

Dear Editors and Reviewers

We have revised our manuscript, “The efficacy of tolvaptan in patients with refractory ascites in a clinical setting”, according to the comments of the associate editor and the reviewers. We are very appreciative of the time and effort they spent in providing us with a lot of helpful suggestions. We believe that the paper is much improved due to the changes that we made, and we hope that you will now find it acceptable for publication.

Yours Sincerely,

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Name of journal: World Journal of Hepatology

ESPS Manuscript NO: 17417

Columns: Original Article

Point by point response

Editors and Reviewers:

1. About this manuscript.

We added sentences about certification in page 2 line 22.

Changes in the revised manuscript

The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see:

<http://www.textcheck.com/certificate/index/bh6GhC>

2. About statements.

We added sentences about certification in page 2 line 8.

Changes in the revised manuscript

Institutional review board statement: This is a retrospective study. We have no statement about institutional review board.

Informed consent statement: For this type of retrospective study formal consent is not required.

Biostatistics: Since our institution is a municipal hospital, we have no biomedical statistician. All statistics was performed by first author using StatView ver. 5 (SAS institute, Cary, NC, USA) and checked by all other authors.

Conflict of interest statement: We have no conflict of interests.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at following e-mail address (anb72547@nifty.com). Participants gave informed consent for data sharing.

3. About abstract.

We changed the abstract according to the advices.

Changes in the revised manuscript

Aims: We conducted this study to elucidate the efficacies of tolvaptan as a treatment for...

4. About CORE TIP.

We added sentences about CORE TIP in page 5

Changes in the revised manuscript

Tolvaptan was effective in 38 (63.3%) refractory ascites patients. The best cut-off values...

5. About COMMENTS.

We added the COMMENTS Page 18 according to the advices.

Changes in the revised manuscript

Backgrounds: Hepatic edema and ascites are common complications in decompensated liver cirrhosis patients. In Japan, ...

6. About REFERENCES.

We changed the references according to the advices.

Changes in the revised manuscript

1. Gines P, Cardenas A, Arroyo V, Rodes J. Management of cirrhosis and ascites. N Engl Med 2004;350:1646-1654 PMID 15084697 DOI 10.1056/NEJMra035021. ...

7. About Table.

We added the locations of table 4 and figure 4 according to the advices.

Changes in the revised manuscript

We added sentences in Page 11 line 25.

We evaluated the changes in urine volume and osmolality between the two groups after administration of TLV (Table 4).

We added sentences in Page 12 line 7.

Figure 4B indicated that a reduction in urine osmolality over 25% was the single best cut-off level to clarify the improvement of refractory ascites with 89.5% sensitivity and 59.1% specificity. A combined measure of urine >1800 mL within the first 24 h and a reduction in urine osmolality >30% were the best cut-off levels to clarify refractory ascites improvements with 84.2% sensitivity and 81.8% specificity (Figure 4A).