Reviewer's report

Title: A phosphodiesterase 5 inhibitor, tadalafil, suppresses stromal predominance and inflammation in a rat model of nonbacterial prostatitis

Version: 0 Date: 17 Jul 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are major issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

No - there are major issues

STATISTICS - Is the use of statistics in the manuscript appropriate?

Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are major issues

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Probably - with minor revisions
GENERAL COMMENTS: In the current study, the authors tried to investigate the role of Tadalafil in a rat model of nonbacterial prostatitis. Their results demonstrated an anti-inflammatory effect of Tadalafil. However, the major mechanism is not anti-inflammation. Tadalafil can increase the intracellular cyclic guanosine monophosphate and reduce smooth muscle tones. These pathological changes can alleviate inflammation too. It is difficult to determine whether the effects of anti-inflammation are directly associated with PDE-5i, or just due to the subsequent effects of the mentioned pathological changes. From this point, they cannot draw a conclusion that tadalafil shows a significant anti-inflammation effect in a rat model with NBP by suppressing inflammatory factors secretion and stroma proliferation. The conclusion should be "Tadalafil could relieve inflammatory effects in the rat NBP model".

REQUESTED REVISIONS:

Major revision

ADDITIONAL REQUESTS/SUGGESTIONS:

In addition to that, I have several concerns about the study design and methods parts.

1. The design is simple. Several other mechanisms were reported associated with the positive effects of PDE5-Is on LUTS/BPH, including increasing intracellular cyclic guanosine monophosphate, reducing smooth muscle tones, altering reflex neurotransmission, increasing blood perfusion and oxygenation, and reducing chronic inflammation in other urinary organs. I am wondering whether the authors found other potential changes in this rat model?

2. The dosage and duration of Tadalafil were determined by what condition? The authors should provide the detailed information.

3. Were the PSA and sexual hormones of the rats detected? How to make sure that all the animal models were established or suffered from "NBP" successfully?

4. prostate weight in NBP, NBP-tadalafil, significantly lower than that in control and control-tadalafil groups. The prostate weight was lower in the animal model. However, we all know that inflammation means swelling, not atrophy.

5. The references were not new and required to be updated.

6. The English requires to be polished by a native speaker.

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.

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**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.

No

**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?

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Are the conclusions drawn adequately supported by the data shown?
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No

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