

Re: "Efficacy and Safety of Modified Tetracycline Dosing in a Quadruple Therapy for Helicobacter pylori: A Retrospective Single Center Study"

May 9, 2023

Dear Dr. Tarnawski:

Thank you very much for your email on April 27, 2023 regarding this manuscript. We are interested in being considered for publication with World Journal of Gastroenterology. We have revised the manuscript to address the comments of the reviewers. Our point-by-point responses are listed below. In the revised manuscript we have highlighted the changes that were made from the original manuscript and have also provided a separate clean version of the revised manuscript.

We eagerly look forward to your final decision.

Sincerely,

Weiling Hu  
Sir Run Run Shaw Hospital

## **Reviewer 1**

Thank you for your approval of our manuscript.

## **Reviewer 2**

**No need to write “Abbreviations” or “Note:” term under the tables or figures. Just write the abbreviations.**

We have now removed “Abbreviations” or “Note:” from all the tables.

**Abbreviation in “Title” is not a preferred style. H. > Helicobacter.**

We have now revised the title to spell out “Helicobacter pylori”.

“Efficacy and safety of modified tetracycline dosing in a quadruple therapy for Helicobacter pylori: a retrospective single center study”

**The title “Efficacy and Safety of Modified Tetracycline Dosing of Tetracycline and Furazolidone Quadruple Therapy for H. Pylori Infection: A Single Center Retrospective Study in China” may be: “Efficacy and Safety of Modified Tetracycline Dosing in a Quadruple Therapy for Helicobacter pylori: A Retrospective Single Center Study.”**

We have now revised the titled to:

“Efficacy and Safety of Modified Tetracycline Dosing in a Quadruple Therapy for Helicobacter pylori: A Retrospective Single Center Study.”

**Indicate all abbreviations under all tables without exceptions. Each table must be self-explanatory.**

We have now provided all abbreviations under the all the Tables.

**Indicate ITT and PP in first usage in manuscript, including Pylori. Indicating just in “abstract” is not sufficient. Repeat also in main manuscript.**

Thank you for your guidance on writing details, and I will repeat it also in main manuscript.

**Correct “eradiation rates” as “eradication rates” in abstract.**

We have corrected to “eradiation” to “eradication” in the Abstract.

**Correct the tautology in keywords. Don’t use abbreviation in keywords. Helicobacter instead of H.**

We have now spelled out Helicobacter as keyword.

**“Following the recognition of H. pylori gastritis as an infectious disease in 2015, guideline recommend that all patients diagnosed with infection should receive eradication therapy [4].” Should be not that distinctive. Instead, Which the cited reference really concludes is: “Following the recognition of H. pylori gastritis as an infectious disease in 2015, guideline recommend that all patients diagnosed with infection should receive eradication therapy. Unless there are competing considerations such as comorbidities, re-infection rates in their communities, competing health priorities of society and financial cost. [4].**

We have now revised the statement in the Introduction section to:

“Following the recognition of H. pylori gastritis as an infectious disease in 2015, guideline recommend that all patients diagnosed with infection should receive eradication therapy in the absence of competing considerations such as comorbidities, reinfection rates, or other societal health and economic priorities. [4]. **(Page 4, Line 9-12)**

**Unfortunately, Figure 1 is not reader friendly. It is very crowded and does not include p values. Instead, a Table will be more explanatory.**

Figure 1 is a summary version of the results in Table2 and Table 3. We have now eliminated Figure 1 to avoid the redundancy.

**Due to drop-outs Intention-to-treat (ITT) success is expected to be lower than per protocol (PP). The possible errors of violation of this general rule must be clearly explained in the manuscript. Mention ITT and PP in statistical methods section.**

ITT analysis and PP analysis are concepts in randomized trials, and generally outcomes of ITT analysis are lower than PP analysis. However, in our retrospective study design, ITT analysis was determined calculating the eradication rate of all 394 patients evaluated in the study while PP analysis was calculated by removing patients who interrupted treatment due to adverse reactions. Despite discontinued treatment due to adverse events, 14 patients including 5 in the tetracycline 500mg twice daily group, 3 in 750mg twice daily group, and 6 in 500mg three times a day group achieve eradication resulting in lower calculated eradication rates in PP analysis than ITT analysis.

We realize that the concept of ITT and PP analysis may not be appropriate for this retrospective study given that the study population were selected by applying inclusion criteria that excluded all patients who lacked follow-up while including those who had documented adverse events leading to bias. Therefore, we would like to remove the concept of ITT and PP analysis and provide one outcome of eradication rate for overall study population throughout the manuscript. Originally the population used for pp analysis, we renamed this part of the population as “removing the Discontinued Treatment Population” and calculated the eradication rate of this part of the population. As shown in Section 3.2.3 of this article, “3.2.3 Eradication Rates of removing the Discontinued Treatment Population”

**(Page 9, Line 23-25, page 10, Line 1-16)**

**Even though “at least “4 weeks interval between the treatment and testing for eradication is accepted, many studies perform 6-8 weeks duration for more accurate results. This issue has to be mentioned in limitations. <http://www.ncbi.nlm.nih.gov/pubmed/15270750>.**

We have now acknowledged that evaluation of H. pylori eradication 4 weeks after completion of treatment may lead to false negative results and provided the reference in the Discussion section.

“Furthermore, evaluation of H. pylori eradication 4 weeks rather than 6-8 weeks from completion of treatment may have led to false negative test, impacting the results [35].”  
**(Page 14, Line 28-30)**

**Mention dosage of other drugs than tetracycline.**

We have now provided the dosage of other medications in the Methods section.

“Specific drugs dosage utilized in the study included furazolidone 100 mg twice daily, colloidal bismuth pectin capsules 400 mg twice daily, bismuth potassium citrate capsules 600 mg twice daily, esomeprazole 20 mg twice daily, rabeprazole 10 mg twice daily, lansoprazole 30 mg twice daily, pantoprazole 20 mg twice daily.” **(Page 6, Line 20-24)**

**Re-evaluate the statistics thoroughly.**

We have recalculated all the statistical analysis of eradication rates and verified the data.