Author's response to reviews

Title: The efficacy and safety of electroacupuncture for women with pure stress urinary incontinence: study protocol for a multicenter randomized controlled trial

Authors:

Zhishun Liu (liuzhishun@aliyun.com)
Huanfang Xu (huanfang_xu@126.com)
Yuelai Chen (chenyuelai@163.com)
Liyun He (hely3699@163.com)
Jia Liu (marie_liujia@yahoo.com.cn)
Shiyan Yan (yanshiyan0927@sina.com)
Ruosang Du (drsmym@sohu.com)
Jiani Wu (handsom_mars@126.com)
Baoyan Liu (liuby@mail.cintcm.ac.cn)

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Author's response to reviews: see over
Dear editors,

Thank you very much for your letter dated August 9th enclosing the reviewer’s comments for our manuscript entitled “Efficacy and safety study of electroacupuncture for women with pure stress urinary incontinence: study protocol for a multicentre randomized controlled trial” (MS:3409607421011967). The comments from the reviewer have been most helpful in revision of our manuscript.

We dealt fully with the criticisms in the revised manuscript. We would like to submit a revised manuscript here. The following are the correspondences to your reviewer concerning the comments and suggestions about the manuscript. I specify changes made in the manuscript, replying point-by-point to the reviewers’ comments.

We wish to take this opportunity to thank your consideration of our paper.

Yours sincerely,

Huanfang Xu
Major compulsory revisions

1. I found this article quite difficult to read. It seemed to jump around a bit, make assumptions about what is known and what is not known and so on. I think it needs a bit of reorganization. If the authors have not read the SPIRIT guidelines I recommend that they do so.

Response: We had our manuscript extensively edited by a native-English speaker with scientific expertise from the professional language editing service Edanz. All language revisions were highlighted with “tracked changes” in red font. Quality of English is much better now. We hope it may be up to the standard of publication now.

Minor essential revisions

2. The trial is about an intervention for stress urinary incontinence and yet this is never defined. It should be done early on.

Response: We added the definition of stress urinary incontinence and pure stress urinary incontinence in the “Background” section highlighted in blue.

3. The author use the term single-blind, and this term can mean anything. It is better to just say who is blind, as they do later in the article.

Response: The term “single-blind” in the manuscript referred to “subject-blind”. Revisions were made according to the reviewer’s advice.
4. There is no information about the generation of the randomization sequence, apart to say that it is block randomized and stratified by centre. At least the block size should be mentioned.

Response: The randomization sequence was generated by the “proc plan” procedure of the SAS9.3 analytic software according to center-stratified, block randomization with a block size of six. Revisions with tracked changes were highlighted in blue in the section of “Study design”.

5. Nowhere does it say who is going to recruit the participants into the study.

Response: Researches nurses or students majoring in acupuncture were responsible for recruitment. Please see the revision highlighted in blue in the section of “Participants”.

6. The abstract defines the sham acupuncture well but I don’t think it clear that the sham needle does not penetrate the skin.

Response: Sham BL33 and BL35 will be needled through adhesive pads to the skin (for the fixation of needles) without penetrating the skin using blunt needles. We specified the non-penetration of the sham needle in the control group using blue color.

7. In the sample size calculation section the authors use plus/minus but don’t say what the number afterwards is. Is it a standard deviation?

Response: Yes, the number afterwards was a standard deviation. We added the
information of our pilot study and reorganized the sentence for clarity. See the words highlighted in blue in the section of “Sample size calculation”.

8. I cannot replicate the sample size calculation. More details should be given.

Response: More details on sample size calculation was added. The pooled standard deviation of our pilot study was 1.74. We expanded it by 1.5 times to 2.61 because there would be a larger variability in multicenter trial. Using a one-sided t-test of difference between means, $\alpha = 0.05$, $1 - \beta = 0.9$, 117 subjects per group will be needed to detect a clinical difference of 1 g urine leakage from a 1-hour pad test. Allowing for a 20% drop-out rate, 140 per group will be needed. Due to the small sample size of our pilot study (20 per group) and a subgroup analysis to be undertaken, we expanded the sample size to 250 per group (total of 500). For revision, please see the section of “Sample size calculation” colored in blue.

9. There is nothing that says what the formula does.

Response: The sample size was calculated based on the formula. Detailed information was added on sample size calculation. To avoid unnecessary confusion, we deleted the formula.

10. Saying that an intention to treat analysis will be done is separated from what the treatment of missing values will be. And it has information about the comparison of drop out rates in between, which makes it more confusing.
Response: We put the ITT analysis and treatment of missing values together in the “Analysis of efficiency” in “Statistical analysis” (see contents highlighted in blue). It’s more clear to understand now.

11. At first in the analysis section it says that t-test will be used for continuous data, but later it says ANCOVA will be used.

Response: For continuous data, ANCOVA will only be used for analysis of primary outcome and subgroup analysis stratified by incontinence severity, and t-test will be used for other continuous data. We supplemented the related information in blue color in the section of “Statistics analysis”.

12. ANCOVA with baseline as co-variants is used to adjusted for baseline imbalance, not for confounding. If there is to be adjustment for confounding the variables to be adjusted for should be specified a priori.

Response: We corrected the mistake that ANCOVA with baseline was to adjust for confounding. It was to adjust for baseline imbalance, in fact. Please see the revision in the section of “Analysis of primary outcome” which was colored in blue.

13. It is the residual that have to be normally distributed, not the data. If non-parametric analysis is to be used how will this use the baseline values? It is not clear.

Response: The expression “if data were normally distributed”, is commonly used in
various literatures. We were confused at this comment at first. Fortunately, we realized our misunderstanding about normality after searching literatures and consulting statistician. We now understand that it is the residual that really needs to be normally distributed. Predictors and/or response variables can have distributions skewed like hell and yet all is fine as long as the residual are normal. We learned from this comment. We’d like to take this opportunity to show our gratitude for the review of Peter Herbison.