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Title: Zinc Carnosine-based Modified Bismuth Quadruple Therapy versus Standard Triple Therapy for Helicobacter pylori Eradication: a randomized controlled study

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Scientific quality

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<th>Grade A: Excellent</th>
<th>Grade B: Very good</th>
<th>Grade C: Good</th>
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<td>Grade D: Fair</td>
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Language quality

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<th>Grade A: Priority publishing</th>
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<td>Grade C: A great deal of language polishing</td>
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Conclusion

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Re-review

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Peer-reviewer statements

Peer-Review: [ ] Anonymous | [ ] Onymous
Conflicts-of-Interest: [ ] Yes | [ ] No
SPECIFIC COMMENTS TO AUTHORS

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes

2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes

3 Key words. Do the key words reflect the focus of the manuscript? Yes

4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes

5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Modifications needed. Details are given later.

6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? Yes. Few modifications are needed. Details are given later.

7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper’s scientific significance and/or relevance to clinical practice sufficiently? Yes. Few modifications are needed. Details are given later.

8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? Yes. Few modifications are needed. Details are given later.

9 Biostatistics. Does the manuscript meet the requirements of biostatistics? Yes

10 Units. Does the manuscript meet the requirements of use of SI units? Yes

11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Yes

12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and
appropriate? Yes. Some editing required. 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? Yes

14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? Yes

Further comments: In the manuscript entitled “Zinc Carnosine-based Modified Bismuth Quadruple Therapy versus Standard Triple Therapy for Helicobacter pylori Eradication: a randomized controlled study” the authors have evaluated the efficacy of H. pylori eradication by Modified Bismuth Quadruple Therapy (MBQT) as compared to proton pump inhibitor and two antibiotic based Triple Therapy (TT). Their data suggest that the MBQT has a better efficacy than the TT (P = 0.003). H. pylori is a class I carcinogen and due to the increased antimicrobial resistance alternative therapeutic approaches need to be evaluated. Therefore, the manuscript is suitable for publication, but it definitely needs some modification. Following are the modifications that I recommend: 1. In abstract, when mentioning for the first time, the name of the bacterium, Helicobacter pylori, should be written in full, but afterwards it should be written as H. pylori. 2. The name of the bacterium should be mentioned once in the introduction in full and in italics. For rest of the manuscript it should be mentioned as H. pylori (in italics). Throughout the manuscript H. pylori is written in various forms (e.g. H pylori, H. Pylori etc.). This must be corrected.
3. Introduction. “Since its first successful culture growth in laboratory 40 years ago, the famous Helicobacter pylori has been a source of debate among medical professionals and the public”. Consider a sentence like ‘Since its first successful culture in laboratory almost 40 years ago Helicobacter pylori infection and gastric diseases have been a source of debate among medical professionals and scientists’. 4. Introduction. This bacterium, which is among very few organisms that can survive in the human stomach, has gained much reputation, majorly a bad one, based on its association with various gastroduodenal diseases. Replace “majorly a bad one” with ‘mostly as harmful bacterium’. 5. Introduction. “Infection can, at a minimum, causes gastritis and is a prominent etiologic agent of gastric and duodenal ulcer disease and gastric adenocarcinoma and lymphoma”. Replace “disease” with ‘diseases’. Replace “lymphoma” with ‘mucosa-associated lymphoid tissue (MALT) lymphoma’. 6. Introduction. “However, due to the increased rate of clarithromycin or metronidazole resistance, standard triple therapy has no longer been effective in regions with high antibiotic resistance”. Replace “has no longer been effective” with ‘is often ineffective’. 7. Materials and Methods. “The patient population comprised 92 consecutive outpatients who presented to outpatient clinic with dyspepsia symptoms and who were found to have H. pylori infection”. Please also mention the clinical status of the patients. 8. Materials and Methods. Please mention inclusion criteria. 9. Materials and Methods. The enrolled patients were randomized by drawing a sealed envelope that contained pre-assigned treatment instructions. Mention mean age of the patients in control vs experimental groups. Also mention the clinical status of different patients in each group. 10. Results. “Most patients (60.9%) were Asian. This was followed by Arab (28.3%) and African (10.9%). Most subjects (81.5%) were non-smokers”. By Arab, which country did the author mean? By Asian, did the authors mean East Asian? Which country? Mentioning country would be better. 11. Results. “Among subjects in the MBQT group, 43 tested negative on the UBT test and 3 tested positive”. Clearly mention
second UBT. Also, mention it in Figure 1. 12. In Figure 2, the color codes for MBQT and TT were not mentioned. 13. Discussion. “In addition to that, our study also showed that being smoker increased the risk of treatment failure by 5 folds, which would be interesting for more investigation and awareness campaigns about its relation with H pylori, its detrimental effect on the gastric mucosa in particular and its role in lowering eradication rate”. Since this is not a new finding this must be discussed by citing other references. 14. Discussion. “Another interesting finding was ethnic variability regarding eradication success, where being of Arabic ethnicity increased the odds of eradication success, but because of the small sample size the true significance of this finding remains questionable”. What could be the reason for this difference in treatment efficacy with ethnicity? Any hypothesis? 15. In Table 1, the authors should mention the numbers of males and females in each group.

Thank you for your valuable and important comments. We did our best to respond to all the questions and adjust the paper based on your recommendations. Modifications were highlighted in the text based on your suggestions. If there is any additional comment or concern, please let me know.

1- Thank you for this remark. The highlights were edited accordingly.
2- The highlights were edited accordingly.
3- Thank you for this remark. The text was adjusted as recommended.
4- Thank you for this remark. The text was adjusted as recommended.
5- The text was adjusted as recommended.
6- Thank you for this remark. The text was adjusted as recommended.
7- The patients of both groups were clinically stable and had no red flags (the exclusion criteria were specified) as mentioned in the manuscript.
8- The inclusion criteria were mentioned in the materials and methods section. It included patients who presented to the outpatient clinic with dyspepsia symptoms, tested positive for H. pylori, and agreed to the H. pylori eradication therapy.
9- The mean age of the patients of both groups was mentioned in the results (Table 1). Also, as mentioned in comment #7, the materials and methods section already included the clinical status of the patients.

10- Thank you for your comment. The countries were added under Table 1.

11- Thank you; it was edited accordingly.

12- The color codes were already mentioned in Figure 2 as a legend.

13- Thank you for this comment. It was adjusted accordingly.

14- Thank you for this remark. We suggested hypotheses.

15- The table was adjusted accordingly.