

Dear Editor,

Thank you very much for considering our manuscript entitled “Itraconazole therapy for infant hemangioma: case report” for publication in the *World Journal of Clinical Cases*. We thank the editor and reviewers for providing constructive comments and suggestions, which improved the manuscript substantially. All items raised have been addressed in the revision, and our point-by-point responses are detailed below.

This revised manuscript has been carefully edited and proofread by *Medjaden Bioscience Limited*.

We hope that this further revised manuscript is now acceptable for publication in your journal, and again, we thank you for your consideration.

With best wishes,

Yours sincerely,

Fu-qiu Li

Responses to Reviewers

We thank you for the comprehensive and thoughtful review, which helped improve the manuscript significantly. We have addressed all points raised and revised the manuscript accordingly. All changes, as well as responses to all questions, are detailed below:

Reviewer 1

1. In the discussion line 160, Bessar et al compared IHs treatment between propranolol and itraconazole, please explain why itraconazole is better and safer than propranolol? If there are other studies compare the comparison of propranolol and itraconazole, please add them in the discussion to increase clinician understanding of alternative therapies for IHs.

Response: Thank you so much for pointing out the critical issue. We chose itraconazole to treat the two IH cases because as compared to propranolol, itraconazole evinces little side effects, non-reliance on electrocardiogram monitoring, and extensively therapeutic capability on cardiovascular diseases. We added this explanation to the discussion in the revised manuscript on Page 8, Lines 203-207. Two more relevant references had been provided and cited.

2. Make conclusions concise and clear. The method of administration of itraconazole can be moved to the Discussion subheading.

Response: Thank you so much for the suggestion. We have revised the Conclusion accordingly and moved the content of medicine preparation to the Discussion.

3. Does itraconazole become the standard therapy for IHs in your hospital? If not,

please attach the ethical clearance of the study and/or the informed consent of therapy in author patients.

Response: Many thanks for the constructive suggestion. Itraconazole has not yet become the standard therapy for IHs in our hospital, so we provided the informed consent of the patients' parents.

Reviewer 2

1. The authors gave two babies oral itraconazole at the dose of 5 mg/kg/d according to the Dr. Ran's report. Then, the authors should explain the prospect of administration period of itraconazole. And the author also needs to explain the skin findings of terminating itraconazole. Because in Case 1, the authors described in page 4 line 98 "On day 80, the size and color of lesions were reduced further (Fig. 1), therefore itraconazole administration was halted.", and in Case 2, in page 6 line 128, "After day 90, the baby's parents decided by themselves to stop the medication and no longer visit the hospital." The reviewer thinks the authors had no plan to administer this drug.

Response: The reviewer's comment has been given full consideration. As shown in the text, we stopped the administration of itraconazole to the patients after the IH condition was controlled. During the follow-up, we did not find any relapse of the skin lesion. However, we do believe that a longer follow-up period is necessary for the confirmation of the long-term efficacy and side effect of itraconazole to IHs.

2. In Figure 1, this case 1 had hemangiomas at on the right hand. However, findings at 43 days and at 124 days after itraconazole treatment showed at the left hand. Please confirm these pictures.

Response: We greatly appreciate that you pointed out this mistake. We must clarify that all photographs were on the right hand of the first baby. The photographs that seem to show the left hand at day 43 and 124 were caused by inversion of the pictures. These have been corrected in the revised manuscript.

3. In CONCLUSION, the authors should describe more briefly. Therefore, the authors can move some sentences from CONCLUSION to DISCUSSION.
4. The authors should explain the reason how oral itraconazole administration was given first in DISCUSSION.

Response: We greatly appreciate your suggestion. We have refined the conclusion and removed some sentences to enhance the conciseness. As recommended, the reason why the oral itraconazole was dissolved in milk has been moved to the middle paragraph of the discussion (page 9, Lines 226-230) in the revised manuscript.

Reviewer 3

1. Long term follow up of these patient is required to see the long term side effects of Itraconazole in these patients.

Response: Thank you for the insightful suggestion. We do believe that a longer period of follow-up is necessary before confirming the long-term efficacy and side effects of itraconazole on IHs. This consideration will be observed and demonstrated in our future studies.

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) *Science editor:* 1 Scientific quality: The manuscript describes a case report of the Itraconazole therapy for infant hemangioma. The topic is within the scope of the

WJCC. (1) Classification: Grade C, Grade C and Grade C; (2) Summary of the Peer-Review Report: These 2 case reports have clearly shown satisfactory outcomes of Itraconazole treatment in infantile hemangioma. Please explain why itraconazole is better and safer than propranolol. If there are other studies compare the comparison of propranolol and itraconazole, please add them in the discussion to increase clinician understanding of alternative therapies for IHs. The authors should explain the reason how oral itraconazole administration was given first in discussion; (3) Format: There are 2 figures; (4) References: A total of 25 references are cited, including 10 references published in the last 3 years; (5) Self-cited references: There are no self-citations; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

2 Language evaluation: Classification: Grade A, Grade B and Grade B. A language editing certificate issued by Medjaden was provided.

3 Academic norms and rules: The authors provided the signed informed consent. The authors should provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. The authors need to fill out the CARE Checklist – 2016 with line/page numbers. No academic misconduct was found in the Bing search.

4 Supplementary comments: This is an unsolicited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJCC.

5 Issues raised: (1) The "Author Contributions" section is missing. Please provide the author contributions; (2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (3) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout; and (4)

The “Case Presentation” section was not written according to the Guidelines for Manuscript Preparation. Please re-write the “Case Presentation” section, and add the “FINAL DIAGNOSIS”, “TREATMENT”, and “OUTCOME AND FOLLOW-UP” sections to the main text, according to the Guidelines and Requirements for Manuscript Revision. 6 Recommendation: Conditionally accepted.

Response: We have made the requested revision.

(2) Company editor-in-chief: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, the author(s) must provide the Signed Informed Consent Form(s) or Document(s). For example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc.

Response: We have uploaded requested files.