Reviewer’s report

Title: Gait analysis following single-shot hyaluronic acid supplementation: a pilot randomised double-blinded controlled trial

Version: 0 Date: 05 Dec 2018

Reviewer: Ahmed Negm

Reviewer's report:

Thanks for giving me the opportunity to review this interesting work.

This manuscript reports the results of a pilot 3-arm RCT to examine the effect of (1) HA+mannitol (n=9), (2) HA+sorbitol (n=5), and (3) saline placebo.

Comments

1. In general, from the abstract, it looks like you aimed to test the effectiveness of the intervention. This is not the purpose of pilot trials, and I am not sure if you have the sample size to test effectiveness. Please make sure you make it clear in the results that the statistical significance is not conclusive and it was not the objective of the trial, as the main objective of the trial is to determine which gait parameters are more sensitive following a single bolus injection of polyol-containing HA for knee osteoarthritis.

2. It would be great if you can report other feasibility outcomes, as suggested by Thabane et al 2010.

3. Abstract, Results, line 53, you need to clarify that mannitol containing viscosupplement effect is different than placebo.

4. Page 7 line 141, who did randomize the participants? Did you use a strategy to conceal your allocation?

5. Page 7: did the 3 types of injections look/feel similar? Did you check if the physician or the participants can figure out the allocation group?

6. Page 7: line 146 what was the physicians'' training, what speciality?

7. Page 7, line 148, what was the assessors' training?
8. Page 8, line 160, more details about the gait analysis is needed, a brief description of the analysis protocol, the test setting.

9. Page 8, line 168, how did you check for data normality? what test did you use?

10. I would change table 2 heading into baseline, instead of visit 1 and 4 weeks, instead of visit 2.

11. Page 11, line 202, how often did you ask about adverse events? And who asked about that?

12. Was the data entry personal or the data analyst blinded?

13. Page 11, line 206, how did you decide that gait speed and stride length are the most relevant gait parameters to investigate when assessing the effects of HA injection in people with knee OA? what was the success criteria? As it is a pilot study, you need to have apriori success criteria.

14. In page 13, line 260, you mentioned "Thus, a single HA injection appears to have a positive impact on pain and function up to six months following injection." Was this study powered to detect between group differences at 6 months? You may need to revise this statement.

15. Page 14, line 271, would you please explain what do you mean by "A sample size of 22 patients is suitable for a pilot study"? Was there a sample size calculation done based on the feasibility outcome? If not, this should be a limitation, even for pilot studies.

16. In page 14 line 276, you mentioned the recruitment difficulty, is it possible to report the recruitment rate and retention rate? These are important feasibility outcomes as well.

17. In the discussion, you may want to comment on that the HA+mannitol group was younger than the other two groups (table 1), also another limitation is including only 5 participants in the HA+sorbitol group, vs. 9 and 8 in the other 2 groups.

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