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OPEN PEER REVIEW

Efficacy of Probiotics in Improving Motor Function and Alleviating Constipation in Parkinson's Disease: A Randomized Controlled Trial

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

1 comment · 12 Jun 2023

Mohammad Sistanizad Reviewer

MINOR REVISION 12 Jun 2023

Sincere greetings to the author(s).
The study and concept are acceptable and may add significant information to what is already known about the complications of Parkinson's disease. Before publication, I suggest correcting the items listed below:
1) The number of patients included in each group and their general characteristics should be reported in the results section of the abstract.
2) In line 38, the phrase “Immune State” is irrelevant.
3) Lactobacillus and bifidobacter were incorrectly introduced as species in lines 42 and 181 and need to be changed.
4) Before they appear for the first time in the text, these two acronyms—"UPDRS on line 49 and FOS on line 191"—should be defined.
5) It appears that the manuscript needs writing improvements; for instance, the sentence in line 53 is deceptive.
6) It is preferable to note the number of each bacterial species separately in the method.
7) Although it is stated that the product under study contains no prebiotics, some pharmaceutical excipients, such as xylitol and lactose, have prebiotic effects. It would be better to discuss this if the excipients had any impact on the findings.
8) In line 161, it is mentioned that two participants with renal disorders had polydipsia; it would be better to specify the type of disorders.
9) Although this is not customary, the word "Placebo" is capitalized throughout the entire manuscript.
10) In line 187, the word "symbiotic" needs to be defined.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewers' Comments:

Reviewer 1:

Comments to the Author

Dear Authors,

Greetings,

I was proud to read the submitted manuscript and there are some comments which should be addressed:

-Thank you for your time

1. This manuscript has a lot of scientific writing mistakes and the English editing should be done prior to re-submission in the IJPR .

-English editing will be revised.

Introduction:

2. In my opinion, it is better to mention the possible etiology of PD associated constipation and probiotics role to regulate these pathways in introduction part instead of various roles of probiotics in non-neurology disease.

-Thank you for your comment. This aspect was added.

Method:

3. The authors mentioned regular use of laxatives were excluded. However, one of the secondary outcomes was reduction of laxative use. Please explain how you measure the frequency use of laxatives among patients without history of laxative use?

-Thank you for your thorough explanation. As patients on regular use of laxatives don’t provide unbiased sight into effects of probiotics on Parkinson’s Constipation patients on regular (like one or twice a day) laxatives were excluded and patients with sporadic use of laxatives were asked to document their use of probiotics in their defecation diary (for example in an specific week an individual had to use twice a week recommended-by-researchers laxatives to have a bowel movement)

4. Please explain about your strategy to modify nutrition training. Various parameters including water consumption, total amount of food, diet components and fiber intake can contribute on bowel movement. If these items were not evaluated, it should be at least included in limitations.

-Thank you for your comment. We have added our strategy on Methods->Requirement->last line to overcome this bias.

5. The calculated sample size was too small in compare with previous studies (e.g. Ibrahim et al, Tan et al,). It seems that 25 patients should be considered for each group of the study. This needs to be clarified

- Thank you for your comment. As stated in Method->Sample size calculation. In a case of not being clear enough it was rewritten. Effect size of the study was significantly high and that shows that significant efficacy can be detected even with small sample size.

Results:

6. Please explain the item of “Times needed to use laxative per week” which is represented in table 2. Does it mean the number of times regarding laxatives use per week?

-Thank you for your comment. A footnote was added to clarify the outcome.

7. In consort chart, the authors mentioned “34 patients not meeting inclusion criteria and 23 patients had exclusion criteria”. Both items seem as a same please re-write the sentences. The legends of Fig 1 and 2 should be added according to IJPR instruction.

- Thank you for your comment. As for not meeting the inclusion criteria if for an instance a patient had constipation based on ROME IV criteria but did not consent to enter the trial, this individual was counted as “not meeting inclusion criteria” but if all inclusion criteria were met but for an example the patient was immunocompromised as in one case he was counted as “having exclusion criteria”. Mentioned legends of figures has been stated.

8. While all recruited patients were more than 60 years old, there was no data in table 1 regarding supplements they use during the study.

- Thank you for your comment. All medicines, supplements and herbal products consumed by the subjects were documented in CRF and the difference of distribution between groups was not significant.

Discussion:

9. In my opinion the results of the study need to be more extensively discussed by comparing them mainly with the previous studies with probiotic (e.g. Ibrahim et al.) Analyzing the possible causes of the differences. The authors should discuss, on the basis of the statistical analysis of the results of their study and of the risk-benefit ratio, whether it is appropriate to start therapy with probiotics early to all those who have an PD with non- motor complication such as constipation.

-Much obliged for your comments. Notes have been added.

10. The role of gut-brain axis in PD and possible effects of dysbiosis on neurodegenerative process in PD should be more discussed as you evaluate the effects of probiotics on UPDRS as secondary outcome instead of animal studies (Lines 186-191)

-Much obliged for your comments. Notes have been added.

Reviewer 2:

Sincere greetings to the author(s).

The study and concept are acceptable and may add significant information to what is already known about the complications of Parkinson's disease. Before publication, I suggest correcting the items listed below:

1) How many patients were included in each group and their general characteristics should be entered in the abstract result section.

-Thank you for your comment. This was noted

2) In line 38, the phrase “Immune State” is irrelevant.

-Thank you for your comment. This was rewritten.

3) Lactobacillus and bifidobacter were incorrectly introduced as species in lines 42 and 181 and need to be changed.

-Thank you for your comment. This was rewritten.

4) Before they appear for the first time in the text, these two acronyms—"UPDRS on line 49 and FOS on line 191"—should be defined.

-Thank you for your comment. This was rewritten.

5) It appears that the manuscript needs writing improvements; for instance, the sentence in line 53 is deceptive.

-Thank you for your comment. This was rewritten.

6) It is preferable to note the number of each bacterial species separately in the method.

-Thank you for your comment. This was added.

7) Although it is stated that the product under study contains no prebiotics, some pharmaceutical excipients, such as xylitol and lactose, have prebiotic effects. It would be better to discuss this if the excipients had any impact on the findings.

-Thank you for your thorough review. As it is mentioned by studies the prebiotic effect of these excipients are dose-dependent and there is a threshold above which they show their prebiotic effect, thus the amount of these ingredients used were minimal and the effects were insignificant.

8) In line 161, it is mentioned that two participants with renal disorders had polydipsia; it would be better to specify the type of disorders.

-Thank you for your comment. This was rewritten.

9) Despite not being customary, the word "Placebo" is capitalized throughout the entire manuscript.

-Thank you for your comment. A Placebo is referring to patients taking placebo group, thus it seemed fit to write this word with capitalized “P”.

10) In line 187, the word "symbiotic" needs to be defined.

-Thank you for your comment. This was rewritten.

2 Revision 1

0 comments

No public comments in this round.