Reviewer’s report

Title: Differential expression of histamine receptors in the bladder wall tissues of patients with bladder pain syndrome/interstitial cystitis – significance in the responsiveness to antihistamine treatment and disease symptoms

Version: 1 Date: 16 Sep 2019

Reviewer: Sanjay Sinha

Reviewer's report:

The authors present an interesting study on histamine receptors in patients with "interstitial cystitis". They performed an initial assessment of 4 different histamine receptors in patients and controls and followed this with a study of H3R receptor in another group of 10 patients and controls. They found that expression of all the 4 histamine receptors was elevated in IC but there were no significant correlations between the expression levels of the four different histamine receptors and the treatment outcome of antihistamine therapy.

This reviewer has the following comments:
1. What type of biopsy (cup or resection) did the authors take?
2. Did the authors record the bladder findings at the time of the biopsy? Did some or all of these patients demonstrate gross changes on bladder assessment either during the initial cystoscopic examination or following distension and evacuation of the bladder?
3. Did the authors classify the patients by their cystoscopy findings (ESSIC class 1, 2 or 3)? Was there any correlation between the cystoscopic findings and histamine receptors? Ultimately most clinicians will not be examining histamine receptors but some might choose to perform a cystoscopy either as a standalone diagnostic procedure or as part of a hydrodistension procedure for treatment.
4. The authors have not described the therapies used and have not defined criteria for classifying patients as 'responders' and 'non-responders'. It is unclear whether some of these patients continued to receive other treatments.
5. The scientific basis for choosing H3R for further study is unclear.
6. Could the authors clarify what each of these imply: H3R receptor, H3R protein level and H3R gene expression and how they are distinct entities? If appropriate, a simple graphic might explain this best. The authors mention that the first and third of these was increased but the second was reduced.
7. Page 5, line 16 (Background): Consider changing 'serious' to debilitating

Current terminology recommended by most guidelines for the condition under study is "Bladder pain syndrome" or "Painful bladder syndrome". It is now widely recognized that not all patients show cystitis on gross or histological evaluation. The term "interstitial cystitis" mostly continues to be used in the USA for reasons related to insurance coding. Would the authors consider using one of these terms rather than 'interstitial cystitis'?
Please confirm that you have included your review in the ‘Comments to Author’ box?
As a minimum standard, please include a few sentences that outline what you think are the authors’ hypothesis/objectives, their main results, and the conclusions drawn. Your report should constructively instruct authors on how they can strengthen their paper to the point where it may be acceptable for publication, or provide detailed reasons as to why the manuscript does not fulfill our criteria for consideration. Please supply appropriate evidence using examples from the manuscript to substantiate your comments. Please break your comments into two bulleted or numbered sections: major and minor comments.

Please note that we may not be able to use your review if no comments are provided.

Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included as text in the ‘Comments to Author’ box.

Yes

Are the methods appropriate and well described to allow independent reproduction of experiments?
Please state in the ‘Comments to Authors’ box below what you think are the strengths and weaknesses of the methods (study design, data collection, and data analysis), and what is required, if anything, to improve the quality of reporting

No

Does the work include the necessary controls?
If not, please explain in the ‘Comments to Author’ box below.

Yes

Are you able to assess the statistics?
- Are the statistical test(s) used in this study appropriate and well described?
- Is the exact sample size (n) reported for each experimental group/condition (as a number, not a range)?
- Are the description of any error bars and probability values appropriate?
- Are all error bars defined in the corresponding figure legends?
- Has a sample size calculation been included, or a description and rationale about how sample sizes were chosen?

Please can you confirm which of the following statements apply to your statistical assessment of the manuscript (Please include details of what the authors need to address in the ‘Comments to Author’ box):

I have been able to assess all of the statistics in this manuscript (please refer to checklist above)
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in the ‘Comments to Author’ box below.

Yes

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Should the manuscript be highlighted for promotional activity?
Articles that are deemed of interest to a broad audience can be promoted in a variety of ways. This could be through email updates, postings on the BioMed Central homepage, social media, blogs and/or press releases. Please indicate in the text box below whether you think this manuscript should be considered for promotional activity, indicating your reasons why (e.g. what is the most newsworthy aspect of the research).

No

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests
I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal