Reviewer's report

Title: Sodium hyaluronate and chondroitin sulfate replenishment therapy can improve nocturia in men with post-radiation cystitis: results of a prospective pilot study

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Reviewer: Andrew Vickers

Reviewer's report:

I hereby submit. Helped by Amy Tin.

The authors carried out a single-arm uncontrolled study to assess the impact of treatment (combination of hyaluronic acid and chondroitin sulfate) on nocturia. The symptom and problem of nocturnal voiding was measured with question 3 of ICSI and question 2 of ICPI, respectively. The change in symptom and problem of nocturia were assessed by paired-sample T-test of scores at baseline and post-treatment. The authors assessed the following correlations at both baseline and post-treatment: the symptom and bother of nocturia; the symptom of nocturia and ICSI total score; the problem of nocturia and total ICPI score. They also assessed the correlation of post-treatment and baseline symptom of nocturia, and finally the correlation of post-treatment and baseline problem of nocturia. The authors concluded by running two multivariable logistic regression models, the first adjusting for age, baseline symptom of nocturia, and baseline ICSI total score; and the second adjusting for age, baseline problem of nocturia, and baseline ICPI score. While it appropriate to utilize paired-sample t-test to test for change in nocturia from baseline to post-treatment, there are changes that should be made to strengthen this paper.

1) The authors should focus on estimation rather than inference in terms of change in score. The authors should report the estimate, including the 95% confidence interval to guide their conclusion regarding a randomized, controlled trial.

2) Based on their study design, the authors should reword their conclusion since improvement after treatment is not equivalent to the treatment reducing the symptom. It is reasonable that if patients were not given the treatment, their symptoms would have also improved.

3) The purpose of assessing and reporting the correlation between every variable is unclear.

4) Although the authors included limitations to their study, it would be beneficial to discuss these limitations in terms of possible bias to their results.

5) Regarding the multivariable logistic model:
   a. it is unclear what the outcome was defined as. Is this the post-treatment score based on a cutpoint?
b. it is also unclear why the baseline score of the individual question and the total score were both adjusted for in the model, as one component consists of the other.

c. with a sample size of 18 patients for the majority of the analyses, multicollinearity would be a concern by incorporating three variables in this model.

d. it is unclear what estimates are being reported in the multivariate analyses (line 152).

e. the author reported the covariates included in the multivariable analyses in the abstract but not in the manuscript, it should be mentioned in both locations for clarity.

6) The first half of Table 3 summarizes the data being reported in Table 1, and therefore does not need to be reported in both ways.