Author’s response to reviews

Title: Efficacy of dapoxetine treatment in Chinese patients with premature ejaculation and possible factors affecting efficacy in the real-world practice

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Dear editors and reviewers:

We thank you very much for giving us an opportunity to revise our manuscript. We have studied comments carefully and have made correction which we hope meet with approval.

Reviewer reports:

Lu Yang (Reviewer 1): Manuscript performed by Peng et. al. verified the pharmacology effects on dapoxetine among Chinese, while there were similar researches in other countries. In this study, the author use one novel measurement called estimated number of intravaginal thrusts before ejaculation (NITBE) to replace the estimated intravaginal ejaculation latency time (eIVELT).

However, there are several details needed further discussion.

1. Compared with eIVELT, NITBE could also be disturbed by the frequency of penile movement. For instance, with high frequency, absolutely the stimulation was strong, which might cause fewer intravaginal thrust times. The superiority of NITBE should be stated in the discussion section.
Response: Thanks for this comment. That’s a very important question. It’s the truth that there’s definitely variation of frequency of penile movement and we listed this possible bias in limitations in Discussion part.

The primary consideration for the proposal of NITBE is to develop a relatively subject factor to evaluate the IELT. Waldinger et al proposed NITBE in 1994 and found that NITBE between patient assessment and partner assessment was consistent, while there’s significant difference regarding eIELT between patient assessment and partner assessment.

In our daily work we asked the patients to try to remain similar frequency in their sexual life. Actually, we have performed another study which demonstrated that the frequency was similar between PE patients and normal control (data not published), which proved that although the frequency varied, the NITBE could initially reflect the length of IELT. Of course, we acknowledge that high-level evidence is required.

Besides since the aim of the current study is to illustrate the change before and after treatment, thus we made the comparison of NITBE of the same patient before and after treatment, which decreased the bias that the frequency of penile movement between different participants.

2. Results showed no statistical differences of eIELT between the two groups stratified by CGIC, only the increase of NITBE could not explain the effect of depoxetine perfectly.
Response: Thanks for this comment. This question raised an important issue: eIELT might not be enough to accurately reflect the treatment effect.
We divided patients into two groups based on the CGIC. Actually, for the two groups, both NITBE and eIELT increased after treatment, which could demonstrate the effect of depoxetine. It’s interesting that the comparison between the two groups only found the difference of NITBE, while eIELT was similar, which demonstrated that there might be different result to evaluate the real-IET by using eIELT versus NITBE. This issue requires further validation. It’s a pity that stop-watch IET was not used in this study, and we have addressed this limitation in discussion. A future study involving stop-watch IELT, eIELT and NITBE would be more informative.

3. The author attempted to find out possible factors affecting efficacy, but baseline characteristics showed no obvious differences. This result should also be expressed in the result section.
Response: By “baseline characteristics” we guess you mean age, PE duration, previous treatment, intercourse frequency. We added a sentence in Results part indicating that these baseline characteristics were similar. Actually, these results (similar baseline characteristics) could prove that these patients were comparable, without obvious bias; only factors related to sexual life (NITBE and PEDT) could be risk factors of PE treatment.

Tommaso Cai, M.D. (Reviewer 2): The manuscript seems interesting but the study schedule does not support the results. The authors performed a retrospective study.
The conclusions are not supported by the methodology. The assessment of PE is critical and the efficacy evaluation is based on questionnaire and PROs. For these reasons, a prospective study is needed.
Response: Thanks for your comment. We need to acknowledge that it is truly a retrospective study. To further validate the usefulness of NITBE a prospective study would be required, yet we think a retrospective study could be a first-step test. Till now most published reports regarding PE used questionnaire and PROs as PE assessment and efficacy evaluation, and we are trying to develop a relatively objective method to assess PE severity and treatment effect. Currently the experience about
NITBE was based on retrospective study, and we think this information might bring some insights into clinicians interested in PE treatment. Hope for your understanding.

Dae Yul Yang (Reviewer 3): Please overwrite this text when adding your comments to the authors.
Response: We guess this reviewer didn’t provide specific comments. We would like to answer if there’s some comments next time.

Mehmet Gokhan Culha (Reviewer 4): The aim of this study was to investigate the factors influencing efficacy of dapoxetine for the treatment of premature ejaculation. The authors evaluated 154 PE patients via intravaginal ejaculation latency time, number of intravaginal thrusts before ejaculation and symptom questionnaires. The authors concluded that dapoxetine was well tolerated and improved for PE patients.

Although the design of the study is appropriate, methodological mistakes and citation errors hamper the overall quality of the manuscript. My other comments are itemized below:

1- In the abstract section, the sentence should not start with numbers.
Response: We have revised the sentence as required.

2- The authors omit to mention if they obtain intuitional review board approval and informed patient consent within the manuscript.
Response: We have provided the information as required in Methods part and Declarations part.

3- Which type of PE patients were included in the study? Has the Acquired-lifelong distinction been made?
Response: As shown in Supplementary file, 119 patients suffered from primary PE, and 39 patients suffered from acquired PE. As shown in Table (the 5th row), the type of PE was similar between CGIC=C=0 and CGIC>C=1 group, indicating that the type of PE might not be a predictive factor for effective of dapoxetine treatment.

4- The authors are requested to indicate if the linguistic validation of the PEP questionnaire has been validated prior to the commencement of the study. If it has been validated, these validation studies must be cited. If it has not been validated, this issue must be discussed under the limitations section.
Response: Thanks for this remind. We added this issue in discussion part as a limitation, and we hope this linguistic validation of PEP questionnaire would be performed in the near future.

5- Mean values should be given with standard deviation in results section.
Response: We have re-calculated the statistics and changed relevant information as required.
6- Drawing an ROC curve on dapoxetine activity and giving a cut-off PEDT value may improve the quality of the study.
Response: Thanks for this good suggestion. We added a figure or ROC curve (Figure 3) and provided a cut-off PEDT score.

7- Figure-1 typo error- ILTE
Response: We have revised the sentence as required. Sorry for this writing mistake.

8- The units in row and column should be specified in Figure-1.
Response: We have changed the figure as required.

9- The values of the questionnaires that are not mentioned in the method section are given in Table-1. These surveys and procedures should be explained in the findings section.
Response: Sorry for the unclear expression. We have changed the figure as required.

We appreciate reviewers very much for the positive and constructive comments and suggestions. Looking forward to hearing from you.

Thank you again for your consideration and assessment.

Sincerely Yours

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