OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://brief.land/briefland/knowledgebase/category/tree.html#opr.html

Archives of Pediatric Infectious Diseases
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Peer Review Report for "Posaconazole-Induced Acute Pancreatitis: A Rare Side Effect in a Child with Chronic Granulomatous Disease"

Author(s): Marjan Tariverdi, Sedigheh Rafiei Tabatabaei, Ali Saffaei, Ladan Ayazkhoo, Bahador Mirrahimi

Review Timeline:

Submit Date:	29 Dec 2019
Revised Date:	13 Jun 2020
Accepted Date:	14 Jun 2020

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Ali Amanati: Reviewer | Revision (0) 13 Jan 2020

Dear AE,
I review with interest a case report entitled “Posaconazole Induced Acute Pancreatitis: A Rare Entity in a Child with Chronic Granulomatous Disease”.
Thanks for this nice case report.
Comments for the authors:
- Please add brief descriptions for suggested comments in the proper position in the text.
Abstract
- Replace "entity" in title with "side effect".
- How did you confirm the causal relationship between posaconazole (PSC) and pancreatitis?
- A brief description should be added in abstract part?
Introduction
- Although brief information is provided about drug induced pancreatitis, more specific

descriptions should be added by relevant known mechanisms that have been described previously.

Discussion

- Discussion is weak.
- Please clarify that if this agent has FDA approve for use in children?
- There is no information regard possible drug-drug interaction in this case.
- There is no information regard effect of CYP2C19 status and azoles side effects.
- There is no information regard importance of TDM in patients who are on azole Px.
- Why did you choose PSC for prophylaxis (Px) despite of other available azoles such as itraconazole?
- What is the best time for initiation of AF Px in such patients? For which reason patient receive late AF Px?
- When all agents are discontinued simultaneously, how could you confirm the causal relationship between PSC and pancreatitis?
- What did you think about the possible risk factors for development of pancreatitis in patients who are on azole Px? How we can prevent such side effect in similar patients?
- Finally, English language could be improved.

Thanks

Parisa Badiee: Reviewer | **Revision (0)** 5 Feb 2020

Dear AE,

The work entitles" Posaconazole Induced Acute Pancreatitis: Case Report of a Rare Entity in a Child with Chronic Granulomatous Disease;" is a well-organized case report on unusual infection in the pediatric patients. This manuscript could be of clinical significance and helpful for the management and treatment of similar cases. It deserves publication in your esteemed journal.

Sincerely

ParisaBadiee
Clinical Microbiology Research center
Shiraz University of Medical Sciences, Shiraz, Iran

peyman arfa: Reviewer | **Revision (0)** 7 Feb 2020

Dear AE;

Thanks for this attractive, useful and novel subject of case report. I have some comments and suggest to some minor revisions for the authors.

1- Please clarify your references for some scientific issues, specially in introduction.

2- Revise your English grammars.

Thanks.

REFEREE: Associate Editor | **Revision (0)** 7 Feb 2020

Dear EIC,

Thanks for this submission titled "Posaconazole Induced Acute Pancreatitis: Case Report of a Rare Entity in a Child with Chronic Granulomatous Disease" in Archives of Pediatric Infectious Diseases.

Based on reviewer's comments and also in my opinion, this manuscript needs major revision.
The authors should follow the reviewer's comments and reply in a point-by-point manner (highlight new changes in the manuscript with yellow color).
In addition, English copy-editing is warranted before next submission.
Best regards

Sedigheh Rafiei Tabatabaei-EIC: EIC | **Revision** (0) 10 Feb 2020

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Reviewer Number	Comment	Reply
Reviewer 1	I review with interest a case report entitled “Posaconazole Induced Acute Pancreatitis: A Rare Entity in a Child with Chronic Granulomatous Disease”. Thank you for your nice case report. Please add brief descriptions for suggested comments in the proper position in the text.	Thanks for your kind words. Your comments are highly appreciated and we employed all forces to revise our manuscript according to your comments. Here, all replies provided point by point.
Reviewer 1	Replace "entity" in title with "side effect".	We modified our title as: "Posaconazole Induced Acute Pancreatitis: Case Report of a Rare Side Effect in a Child with Chronic Granulomatous Disease"
Reviewer 1	How did you confirm the causal relationship between posaconazole (PSC) and pancreatitis?	We used Naranjo scale in this regard and we found a definite probality in this regard. Below paragraph added to the manuscript: "The Naranjo Adverse Drug Reactions Probability Scale (NADRPS) used for evaluation of the causality of this event with definite probability."
Reviewer 1	A brief description should be added in abstract part?	We added more descriptions about pancreatitis and CGD to the abstract.
Reviewer 1	Although brief information is provided about drug induced pancreatitis, but more specific descriptions should be added by relevant known mechanisms that have been described previously.	We described all probable mechanism in the text. Below paragraph added to the manuscript: "Possible mechanisms for drug-induced pancreatitis include cytotoxic effects, pancreatic duct constriction, accumulation of toxic metabolites, and hypersensitivity reactions."
Reviewer 1	Discussion is weak.	Thanks for your comment. We used your precious comments to improve the discussion section.
Reviewer 1	Please clarify that if this agent has FDA approve for use in children?	We added a paragraph in this regard as below: "The use of Posaconazole in children under 12 years of age is not FDA approved but unlabeled use of drugs in children is common because of lack of data in this population. The majority of data regarding safety of drugs in children is based on reports"

