Reviewer's report

Title: Levels of NPY in synovial fluid relate to pain in patients with knee osteoarthritis

Version: 4 Date: 18 March 2014

Reviewer: Nicole Cattano

Reviewer's report:

Major Compulsory Revisions:
Title:
- Spell out NPY in title

Abstract:
- Clarify methods (120 total participants)
- Correct capitalization/spacing issues throughout.
- First line of background Knee osteoarthritis (K doesn’t need to be capitalized).
- Last sentence “effects of neuropeptide Y(NPY) need space in between end of Y and the abbreviation.
- Space after period “advanced stage group 17. And”
- These are just some examples of the multiple issues throughout the abstract and the entire manuscript.
- Results indicated a significant increase in NPY concentrations. Increase does not appear to be the correct word; it implicates an entirely different methodology.
- Select keywords that are NOT found in the title.

Background:
- Knee Osteoarthritis (KOA) - O should not be capitalized
- KOA Patients’ – P should not be capitalized
- Line starting with “Many studies have been performed to unravel…” This idea is very unclear and confusing. Please clarify what you mean by stating probably include…
- End of this 1st paragraph-the sentence stating that there is no known effective treatment is confusing and detracts from the primary purpose of this specific study.
- Consider 2nd paragraph rewording to active voice.

Methods:
- Spell out January in the Patients section
- Need to better define the inclusion and exclusion criteria.
- Need to better state how patients were recruited...was it from an office visit for pain or some other type of treatment?
- Virtually no information is provided regarding the control participant recruitment.
- In case of bilateral KOA, how as “the serious side” defined to be assessed?
- Exclusion criteria seems to contradict the previous statement. It appears that you permitted bilateral KOA patients, however, the exclusion criteria included another symptomatic OA joint. Is this actually other than the knee???
- Within the exclusion criteria—the use of e.g., implies a list, therefore “on and on” can be removed.
- Last sentence of exclusion criteria regarding anti-inflammation therapy...This sentence is a fragment, please revise. Also, it is unclear as to whether oral NSAID use was permitted or not. It appears possibly this would be an exclusion criteria?? And why exclude those that were planning to get an injection or surgery within the next 3 months?
- Arthrocentesis section: All needs to be written in the past tense. This entire 2 paragraph needs to be re-written to provide clarity.
- KOA pain assessment: this section is extremely vague and does not allow a reader to understand HOW this assessment was done.
- KOA radiographic grade: Same as above...when were radiographs taken in relationship to arthrocentesis? Who read them and assigned grade? Did all have radiographs done at time of visit?
- NPY in synovial fluid: Reword first sentence: Radioimmunoassay was performed to determine NPY concentration in KOA synovial fluid.

Statistical Analysis:
- Please state what statistical procedures were done and on what statistical package.
- In order to run Post Hoc testing, should have run an ANOVA first?? Also-Why not Tukey’s?

Results:
- Perhaps present results information on the primary aim first, and consider the demographics for each subcategory (age and SD?)
- Doesn’t appear to have controlled for body weight?
- Same information is presented in Table 3 and Figure 1...perhaps pick which you feel better presents information.
- “NPY in synovial fluid demonstrated a significant increase in KOA patients... compared with healthy participants.” This sentence is confusing. NPY concentrations were significantly higher...
- Within KOA group, significantly higher NPY concentrations were found in each subgroup as pain increased?
- KOA radiographic grade and NPY section....same concerns as above.
-Were you appropriately powered to look at these subgroups?

Discussion:

-The entire first paragraph of this section is redundant with previous information. I do think there is value with the last 2 sentences to lead into the discussion.

-2nd paragraph states that this study is aimed at evaluating the effects of NPY in the development of pain in patients with KOA. This seems inappropriately worded as previously it was more the association between pain and NPY concentrations. This purpose should be clarified and consistent throughout the entire document.

-The authors do not get to their specific study results until the 3rd paragraph. This should be incorporated earlier.

-Same concerns within this section as the results…a significant INCREASE is confusing.

-3rd paragraph when stated that “NPY concentrations were found in significantly higher concentrations in the synovial fluid of patients with arthritis of the knee than in controls with non-inflammatory joint disorders” Seems that your study reinforces this finding..however, it is unclear as to what kind of arthritis of the knee from this previous study (e.g., rheumatoid or osteo-) as well as what non-inflammatory joint disorder the controls may have had.

-Sentence starting with “And as pain intensified…” is very confusing and needs to be clarified.

-Within 3rd and 4th paragraphs the use of down/up ward trends or increases in concentrations is confusing and misleading.

-Within 4th paragraph….try to avoid the use of direct quotations

-5th paragraph-based on CURRENT STUDY (instead of our studies…)

-“NPY as a putative regulator of pain transmission…” Putative does not accurately add value to this statement. I would consider removing.

-5th paragraph could be teased out throughout the discussion more. Seems to be where the bulk amount of the literature is found and reinforced or refuted.

-NO LIMITATIONS DEFINED – should be stated here

Conclusion

-First sentence is not accurate. Change of NPY is not what this study looked at. Cannot made deductions based on current study to this level. The way this sentence is written it appears that an increase in NPY leads to increased knee pain. Since this is a cross-sectional study you cannot make this assumption.

Minor Essential Revisions

Title: none

Abstract: correct spacing

-Grammatically consider rewording last sentence of methods to more active
Radioimmunoassay was used to examine NPY concentrations in knee synovial fluid

Background:

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

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.