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Possible anaphylaxis to palonosetron

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Abstract

Anaphylaxis related to drug therapy with 5-HT₃ antagonists, in particular, palonosetron has not been reported frequently in the literature. Here a case is presented where the patient possibly had an anaphylactic reaction to palonosetron. In this case report, a 40-year-old female with ovarian cancer developed shortness of breath and hypotension after receiving her palonosetron as part of her premedication for chemotherapy. The patient recovered successfully with fluids and supportive care. This case demonstrates that even after successful treatment in the past with palonosetron a patient may later develop a hypersensitivity to the agent.

Keywords

Palonosetron, anaphylaxis, hypersensitivity, 5-HT₃ receptor antagonist

Introduction

Anaphylaxis is a serious, potentially fatal, multi-organ systemic reaction that can result from drug administration.¹ The most common organ systems include the respiratory, cardiovascular, gastrointestinal, and cutaneous systems.¹ The etiology of drug reactions can be classified into immunologic and nonimmunologic.² The majority of adverse drug reactions (about 75–82%) are caused by predictable, non-immunologic effect with the remaining are caused by unpredictable effects that may or may not be immune mediated.² Adverse drug reactions by either etiology are a major cause of morbidity and mortality worldwide and complicate 5–15% of therapeutic drug courses.^{3,4} More than 100,000 deaths in the United States every year are attributed to adverse drug reactions and consist of 3–6% of all hospital admissions.^{3–5} In the clinical setting, anaphylaxis is considered likely if any one of the three following criteria are met within minutes to hours:¹

- Acute symptoms involving skin, mucosal surface, or both, and at least one of the following: respiratory compromise, hypotension, or end-organ dysfunction.
- Two or more of the following occur rapidly after exposure to a likely allergen: hypotension, respiratory compromise, persistent gastrointestinal symptoms, or involvement of skin or mucosal surface.

- Hypotension develops after exposure to an allergen known to cause symptoms for that patient: age-specific low blood pressure of more than 30% compared to baseline.

Immunologic drug reactions can be caused by a number of factors. They can be IgE-mediated (Type I), cytotoxic (Type II), caused by immune complexes (Type III), or delayed, cell mediated (Type IV).⁶ A classic example of a Type I reaction is anaphylaxis from a β -lactam antibiotic and Type IV reactions are generally a delayed hypersensitivity that appears when antigen sensitized cells release cytokines upon re-exposure to the sensitizing agent.⁷

Here we describe a case of a patient who developed possible anaphylaxis following the administration of intravenous palonosetron.

Case report

A 40-year-old Caucasian female with a stage III-A ovarian cancer was scheduled to receive her fourth

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cycle of chemotherapy with paclitaxel followed by carboplatin. As part of the standard pre-treatment, the patient had taken aprepitant orally, then palonosetron and dexamethasone were administered intravenously, which finished without complications. Immediately following the completion of palonosetron and dexamethasone, intravenous diphenhydramine was then started. Within minutes after the start of the diphenhydramine infusion, the patient reported that she was not feeling well. She reported feeling dizzy, weak, and short of breath. The infusion was stopped and her vitals were recorded. Her blood pressure was in the 70s/40s; her heart rate was in the 40s; oxygen saturation was 100%. The patient's baseline blood pressure earlier in the day before any drugs were administered was 110/73 with a heart rate of 69 and respiratory rate of 18. The patient was put in a lying position and given 500 mL of 0.9% sodium chloride solution. A physical examination was performed and found to be within normal limits. Within 10 minutes, her blood pressure was in the 100s/50s and heart rate was in the 50s. Her vitals then remained stable. The patient then received her planned chemotherapy and was discharged home. No further reaction was noted by the patient in the 72 h that followed. Several weeks after the chemotherapy was given, hives were reported under the patient's arms, under the breasts, and in the groin area. The patient reported no changes in laundry detergent, cleansers, or soaps. This was successfully treated with oral diphenhydramine.

