 20 minutes after drug administration, she started developing rashes all over the body with swollen lips, sweating, light-headedness and difficulty in breathing and her blood pressure had lowered to 85/60 mmHg, heart rate elevated to 101 beats per minute, and her oxygen saturation level was 88% on room air. She received prompt diagnosis of anaphylactic shock and was treated with normal saline, intramuscular epinephrine, intravenous hydrocortisone 100 mg, and chlorpheniramine 4 mg. Oxygen was provided at a rate of 6 liters per minute via an oxygen mask.

After one hour, her symptoms began to improve, and she became stable. She was monitored for 12 hours following which she was discharged.

By history it was verified that she had previously developed a similar reaction to pantoprazole with a different brand and was a food allergy patient also.

Her hospital stay was uneventful, thus she was discharged and instructed not to use pantoprazole again. It was clearly written on her prescription with advice to show to any doctor she visited in future.

On causality assessment, the ADR was categorised as "certain" as previously she gave a similar history and was entered on Vigiflow

DISCUSSION

Proton pump inhibitors (PPIs) play a key role in managing acid related gastric disorders. According to Uppsala Monitoring Centre database the occurrence of adverse drug reactions for H₂ receptor antagonists and PPIs ranges was noted and it ranges from 0.2% to 0.7% of all cases of drug-induced anaphylaxis.⁴ These medications are usually safe and tolerable. While side effects have been documented with pantoprazole use, instances of drug-induced anaphylaxis are rare.⁵

In our case studies, the patients developed anaphylactic reactions, presenting as critical episodes of oedema, urticaria and hypotension after i.v and oral administration of pantoprazole. Anaphylaxis is a fulminant reaction leading to respiratory and cardiovascular complications though affecting multiple organs. Drug allergy or hypersensitivity reaction has an immunological basis. The individual may have been previously sensitized with prior administration of the same drug or structurally related drug. The medication induces an immune response and acts like a hapten. It binds to receptors located on mast cells and basophils and reacts with immunoglobulin E, resulting in cellular degranulation and release of proinflammatory mediators such as histamine, prostaglandins, leukotrienes, and PAF. These mediators subsequently increase the contraction of bronchial smooth muscles, precipitate vasodilation culminating in oedema (angioedema, laryngeal oedema or even generalised oedema) and sudden fall in blood pressure. The release of histamine also triggers urticaria, itching and erythema.⁶

Causality assessment of the ADRs was done by the WHO-UMC (World Health Organization-Uppsala Monitoring Centre) and Naranjo's scale which designated the ADRs as "probable" in 1st case and "certain" in 2nd case.

In addition to affecting the ability of orally eaten proteins to become sensitized, acid suppressing medications increase the likelihood of food allergies in their users. Fungal and bacterial cell membranes also present H+/

K⁺-ATPase, which is inhibited by PPIs hence PPIs may exert an antimicrobial effect on certain pathogens. This influences the intestinal flora leading to lack of gastrointestinal protein degradation causing food allergies and could also offer an increased susceptibility to drug hypersensitivity reactions. Indiscriminate use of acid suppressing agents can be the causative factor for anaphylactic reactions induced by PPIs.⁷

A low pH is required to activate the pepsin enzyme and stimulate the secretion of pancreatic enzymes and the acid also destroys the allergenic component of food. Use of drugs inhibiting the acid secretion causes the food allergen to remain intact leading to allergic sensitization.⁸

Complete suppression of gastric acid, as seen in patients receiving long-term PPI treatment, is thought to increase the risk of allergy sensitization as the drug carrier/protein complexes develop immunogenicity.⁹

Several cases of Type I IgE-mediated hypersensitivity responses have been reported. Delayed hypersensitivity reactions associated with PPIs are infrequently documented in the literature. Reports of cross-reactivity amongst PPIs have also been recognised.¹⁰

Ottervanger et al. observed that after omeprazole 40 mg i.v. injection anaphylaxis occurred within a few minutes. Even after 6 weeks of taking oral omeprazole 20 mg, the same patient developed urticaria.¹¹ A 50-year-old male in China encountered anaphylactic shock after receiving an IV pantoprazole under general anesthesia.¹²

A case study by Gupta et al. documented two incidences of anaphylaxis after consuming oral 40 mg pantoprazole. Both patients were kept monitored for 12 hours and advised not to take pantoprazole in the future.¹³ Another case study by Faridaalae et al. revealed that two minutes after receiving 40 mg of intravenous pantoprazole—a medication prescribed for acute gastritis—a female patient experienced anaphylaxis, hives, cyanosis and dyspnea. Her blood pressure also dropped to 86/60 mmHg, heart rate shoot-up to 101 beats per minute, and oxygen saturation dropped to 78%.¹⁴

A case of pantoprazole induced anaphylaxis was also reported by Kakode K.P et al. in a male patient on 3 occasions.¹⁵ A similar reaction was also reported by Yousefi H et al. in a male patient 3 minutes following 40 mg pantoprazole injection for peptic ulcer.¹⁶

Drug allergy is a Bizarre, type-B adverse drug reaction. To avoid similar incidents in the future, the patient must be educated on how to avoid taking that drug, and adequate records of the patient's allergic history must be kept so that he can show it to his treating physician in future. Moreover the doctors/residents also have to elicit complete and proper history from the patient before starting any treatment.

CONCLUSION

The current evidence supports that taking PPIs without caution increases the risk of anaphylactic reactions among subjects. As anaphylaxis jeopardizes the life of an individual, health care professionals must execute caution in prescribing pantoprazole. The need of providing patients with appropriate information and raising their knowledge of adverse drug reactions is emphasized by these case studies.

Aware patients can play a very useful role by notifying such ADRs to the nearest ADR monitoring centres. Meticulous history taking by doctors regarding drug allergies can also rule out such ADRs of commonly prescribed drugs.

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