Author’s response to reviews

Title: Pharmacokinetic Study of Single- and Multiple-dosing with Metolazone Tablets in Healthy Chinese Population

Authors:

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Accompanying Letter

Reviewer reports:

Reviewer #1: The design study is correct. The used methods are appropriate and the results are clearly presented and extensively discussed. Unfortunately, often the data obtained in healthy volunteers is non applicable to patients. This issue is important in the management of population suffering from diseases. I recommend to discuss this matter (see Pharmacokinetic interaction between levofloxacin and ciclosporin and tacrolimus in kidney transplant recipients: ciclosporin, tacrolimus and levofloxacin in renal transplantation. Clin Pharmacokinet. 2006; 45(2):169-175). Obviously, I recommend to add the proposed reference in the appropriate sections.

Answer: Thank your precious recommendation, I have been add the proposed reference in the appropriate sections of my revised manuscript.

Reviewer #2: The manuscript by Li et al evaluates the pharmacokinetics of metolazone after single and multiple oral doses, as well as a food effect study. The authors utilized non-compartmental analysis of determine the influence of dose and gender on pharmacokinetic parameters. The study design and analysis methodology was suitable for the goals outlined by the authors; however, I have a few concerns about the manuscript and presentation of the data.

1) The figures are unclear due to the connecting lines that are present between all data points. It would be advisable to remove figure 7 (mean data) and present mean ± SD data in the earlier figures, possibly combining all of the single dose data into a single figure. This would make it easier for the reader to evaluate differences between doses. Within figure 5 there should be a distinction made between the fed and fasted data points. The figure legends should also contain additional information so that they stand alone from the text of the manuscript.
Answer: Thank your precious recommendation, I have been removed figure 7; I have combined all of the single dose data into one figure; I have listed the figure legends at independent section of our manuscript.

2) The manuscript should be revised for English grammar and readability. In some cases there are run-on sentences and paragraphs containing a single sentence.

Answer: I have try my best to improve grammar and readability of our manuscript.

3) Methods, page 6. Were women on hormonal birth control included in the study?

Answer: Women on birth control included in the study.


Answer: I added some details about process of drug administration to this section (Single dose, multiple dose and food effect of study design).

5) Methods, page 10. What parameters were used for the linear regression model to determine dose proportionality? Why was superposition not considered?

Answer: I added the expressions about statistical analysis to this section.

6) Results, page 12-13. The paragraph contains data that was included within the tables. The numbers can be removed with a reference to the table.

Answer: I have removed the numbers which can be reference to the following table.

7) Results, page 14. Elimination half-life of 8.97 hours (line 59) is not consistent with the data in Table 1, which listed the elimination half-life as 7.61 hours.

Answer: I have corrected my mistake in here, the elimination half-life is 7.61 hours. thank you very much!

8) Discussion, page 17. Include any comparative literature data on the pharmacokinetics of metolazone or similar compounds.

Answer: I have make more comparison added to my manuscript from other literature data on the pharmacokinetics of metolazone. thank you very much!