Reviewer 1	There is no information regard possible drug-drug interaction in this case.	We added a sentence in this regard as below: "The drug-drug interactions reviewed for the drugs. Only interaction was between Pantoprazole and Posaconazole, which may reduce the Posaconazole plasma levels"
Reviewer 1	There is no information regard effect of CYP2C19 status and azoles side effects.	Thanks for your precious comment. Although CYP2C19 has a great impact on the azole metabolism but we have not any facility to measure the enzyme activity. However we added this limitation as a suggestion to the manuscript. "Also, it is recommended to evaluate the Posaconazole metabolism through therapeutic drug monitoring programs or measuring the CYP2C19 activity."
Reviewer 1	There is no information regard importance of TDM in patients who are on azole Px.	Thanks for your comment. We added the importance of TDM and we suggested to use TDM for future cases as below: "Also, it is recommended to evaluate the Posaconazole metabolism through therapeutic drug monitoring programs or measuring the CYP2C19 activity."
Reviewer 1	Why did you choose PSC for prophylaxis (Px) despite of other available azoles such as itraconazole?	You are right. However we must use the syrup dosage form of Iitraconazole and it was not available in the Iranian pharmaceutical market. But after this event we use Iitraconazole tablets inevitably. We added a paragraph to clarify this issue: "At the last admission, the Syrup of Posaconazole 5 cc every 8 hours was added to her drugs according to available medications in the Iranian pharmaceutical market. Although we could not use other azoles because the syrup dosage forms of them were available in the in the Iranian pharmaceutical market"
Reviewer 1	What is the best time for initiation of AF Px in such patients? For which reason patient receive late AF Px?	CGD is a rare disorder in which the phagocytes fail to produce hydrogen peroxide. The patients are predisposed to bacterial and fungal infections. Prophylactic antibiotics and interferon gamma have reduced bacterial infections, but there is also the danger of life-threatening fungal infections. Although there are some reports of prophylactic role of

		Iitraconazole in CGD but in the presence of fungal, it is necessary in initiate it. However, the AFs must be imitated sooner, but the patient and her family has a poor adherence to follow their medical problems.
Reviewer 1	When all agents discontinued simultaneously, how could you confirm the causal relationship between PSC and pancreatitis?	You are right and we added our causality assessment method for more clarification as below: "We used Naranjo scale in this regard and we found a definite probality in this regard. Below paragraph added to the manuscript: "The Naranjo Adverse Drug Reactions Probability Scale (NADRPS) used for evaluation of the causality of this event with definite probability."
Reviewer 1	What did you think about the possible risk factors for development of pancreatitis in patients who are on azole Px? How we can prevent such side effect in similar patients?	We added a sentence in this regard to improve our manuscript: "Any underlying causes which alter the azole metabolism such as renal and liver failure and drug-drug interactions may lead to such adverse drug reactions".
Reviewer 1	Finally, English language could be improved.	Thanks for your comment. We consulted with a native English speaker to improve the language.
Reviewer 2	The work entitles" Posaconazole Induced Acute Pancreatitis: Case Report of a Rare Entity in a Child with Chronic Granulomatous Disease;" is a well-organized case report on unusual infection in the pediatric patients. This manuscript could be of clinical significance and helpful for the management and treatment of similar cases. It deserves publication in your esteemed journal. Sincerely	Thanks for your kind comment.
Reviewer 3	Thanks for your attractive, useful and novel subject of case report. I have some comments and suggest to some minor revision.	Thanks for your comment. All your comments had been addressed in the text.
Reviewer 3	1- Please clarify your references for some scientific	We added some references in this regard and some

	issues, especially in introduction.	modifications done.
Reviewer 3	2- Revise your English grammars.	Thanks for your comment. We consulted with a native English speaker to improve the language.

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Ali Amanati: Associate Editor | **Revision** (1) 3 Jun 2020

Dear EIC,
The overall presentation of the manuscript is improved after amendments. However, a few points still need the authors' consideration.
- Provide a screenshot from your responses to 10 items in Naranjo scale, and upload it as a supplementary file in the new submission. Reference to the supplementary file in the text.
- In this part: "the Syrup of Posaconazole 5 cc every 8 hours was added to her drugs according to available medications in the Iranian pharmaceutical market", "unavailable" seems to be correct.
- About your response to this comment: "What is the best time for initiation of AF Px in such patients? For which reason the patient receives late AF Px?"; please add a brief description in the proper position in the text.
Thanks.

REFEREE: EIC | **Revision** (1) 4 Jun 2020

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Comment	Reply
The overall presentation of the manuscript is improved after amendments. However, a few points still need your consideration.	Thanks for your comment. Other minor comments also addressed here point by point.
Provide a screenshot from your responses to 10 items in Naranjo scale, and upload it as a supplementary file in the new submission. Reference to the supplementary file in the text.	We provided our calculated scale as a supplementary file.
In this part: "the Syrup of Posaconazole 5 cc every 8 hours was added to her drugs according to available medications in the Iranian pharmaceutical market", "unavailable" seems to be correct.	We correct this issue
About your response to this comment: "What is the best time for initiation of AF Px in such patients? For which reason the patient receives late AF Px?"; please add brief description in the proper position in the text.	We added this point in the middle paragraphs of "case report" section.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Ali Amanati: Associate Editor | **Revision** (2) 13 Jun 2020

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (2) 14 Jun 2020

Dear Author,
Thank you very much for the revised manuscript.
It is a pleasure to inform you that your manuscript, has been accepted for publication in APID.
Thanks again.