The patient has no prior history of any allergies to drugs or food. However, the patient does report that the smell of isopropyl alcohol makes her dizzy. The only concomitant medications that the patient reported that she was taking was an estradiol patch, applied weekly and hydrocodone/acetaminophen taken on an as needed basis, with no reported usage in the days leading up to her planned chemotherapy. No chronic medical conditions are noted on physical exam. Due to the severe nature of the blood pressure drop accompanied with shortness of breath, subsequent re-challenge with palonosetron, or other 5-HT₃ receptor antagonists was not performed. During subsequent cycles of chemotherapy, dexamethasone, aprepitant, and diphenhydramine were administered with no reaction. The causal association of aprepitant, palonosetron, dexamethasone, and diphenhydramine were evaluated using the Naranjo algorithm and a score of 5 indicating 'probable' for palonosetron, a score of 4 indicating a 'possible' reaction to diphenhydramine. Dexamethasone and aprepitant both scored a 3, which indicates a 'possible' reaction. According to the NCI CTCAEv4.03 (National Cancer Institute Common Terminology for Adverse Events), this would rank as Grade 3 anaphylaxis.

Discussion

Palonosetron is a newest available agent in the 5-HT₃ receptor antagonist class of drugs. It was approved in 2003 by the FDA. The current approved indications are the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderate and highly emetogenic chemotherapy regimens. It is also indicated for the prevention of post-operative nausea and vomiting for up to 24 h following surgery.⁸ Palonosetron has a prolonged half life of about 40 h and a greater binding affinity for the 5-HT₃ receptor.⁹

In a literature review, only one case report of anaphylaxis was found with palonosetron.¹⁰ The product labeling lists hypotension as occurring in less than or equal to 1% of patients and hypersensitivity as less than 1% of patients.⁶ In general, the 5HT₃-receptor antagonists are generally well tolerated with minimal adverse drug reactions and no limiting toxicities at typical doses. The most common adverse events include mild headache, transient elevation of hepatic aminotransferase levels, and constipation.¹¹ Generally, there is no cognitive, psychomotor, or affective disturbances associated with the drug class.¹² A literature review was also done for aprepitant with no cases of anaphylaxis reported.

Palonosetron is not the only drug the patient received that may have caused hypotension. According to the product information, hypotension associated with palonosetron was reported in 1% of the patients.⁸ Aprepitant is associated with hypotension with a similar frequency, of greater than 0.5% of patients.¹³ The prescribing information for diphenhydramine also mentions hypotension with no frequency given.¹⁴ Hypotension is not listed as a reaction to dexamethasone in the prescribing information, but both hypertension and hypersensitivity reactions are mentioned with no given frequency.¹⁵ In this case, palonosetron is the only medication that patient did not receive during her remaining cycles of chemotherapy. She did not experience any hypotension, rash, or other reaction during subsequent cycles.

It is of interest that the patient reported a rash several weeks after she was treated with chemotherapy. Cutaneous drug reactions occur in 2–3% of hospitalized patients and thousands of outpatients have severe cutaneous drug reactions every year.¹⁶ According to the prescribing information, each drug the patient received can cause a rash. Carboplatin in particular is known to cause delayed hypersensitivity.^{7,17,18} One common feature of a Type IV reaction (delayed or T-cell mediated) is as an allergic contact dermatitis.¹⁶ In the past, this reaction was thought to be a Type I reaction, but more recent data suggests a role for Type IV, as a result carboplatin reactions are more heterogeneous in

nature.^{7,17,18} Reactions after rechallenge are generally worse than the original reaction.¹⁶ The patient received two further cycles of chemotherapy with both paclitaxel and carboplatin without further incident, so it is unlikely that the subsequent rash was due to a delayed hypersensitivity reaction to carboplatin. The treating service did not think the rash was related to drug therapy, however, since the patient was not retreated with palonosetron, that possibility does remain.

Based on the widespread use and generally good tolerability palonosetron, clinicians should be aware that, while not common, patients may experience a severe adverse reaction to it.

Conflict of Interest

The author declares there is no conflict of interest.

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