

ANSWERING REVIEWERS



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2429-review.doc).

Title: Mucocele of the appendix: An unusual cause of lower abdominal pain in a patient with ulcerative. A case report and review of the literature

Author: Sofia Forssten, Malkanthi Evans, Dale Wilson, Arthur C Ouwehand

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 8550

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer 00166494

WGE-EPS-8550 The influence of a probiotic mixture on antibiotic induced microbiota disturbances
Assigned: 30-Dec-2013 Due: 13-Jan-2014 Report sent: 03-Jan-2014

General Statement This paper essentially shows that an 8 days treatment with amoxicillin-clavulanic acid (AUGMENTIN?) for 7 days causes only very minimal changes in the intestinal microbiota, and also minimal changes in gastrointestinal symptom rating score, bowel habits and Bristol stool scales (using validated instruments). Moreover, simultaneous administration of probiotics did not provide really significant protection against the minimal changes that were observed in their absence. Thus, by and large, the study is negative. In this respect, it may be worth to be published because of all the uncertainties around the use of probiotics to prevent gastrointestinal disorders related to antibiotic treatments.

However, the limitations of the study (small number of subjects; use of only one antibiotic preparation and one type of treatment) need to be carefully underlined.

We mention that the results cannot be used to draw conclusions on other antibiotics or probiotic.

Also, the conclusions need to be much more straightforward (say plainly that there are no real difference).

We have made the conclusions more straightforward concluding basically the antibiotic consumption that the consumed species slightly increased in numbers.

Lastly, the paper is quite long and could easily be pruned by 30-40 %, especially since there is not much to discuss (the data speak for themselves if taken at face value and in the context of a biological investigation where minimal changes are probably unimportant).

We shortened the body text by approximately 30%.

Specific points: The authors provide detailed tables with statistical analyses. This is good, but data need also be looked at face value. Thus, some of the differences may be statistically significant (using the appropriate test) but are those biologically meaningful? For instance, the authors go a long way in explaining that *B. lactis* CFUs significantly decreased during the study ($p < 0.001$) but the actual largest change is from 8.82 ± 0.69 to 8.20 ± 0.64 . I really question the biologic significance of such a small change. Thus, the Discussion should be more critical and go beyond the mere acceptance of statistical significances.

We indicated in the discussion that the changes in the microbiota, over all, are small and that the biological relevance of these changes may be limited.

Commercial names must be avoided in scientific publications and only used once if needed to clearly identify the product in use. So, please, use amoxicillin/clavulanic acid throughout and cite AUGMENTIN? only once when you define the product you used.

We changed Augmentin to amoxicillin/clavulanate; with the exception of the materials and methods section.

The description of the study design is a bit confusing as the first line suggests to the reader that there are 3 groups, namely placebo and two study (non-placebo) groups.

We described the study design in a more concise way.

A strain of bacteria is susceptible, not sensitive, to an antibiotic (hence the title of the CLSI document describing the standard methodology for testing antibiotic activity: "Performance Standards for Antimicrobial Susceptibility Testing" [see <http://www.clsi.org/standards/micro/sub-ast/>]) or the name of the European committee defining the corresponding standards: "European Committee on Antimicrobial Susceptibility Testing" [<http://www.eucast.org>])

This has been corrected in the manuscript.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.