Author's response to reviews

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

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Author's response to reviews: see over
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Reply to referees’ comments

Reviewer- Kohei Takahashi
Comment- Would you like describing the result of skin test or serum IgE level if performed
Reply: We did not perform either. The skin test would have needed to be carried out in the intensive care setting given the intensity of the reaction, and hence was not done.

Reviewer- Rui Sato
Comments:
1. The word Naranjo’s causality assessment scale was misspelled as “Noronjo. It should be corrected.
Reply: This has been done

2. “In our case, we suspect an IgE mediated anaphylactoid reaction.” This is not correct I am afraid. IgE does not mediate an anaphylactoid reaction, if so, it is anaphylaxis. If possible, the information is desirable how rare this side effect of ondansetron or other 5HT3 antagonists is.
Reply- The difference between IgE and non IgE reactions is now given in the text. In the absence of a skin test and IgE levels, it is difficult to determine whether the reaction was anaphylaxis or anaphylactoid. The exact incidence of these reactions is unknown. A paper giving the number of such reactions reported to the US FDA is quoted.

Reviewer- Parathasarathi Gurumurthy
Comments:
1. Authors have used the term anaphylaxis in the title and later in the text (Introduction of abstract and article and under discussion) call it as IgE mediated anaphylactoid reaction. Anaphylactoid reactions are very similar to anaphylaxis but are not IgE mediated. Both anaphylaxis and anaphylactoid reactions are expected to have involvement of CVS or RS. But there is no hypotension or bronchospasm in this patient. I would rather suggest it as ondansetron induced urticaria. The title may be suitably modified.
Reply: The difference between IgE and non IgE reactions is now given in the text. In the absence of a skin test and IgE levels, it is difficult to determine whether the reaction was anaphylaxis or anaphylactoid. In this patient, urticaria was also accompanied by a wheal and the treatment was immediate since she was already in the emergency department. It is thus difficult to say whether it was just urticaria or could have progressed further. Hence, we would like to retain the title of “hypersensitivity”

2. Under discussion on Page 6, authors say “we suspect an IgE mediated anaphylactoid reaction” to ondansetron. It is advisable to replace the anaphylactoid reaction with IgE mediated urticarial reaction. While it is said as IgE mediated urticarial reaction, we have to demonstrate previous exposure to ondansetron or cross reactivity to any other drug. This issue may have to be addressed.
Reply: As above. There was no previous exposure. This is now mentioned.

3. On Page 6, para 2 last sentence, authors say, “an immunological component cannot be ruled out as there have been reports of positive lymphocyte transformation tests to ondansetron.” This sentence reads completely out of place. What possible relation are the authors trying to draw between lymphocytes and IgE mediated type 1 reactions.
Reply: Sentence deleted

4. As per Naranjo’s scale causality assessment, score 6 refers to a “probable” reaction, not “possible” reaction. This should be corrected.
Reply: Corrected

5. The incidence of IgE mediated urticarial reactions to ondansetron is rare, but not extremely rare. This may be corrected in the first para of introduction.
Reply: Corrected.