Reviewer’s report

Title: The influence of probiotics on genital high-risk human papilloma virus clearance, associated lesions and quality of cervical smear: A randomized placebo-controlled trial

Version: 0 Date: 13 Mar 2019

Reviewer: Alessandra Pierangeli

Reviewer's report:

The study "The influence of probiotics on genital high-risk human papilloma virus clearance and quality of cervical smear" gives a contribution on the important issue of the probiotics effectiveness in reducing vaginal colonization of HPV. In a randomized, double-blinded, placebo-controlled trial 121 women were enrolled (62 in the study group and 59 in the control group). The study group received the probiotic bacteria Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14 and all women were tested every 3 months with cytology and HR-HPV until a negative result was obtained. There was no significant difference in HPV clearance whereas HPV load estimated with the HC2 test was found as an independent factor predicting HPV clearance in both groups.

The interest is related to the finding of significant decrease in mildly abnormal cytology, in the study group (13 to 4) compared to the control group (9 to 6) (p=0.017). The authors also consider relevant the differences in the unsatisfactory reports between the two groups.

This study is well written but has some weakness in the study design. First of all, the sample size was small and second, it is not clear whether enrolled patients had a clinical diagnosis of bacterial vaginosis (BV), that as the authors stated, may have a strong influence on the clearance of HPV-associated lesions.

Moreover, it should be revised in several points, as detailed below.

Title: "The influence of probiotics on genital high-risk human papilloma virus clearance" is not entirely correct: it should be modified in high-risk human papilloma virus-associated lesions.

Methods

A definition of unsatisfactory cervical smear should be given.
Discussion

The sentence "BV was independently associated with HPV infection" is not referenced and it is not clear whether it refers to this study group.

Findings from other recent papers on the use of probiotic strains in HPV-positive patients should be discussed

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?
4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests' below

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal