

Letter to the Editors

Palonosetron induced anaphylaxis in an adult female

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We report a case of anaphylactic shock following intravenous (i.v.) administration of palonosetron. A 40 year old woman with relapsed breast cancer was scheduled for first cycle of chemotherapy with cyclophosphamide, epirubicin, 5-fluorouracil and docetaxel. Prior to the start of chemotherapy, i.v. palonosetron 0.25 mg (5 ml) was administered to prevent nausea and vomiting. Within a few seconds the patient experienced difficulty in breathing, generalized itching and dizziness. Bronchial wheeze was present, blood pressure was unrecordable and oxygen saturation by pulse oximetry was 75%. She was immediately moved to the intensive care unit and was resuscitated with oxygen, i.v. crystalloid and i.v. adrenaline (1 : 10 000), hydrocortisone and pheniramine. Within 1 h the patient was haemodynamically stabilized. Laboratory tests revealed no abnormality in liver or renal function. Palonosetron was discontinued and the next day she was premedicated with i.v. metoclopramide, dexamethasone, pheniramine and ranitidine and chemotherapy was initiated. Thereafter, the patient did not develop any other problem and was asymptomatic after 72 h of follow-up.

The patient had no history of concomitant medications (including herbal medicines), allergy to food or other drugs (including other 5-HT₃-receptor antagonists) or addiction to tobacco or alcohol. Medical history of any chronic systemic disease was also absent. However, she revealed a history of allergic dermatitis to household detergents and caustic soda. Re-challenge with palonosetron was not carried out due to the life threatening nature of the adverse drug reaction (ADR). Causality assessment was carried out using the World Health Organization-Uppsala Monitoring Centre criteria and the adverse reaction had 'certain' relationship with palonosetron administration. The strong temporal relationship between administration of palonosetron and onset of symptoms of anaphylaxis and their amelioration with discontinuation of the drug suggested this relationship. The casual association was also evaluated using the Naranjo algorithm and a score of 7 indicated a 'probable' relationship [1]. The ADR was reported to the national pharmacovigilance centre under the National Pharmacovigilance Programme, India.

Palonosetron is a relatively new 5-HT₃ receptor antagonist that was approved in 2003 by the US FDA for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderate to highly emetogenic cancer chemotherapy. It has at least 30-fold higher affinity for the 5-HT₃ receptor compared with the first-generation 5-HT₃ receptor antagonists like ondansetron, granisetron and dolasetron. In addition, palonosetron also has higher potency and is three-fold more potent than granisetron and up to 55-times more potent than ondansetron [2]. It is generally well tolerated, and in clinical trials, headache (9%) and constipation (5%) were the most commonly reported adverse drug reactions. Less frequently reported adverse reactions include diarrhoea, dizziness, fatigue, abdominal pain and insomnia. The severity and frequency of the adverse reactions are similar to those observed with ondansetron and dolasetron [3]. A recent case report described the occurrence of generalized tonic clonic seizures after i.v. palonosetron in a patient with breast carcinoma scheduled for chemotherapy [4].

To the best of our knowledge, this is probably the first case of i.v. palonosetron-induced anaphylaxis to be reported. However, anaphylactoid reaction has been reported with the use of i.v. ondansetron. The very rare (less than 1/10 000) incidence of hypersensitivity encountered during post marketing surveillance of palonosetron has been mentioned in its package insert and the use of palonosetron has been contraindicated in patients who are hypersensitive to it or other 5-HT₃ receptor antagonists [5]. Although this patient did not have a history of drug allergy, it is possible that she may have been pre-sensitized to 5-HT₃ receptor antagonists during her earlier hospital visits for surgery of the tumour.

The widespread and easy availability of 5HT₃-receptor antagonists in the Indian market has promoted the off label use of these drugs, such as in the treatment of antimalarial-induced vomiting, gastritis, migraine and other emetogenic conditions [6]. In view of the life threatening yet avoidable nature of the anaphylactic reaction developing after i.v. palonosetron, those prescribing it or other 5-HT₃ receptor antagonists should exercise extreme caution, especially in patients with history of any sort of

hypersensitivity. Whenever possible, alternatives like metoclopramide or domperidone should be prescribed for such patients.

Competing interests

There are no competing interests to declare.

REFERENCES

- 1 Farcas A, Bojita M. Adverse drug reactions in clinical practice: a causality assessment of a case of drug-induced pancreatitis. *J Gastrointest Liver Dis* 2009; 18: 353–8.
- 2 Aapro MS. Palonosetron as an anti-emetic and anti-nausea agent in oncology. *Ther Clin Risk Manag* 2007; 3: 1009–20.
- 3 De Leon A. Palonosetron (Aloxi): A second-generation 5-HT₃ receptor antagonist for chemotherapy-induced nausea and vomiting. *Proc (Bayl Univ Med Cent)*, 2006; 19: 413–6.
- 4 Zambelli A, Sagrada P, Pavesi L. Seizure associated with palonosetron. *Support Care Cancer* 2009; 17: 217.
- 5 Daily Med. Aloxi (palonosetron hydrochloride) injection [MGI Pharma]. Available at <http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=9053> (last accessed 15 November 2009).
- 6 Mehra KK, Gogtay NJ, Ainchwar R, Bichile LS. Hypersensitivity to intravenous ondansetron: a case report. *J Med Case Reports* 2008; 2: 274.

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