

World Journal of Gastroenterology

Science Editor, Editorial Office

Yuan Qi

Re: Ms: No. 32817

Dear Dr. Yuan Qi,

Re: Ms: No. 32817 Recent advances in the management of pruritus in chronic liver diseases

Thank you for considering our manuscript for publication and providing us with useful comments and advice which has helped to improve the article. We have made revisions, in accordance with the Reviewers' comments, which are shown **red font**.

Below we include a list of our responses to the Reviewers' comments.

We hope that the manuscript is now acceptable for publication in *World Journal of Gastroenterology*.

Yours sincerely,

Kazuto Tajiri

Assistant Professor

Department of Gastroenterology

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Responses to comments

Reviewer 02529807

I commend you for a very nice summary of the evidence related to pruritus. It is well written and the literature review is quite thorough.

Response

Thank you for your comments.

Reviewer 02445541

This review describes the present knowledge about the pathophysiology and possible treatments of pruritus in chronic (cholestatic) liver disease. Literature is well covered and Figs 1 and 2 show comprehensible summaries of both main items. The paper is well written and quite understandable.

I have only a few minor comments:

1. In Fig 1 the distinction between periphery and central nervous system is not clearly marked: does the spinal cord belong to CNS or is it intermediate and are endorphins exclusively acting there or also in thalamus and other parts of the CNS?

Response

We have corrected Fig.1 with the distinction between periphery and CNS. The spinal cord belongs to the CNS, and it has been shown in new Fig. 1. Opioid receptor had been known to play a role in the CNS including thalamus (Umeuchi H, et al. Eur J Pharmacol. 2003), but it has been shown to be working also in the periphery. We have added the description about them (page 8, lines 13 to 17).

2. I miss in the list of cholestatic diseases BRIC, which is dominated by itching as an important quality of life destructing symptom.

Response

As reviewer suggested, BRIC is a cholestatic disease showing pruritus. We have added the information about BRIC (page 10, lines 2 to 8).

3. At several places, even in the abstract, pruritus (which is correct) is written as pruritis.

Response

We have corrected the spelling of pruritus to right one.

4. The role of NO remains unclear in the text and also in Fig 1. Confusing is its role in the periphery, but it has also a role in the CNS. This should be clarified.

Response

We have added the description about NO in the text and Fig. 1 to understand the role in the periphery and CNS (page 8, lines 4, 5, 9, 11 and 12).