

Dear editors and reviewers,

We, the authors of World Journal of Clinical Cases Manuscript NO: 62890, appreciate the three anonymous reviewers' comments and the additional comments from the science editor and the company editor-in-chief, which helped us revise the manuscript. We paid heed to all of your advice and suggestions, and the manuscript has been revised accordingly. We believe that the contents and the clarity of our paper are much improved in the revised version.

Reviewer #1 comments: *First, this manuscript's original findings is that escitalopram can cause drug-induced hepatotoxicity and cholestasis, generally within a week after initiation. Second, this is the first reported case of cholestasis where the treatment with escitalopram is the only possible cause, with a highly probable causality. This manuscript find that the serotonergic antidepressants in patients with non-severe depression is the ineffectiveness and harmfulness. Third, the limitations of the study is lacking of course of clinical recovery and biological normalisation after escitalopram withdrawal in the literature review.*

Recommendation: *It is recommended to add a picture of liver pathology or biochemical results to support the evidence of "inflammatory syndrome, cholestasis with a conjugated hyperbilirubinemia and cytolytic hepatitis".*

Answer: dear reviewer, table 1 (line 80) now represents C-reactive protein (CRP), total bilirubin, conjugated bilirubin, unconjugated bilirubin and alanine transaminase levels before, during and after the course of treatment with escitalopram. We specifically added the CRP levels to support the evidence of an inflammatory syndrome.

Reviewer #2 comments: *Escitalopram-induced hepatitis is extremely rare, which is very interesting. And, the authors also performed VigiBase analysis in the manuscript. But I have some questions.*

Question 1: *This is a case report on escitalopram-induced hepatitis, therefore without the need for an extensive description of depression in the background.*

Answer 1: dear reviewer, we agree with your comment and the description of depression in the background has been deleted, improving the clarity of our manuscript.

Question 2: *In the line of 72," without any pain or hyperthermia", but in the line of 87 "the pain stopped". Is there with or without "pain" of the patient?*

Answer 2: dear reviewer, there was indeed a mistake, so we corrected the manuscript to delete the mention of pain: "The pruritus stopped two days after escitalopram withdrawal" (line 71).

Question 3: *I can't find figure 1 in the manuscript.*

Answer 3: dear reviewer, this was a mistake in the first place, the mention of figure 1 has been deleted in the reviewed version.

Question 4: *Whether to screen autoantibodies and immunoglobulin levels of the patient ?*

Answer 4: dear reviewer, unfortunately, autoantibodies and immunoglobulin levels weren't screened. However, since it would have been interesting to do so, we mentioned it in the reviewed version (line 67).

Question 5: *It is not necessary to describe RUCAM in detail in the manuscript.*

Answer 5: dear reviewer, we deleted the RUCAM detail in the manuscript, and we put it in appendix 1.

Question 6: *Why does bilirubin fall more quickly than transaminases during recovery of the patient ? It is not common in the clinic, especially in DILI.*

Answer 6: dear reviewer, you raise an interesting question but we are unable to explain why. We mentioned it in the reviewed version (lines 72-74), and we also referred to the time course of serum test results in DILI from several real cases (reference 5).

Reviewer #3 comments: *This is an interesting case with a thorough review of the literature. The Authors also performed an analysis of the data available on Vigibase, which is the largest pharmacovigilance database. I have few comments:*

Comment 1: *Define the abbreviations at the first mention.*

Answer 1: dear reviewer, all the abbreviations are now defined at first mention in the reviewed version.

Question 2: *Line 65: To which category does escitalopram belong?*

Answer 2: dear reviewer, we specifically mentioned in the reviewed version that escitalopram is a selective serotonin reuptake inhibitor (line 47).

Question 3: *typo mistakes Line 88 (live) and line 118: do you mean "all over the world" instead?*

Answer 3: dear reviewer, we apology for the typo mistakes which have been corrected.

Science editor comments: This article reports a novel case of hepatitis caused by the use of escitalopram. The article not only described the cases in detail but also carried out corresponding literature induction and Vigibase analysis, which made the conclusions more convincing. However, we have the following comments:

Question 1: *The topic of the article is hepatitis caused by escitalopram. The background part has too many explanations about depression. Should this part be deleted to highlight the topic?*

Answer 1: dear editor, we agree with your comment and the description of depression in the background has been deleted, improving the clarity of our manuscript.

Question 2: *Figure 1 is mentioned in lines 73-74 of the article, we did not find it in the article.*

Answer 2: dear editor, this was a mistake in the first place, the mention of figure 1 has been deleted in the reviewed version.

Question 3: *It is interesting to note in the second half of the results that there is a difference between clinicians giving antidepressants and recommending psychotherapy when treating patients with depression. However, the discussion in this part is not closely related to the theme of this paper, so it is suggested that the author can draw closer to the theme appropriately.*

Answer 3: dear editor, we agree with your comment and the second part of the discussion about psychotherapy or general considerations on depression treatments have been deleted, improving the clarity of our manuscript.

Question 4: *The references in this article are relatively old, and it is recommended to choose more references from the past 5 years.*

Answer 4: dear editor, we deleted the references of two “old” articles (former references 12 and 13), and we added four new references of more updated articles (5, 7, 10 and 15; respectively from 2018, 2019, 2017 and 2018). The other “old” articles have not been deleted because it is either a reference to the RUCAM score (reference 6), references to the methods used in pharmacovigilance analysis (references 8 and 9) or the full review of the literature (references 11, 12, 13, 14).

Overall, in the first version, 3 references out of 13 were recent (from the past 5 years). In the revised version, 7 references out of 15 are recent (from the past 5 years). We hope this improvement will meet your satisfaction criteria.

Company editor-in-chief comments: I have reviewed the Peer-Review Report, 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. 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.

Thank you very much.