

Peer Review File

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Reviewer A

This is a very nice systematic review and meta-analysis on a much debated and very relevant topic in abdominal surgery.

Comments (minor revisions):

Please add the number of included patients in tables 1-3, and please use mg instead of gm.

Table 1: variables should be presented as follows: Age (years) (Median)

Reply A

Thank you for the review and comments.

1. We have added the number of patients in tables 1-2, since table 3 is quality of included studies we haven't added the included number of patients in this table.
2. Changed dose from gm to mg.
3. We have represented the age as it is given in published papers, and unfortunately, Park et al. have represented age as a mean.

Reviewer B

The authors have performed a meta-analysis of three articles, comprising a modest number of patients, and claim that the data show that antibiotic prophylaxis is unnecessary for "acute cholecystectomy" in their words. There are substantive questions for the authors.

Major comments:

1. Imprecise terminology impairs the interpretability of the paper, and its readability. It needs to be made clear that his paper is about laparoscopic cholecystectomy. The term "acute cholecystectomy" is not in standard usage and leaves much to be desired. Please refer to "emergency laparoscopic cholecystectomy for mild-moderate acute cholecystitis."
2. It is not actually stated whether the comparison is between single-dose prophylaxis and nothing/placebo, or single- vs. multiple-dose prophylaxis. The reviewer had to read the source documents; please don't make the general readership do the same to figure out what you are comparing.
3. The authors have not mentioned all of the relevant guidelines. Please cite and discuss Colling KP, Besshoff KE, Forrester JD, et al. Surgical Infection Society Guidelines for antibiotic use in patients undergoing cholecystectomy for gallbladder disease. Surg

Infect (Larchmt) 2022;23(4):339-350. doi: 10.1089/sur.2021.207.

4. Because your recommendation to not provide antibiotic prophylaxis is not only counter to current guideline recommendations, but arguably lacks face validity considering the 18+% infective complication rate you cite, your argument needs to be more robust. Granted, not all of those infections are surgical site infections, but that is not discussed.

5. It is strongly suggested that you restructure your current, relatively scant discussion with a compare/contrast of all relevant guideline recommendations. The extensive literature regarding no antibiotic prophylaxis for elective laparoscopic cholecystectomy should also be contrasted.

6. The upper limit of your confidence interval is 1.03. Additional trials (if performed) are more likely to narrow the confidence interval than change the point estimate meaningfully, raising the possibility that you are basing your recommendation on a Type-II error. You impugn the Tokyo guidelines for poor data quality, but your included data may be no better. Your discussion should discuss that possibility as a limitation, including a hypothetical power calculation in the discussion may help strengthen your argument.

7. The paper would benefit from a funnel plot as a figure.

8. Quality scores (e.g., Jadad) were described but not reported. Please provide the data.

9. The authors are advised that, considering that a major re-write of the paper is being recommended by this reviewer, the formatting, grammar/punctuation, and references have not been scrutinized. Please do so, in the hope of avoiding another cycle of re-revision for the revised manuscript.

Reply B

Thank you for the review and comments.

1. We agree with this comment and have made the changes in the title, abstract and introduction.
2. We apologize for the confusion. We have mentioned the comparison between the single-dose antibiotic prophylaxis versus placebo in the inclusion criteria in methods and in the treatment protocol.
3. We apologize for not mentioning these guidelines in our earlier manuscript, we have made the necessary changes.
4. We completely agree with your comments and we have stated in the implication section of our discussion that the use of preoperative antibiotics can be advised in cases where the operating surgeons feel the need. Since we have data from three randomized control trials, therefore we recommend a major multicenter randomized control trial is needed to confirm these findings.
5. We appreciate your comment, and we have made the necessary changes in the discussion regarding comparison with the existing literature on the use of preoperative antibiotic prophylaxis for elective laparoscopic cholecystectomy.
6. Thank you for your comment and we understand that one of the limitations of this systematic review is the paucity of randomized control trials and the number

of patients. Since, this is a systematic review we have not done a hypothetical power calculation, but we have recommended the need for a major randomized control trial with adequate power calculation to strengthen our findings.

7. We completely agree with your comment and we have added a forest plot as a supplementary file.
8. We appreciate your comment and the quality of the included trials has been demonstrated in Table 3, and has been discussed in the discussion as well.
9. Thank you for your comment we have rewritten the entire manuscript and have tried to eliminate all the existing flaws in the current manuscript.

Reviewer C

Something is missing at the end of the part Key Findings.

Good work, amazing how few studies and patients included worldwide considering the Numbers of cholecystectomies performed.

Perhaps a final language control should den considered.

(like “no-antibiotics group”)

Reply C

Thank you for the comments.

1. We have readjusted the box of the key findings.
2. A final change in the language has been made.

Reviewer D

Line 305, Title of figure is incomplete.

Line 172 it should be "dose" instead of "dose".

My main peeve about this paper is the selection of trials in this systematic review. It is not true in line 189 that there is no existing systematic review or meta - analysis on this topic.

Similar publications include:

Zhou H, Zhang J, Wang Q, et al. Meta-analysis: antibiotic prophylaxis in elective laparoscopic cholecystectomy. 2009. In: Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]. York (UK): Centre for Reviews and Dissemination (UK); 1995-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK78426/>

Liang, B., Dai, M., and Zou, Z. (2016) Safety and efficacy of antibiotic prophylaxis in patients undergoing elective laparoscopic cholecystectomy: A systematic review and meta-analysis. *Journal of Gastroenterology and Hepatology*, 31: 921–928. doi:

10.1111/jgh.13246.

Matsui Y, Satoi S, Hirooka S, et al. Reappraisal of previously reported meta-analyses on antibiotic prophylaxis for low-risk laparoscopic cholecystectomy: an overview of systematic reviews. *BMJ Open* 2018;8:e016666. doi:10.1136/bmjopen-2017-016666

Reply D

Thank you for the comments.

1. We have completed the title in figure 2.
2. The spelling error in line 172 has been made.
3. We appreciate your comment and the comparison with the use of preoperative antibiotic prophylaxis in elective laparoscopic cholecystectomy has been added in the discussion.