Author's response to reviews

Title: Hypersensitivity to Intravenous Ondansetron in a 19 year old female: Case Report

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Abstract

Introduction:

Ondansetron, a widely used 5-Hydroxytryptamine$_3$ (5-HT$_3$) receptor antagonist in the prevention and treatment of chemotherapy-induced nausea and vomiting is associated with various unusual adverse drug reactions. Here we describe an anaphylactoid reaction to a single intravenous dose of Ondansetron.

Case Presentation:

A 19 year old female presented with 3-4 episodes of nausea, vomiting, and epigastric distress. She was a known case of polycystic ovarian disease (PCOD) on treatment with cyproterone acetate 2mg, ethinyl estradiol 0.035mg, finasteride 5mg and metformin 500mg for one month. She was also taking oral Roxithromycin 500mg per day for the past 3 days for treatment of a mild upper respiratory tract infection. She also occasionally took rabeprazole 10mg for gastritis which worsened after treatment with roxithromycin. She was treated with a single 4mg dose of ondansetron intravenously. She immediately developed urticaria, which was treated with intravenous dexamethasone 4mg and chlorpheniramine maleate 20mg. The reaction abated within a few minutes and she was discharged within an hour. She was asymptomatic at 72 hours of follow up.

She had no history of ondansetron exposure, or drug or food allergies. The adverse event on the Naronjo’s causality assessment scale was 6 indicating a “possible” reaction to ondansetron.
Discussion

5-HT₃ receptor antagonist have been associated with life threatening adverse reactions like hypotension, seizures and anaphylaxis. The wide availability of these drugs in India has promoted their off label use in the treatment of gastritis, migraine and so on. Our case represents an off label use in a patient who could have been treated with a safer drug. Some authors have suggested that anaphylaxis may be a class effect while others think it may be drug specific. In our case, we suspect an IgE mediated Anaphylactoid reaction to Ondansetron. Considering all the existing evidence we need to be more cautious whilst using Ondansetron and also be aware of the various unusual side effects, especially when used in an out-of-hospital set up. Our case report underscores the importance of physician judiciously using the drug so as to reducing the incidence of avoidable adverse drug reactions.
**Case Report**

**Introduction:**

Ondansetron is a widely used 5-Hydroxytryptamine$_3$ (5-HT$_3$) receptor antagonist in the prevention and treatment of chemotherapy-induced nausea and vomiting, especially that caused by highly emetogenic drugs such as cisplatin, and is considered a gold standard for this purpose [1]. It may also be used in the prevention and treatment of radiation induced nausea and vomiting as well as post operative nausea and vomiting. Commonly seen side effects include constipation or diarrhea, headache, and dizziness. All 5-HT$_3$ receptor antagonists have been associated with asymptomatic electrocardiogram changes, such as prolongation of the PT and QTc intervals and certain arrhythmias [2]. The clinical significance of these side effects is unknown. Hypersensitivity to Ondansetron is an extremely rare side effect. The authors describe in this paper a case of anaphylactoid reaction to a single intravenous injection of Ondansetron.

**Case Presentation:**

A 19 year old female patient visited the emergency department (ED) of a tertiary referral centre with 3-4 episodes of nausea, vomiting, and epigastric distress. She was a known case of polycystic ovarian disease (PCOD) on treatment with cyproterone acetate 2mg, ethinyl estradiol 0.035mg, finasteride 5mg and metformin 500mg for one month. The patient was taking oral Roxithromycin 500mg per day for the past 3 days along with PCOD medication for treatment of a mild upper respiratory tract infection. The patient also occasionally took single dose rabeprazole 10mg for gastritis. The gastritis had
worsened after treatment with roxithromycin which was the cause of her visit to the ED. The patient was treated with a single 4mg dose of ondansetron intravenously. Within a few seconds of the patient developed redness, wheals around the injection site along with urticaria. There was no hypotension or bronchospasm. She was immediately treated with intravenous dexamethasone 4mg and chlorpheniramine maleate 20mg. The reaction abated within a few minutes. The patient did not complain of any other symptoms and was discharged after an hour of observation. She was asymptomatic at 72 hours of follow up.

On further history taking, the patient gave no previous history of ondansetron exposure, or drug or food allergies. There was no history of a similar episode in the past. She gave no personal or family history of atopy, asthma, or bronchitis. The adverse event on the Naranjo’s causality assessment scale was 6 indicating a “possible” reaction to ondansetron. [3]

Discussion

5-HT₃ receptor antagonists such as ondansetron, tropisetron, granisetron and palonosetron are generally associated with a wide safety margin and widely used in cancer chemotherapy. There are however reports of life threatening adverse events conditions such as generalized tonic clonic seizures, hypotension [4], chest pain, and dystonia [5]. To date, all anaphylaxis and anaphylactoid reactions induced by ondansetron have been in patients receiving the drug for cancer chemotherapy. This has prompted some authors to suggest that the drug’s use should be restricted [6]. In the
Indian market, the drugs have a wide availability with over 43 different brands.[2]. Such wide availability of this class of drug has promoted the off label use of these drugs, such as in the treatment of anti malarial induced vomiting, gastritis, migraines, and other emetogenic conditions. The present case also represents the off label use of the drug in a patient who could have probably received safer medication such as Domperidone or Metoclopramide.

Some authors have suggested that anaphylaxis may be a class effect [7], while others think it may be drug specific [8]. Ondansetron and tropisetron share an indole heterocycle, ondansetron while granisetron does not. This may justify the reports contradicting anaphylaxis as a class effect. In our case, we suspect an IgE mediated Anaphylactoid reaction to Ondansetron considering the rapidity of events following the administration of the drug [9]. An immunological component cannot be ruled out as there have been reports of positive Lymphocyte Transformation Test to Ondansetron [10].

In the wake of the above evidence, and the increasing availability and off label use of Ondansetron and other 5-HT₃ receptor antagonists, we need to be more cautious whilst using this drug and also be aware of the various unusual side effects, especially when used in an out-of-hospital set up where prompt treatment of the reaction may not be possible. Our case report underscores the importance of physician judiciously using the drug so as to reducing the incidence of the above mentioned avoidable adverse drug reactions.
Conclusion

We emphasize the need to be judicious in the use of Ondansetron and other 5 HT₃ receptor antagonists due to their association with various unusual and life threatening reactions. We also caution against the off label use of the drugs especially in an out-of-hospital setup.

Consent: Written informed consent was obtained from the patient for publication of this case report. A copy of the written informed consent is available for review by the Editor-in-Chief of this journal.

Competing Interests: None

Authors Contribution:

KM: Identified the Adverse Drug Reaction and wrote the first draft of the paper.

NG: Conceived the manuscript, performed literature search and causality analysis and wrote the final draft of the paper.

RA: Was the physician who treated the Adverse Drug Reaction.

LSB: Helped to draft and finalise the manuscript.

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References


