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

Version: 2  Date: 3 October 2014

Reviewer: Sara Lenherr

Reviewer's report:

My primary concern about this paper is that subjects are included based on the fact that they have “symptomatic cystitis” (which is a troublesome diagnostic term already) and then a sub-analysis was done on those with nocturia. By this stepwise inclusion, it is already obvious that this study was not designed to monitor this endpoint. Rather, the appropriate design would be to identify those patients that had RT, then query for nocturia.

Minor Essential Revisions

Please define “symptomatic cystitis”- is that lower urinary tract symptoms? Based on what scale? (line 75)

Please cite a reference for the instillation recipe and protocol. (lines 80-82 and 102-106) The recipe for the solution is redundant and does not need to be re-stated twice. Regardless, if this is not a published protocol, please state so. Are there any animal studies?

Please address why LUTS and nocturnal voiding frequency are evaluated with the ICSI/ICPI rather than the AUA-SI or other more widely accepted tool outside the interstitial cystitis field. The authors comment that the ICSI/ICPI is one of the “most accurate tools to identify the most relevant voiding and pain symptoms due to bladder pain” however the outcome of interest is nocturnal voiding episodes. (line 110) Please verify that the ICSI/ICPI is validated to “diagnose,” not just “monitor” symptoms/problems. Is this the only survey that was administered to this patient population?

From what I can tell, the statistical model is multivariable not “multivariate” because I do not think all of the repeated measures were all put into the model, just the baseline and end of the study survey results. Please confirm model type. (lines 120, 151 and 189)

Appropriate multivariable logistic model building should not just include variables because they are “significant” but rather are clinically pertinent. (line 120)

Please define “grade 2 toxicity” (line 132)

I am confused by lines 139-140: These lines suggest that they treated the patients that had no nocturia at baseline. Is that correct?
I question the validity of using the total ICSI and total ICPI scores - this is a survey for interstitial cystitis. Is it validated in radiation cystitis populations? (lines 146-148)

Figure 1: The figure should be able to stand on its own. Please show p-values on the figure (not refer to it in the text). Also, the y-axis is not 95% CI, but score value for each respective domain.

Table 1: Please label “end point” as Week 12. The table is sparse and actually a bit confusing. If there are no subjects who had baseline nocturia=1, remove that row, etc. There is no need to have Week 12 columns of 4 and >=5. The information from line 294 should be able to be integrated into the table.

Table 2: Similarly lines 297-298 should be able to be integrated into the table in a standard fashion.

Table 3: This is not a very informative table. Would remove this table or at least remove all the 0 (0%) results. Very difficult to look for what is important. Lines 302-303 are redundant from the table title.

Type-o’s/word choice errors:
Line 131: intermediate risk
Lines 137 & 139: remove “about”

If you adjust for a variable, then it can’t correlate with the outcome in that same model.

Line 151-153: "At age-adjusted multivariate analyses, both age and baseline ICSI-Q3 correlated with post-treatment ICSI-Q3 (r=0.293, p=0.011 and r=0.970, p<0.001, respectively)…"

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests