Author’s response to reviews

Title: Acupuncture for chronic prostatitis/chronic pelvic pain syndrome: study protocol for a randomized controlled trial

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Author’s response to reviews:

Dear Dr. Møller,

RE: Acupuncture for chronic prostatitis/chronic pelvic pain syndrome: study protocol for a multicentre randomized controlled trial (Manuscript ID: Trials-TRLS-D-17-00602)

Many thanks for reviewing our manuscript, which has been revised taking into consideration all editorial comments and reviewers’ comments. This document includes our responses to the reviewers’ comments point by point. All changes have been highlighted in RED in the revised version of the manuscript.

We hope the revised version of the typescript is now suitable for publication in the Trials.
Looking forward to hearing from you,

Best wishes

Zhishun Liu

Reviewer #1

General observation

My general observation is that the study protocol is quite interesting but the paper requires a thorough editorial review by the authors for English grammar (e.g. tenses, the protocol has to be written in present and future tenses, not in the past tense, since the study did not start yet).

For example:

1. Page 4 - Line 60: replace "notified" with "will notify".

2. Page 8 - Line 58: replace "manipulate" with "handle".

3. Page 10 - Line 16: replace "discontinued" with "discontinue"

Answer:

Thanks for your suggestion. The manuscript has been polished, and mistakes of grammar have been revised.

Methodology

The following points should be considered.
1. GCP: There is no statement whether the protocol complies with GCP. Please clarify how it complies or not.

Answer:

This trial protocol is developed in accordance with the Declaration of Helsinki Good Clinical Practice guidelines for trial conduct [29], and has been approved by the Research Ethics Committee of the aforementioned hospitals. Please see Methods section in page 5.

2. Blinding: Probably the biggest problem with acupuncture studies is the lack of blinding. Despite the use of a sham procedure, it seems unlikely that patients would not guess which procedure is which, especially that patients will receive shallow needling. My guess is that most patients would know which treatment is which. This is particularly important for a subjective outcome measure like pain. Also, the blinding assessment can be biased, but in my opinion no better alternative is available.

Answer:

This trial will have some limitations: the blinding of acupuncturist will not be conducted; the location of sham acupoints are close to real acupoints; the sham acupuncture needle will be penetrated subcutaneously. Please see page 12, we have added this limitation at the end of Discussion section.

3. Inconsistency in the definition of the primary outcome:

   a. If you look at the abstract, the coprimary outcomes are the proportion of responders at 8 weeks and 32.

   b. If you look at the main text, the coprimary outcomes are the proportion of responders at the end of 8-week treatment and 24-week after treatment weeks.

   c. If you look at the study record detail on clinicaltrials.gov, you see that the original primary outcome measure is the 'proportion of responders at the end of 8-week treatment'.
Answer:

The expression caused the confusion, in fact, it is consistency of primary outcomes in the abstract, main text, and the information on clinicaltrials.gov. Owing to we set an 8-week treatment in this trial, which means that “24-week after treatment” is equal to “32-week”. To avoid the confusion of primary outcomes, we have exchanged all “24-week after treatment” to “32-week”.

4. Needles dispensation: provide details of how the needles will be dispensed and who provides the needles in this multi-center trial e.g. supplied locally or centrally. In case the needles to be used are the conventional needles, specify whether the needles in all centers are the same.

Answer:

Guang’anmen Hospital will supply the acupuncture needles. Other details such as how the needles will be dispensed and the parameters of needle has been described in the methodology section.

5. Acupuncturists: it is not well defined if the procedures are to be done by a single acupuncturist per site and if both treatment groups will be treated by the same therapist by site. If all interventions are to be delivered by a single therapist by site, that is both a strength and a weakness. It is a strength as it reduces variability, but a weakness as is limits generalizability. We have no way of knowing whether results would be completely different if delivered by a different therapist.

Answer:

In each center, two acupuncturists will provide acupuncture or sham acupuncture treatment. To improve the consistency of treatments, acupuncturists will receive trial specific (standardized operation procedure) training prior to performing treatments. The training includes a video showing detailed information on how to perform the acupuncture and sham acupuncture.
6. Rescue medicine: in case lots of analgesics will be used in this study, the results might be affected. All we can do is to wait for the results.

Answer:

Yes, the use of medicine will happen and it will affect the results. Thus, the information of using rescue medicine will be carefully recorded during the whole trial.

7. Insurance/indemnity: no information on insurance and indemnity are provided in the main text.

Answer:

The information of insurance has been described in the consent, and we have added following statement in the Safety assessment section. “Guang’anmen Hospital has insurance to cover for harm associated with the interventions during this trial.” Please see page 9.

8. Study flowchart: it is recommended to include the study flowchart:

columns: Screen Visit , Week 1, Week 2

rows: Patient information and informed consent, Physical examination

Answer:

Thanks for your recommendation. Accordingly, we’ve revised the flowchart.