Author's response to reviews

Title: P6 acupoint stimulation for prevention of postoperative nausea and vomiting in patients undergoing craniotomy: study protocol for a randomized controlled trial

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Version: 2 Date: 28 April 2013

Author's response to reviews: see over
Dear Editors and Reviewers,

Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled “P6 acupoint stimulation for prevention of postoperative nausea and vomiting in patients undergoing craniotomy: study protocol for a randomized controlled trial” (MS: 1586134170908618). The comments are all valuable and very helpful for revising and improving our paper. We have studied the comments carefully and have made a few revisions. Our revised submission is a copy of the manuscript with highlighted changes. The main corrections in the paper and the responses to the reviewers’ comments are as follows:

**Replies to Reviewer #1:**

1. **Use letters, not numbers: not 2, but two.**
   
   Answer: Thanks for the reviewer’s suggestion. We have changed "2" into "two" in the revised manuscript.

2. "Effectiveness" is a term normally used in pragmatic RCTs. Since this mainly is an explanatory design of RCT, I will recommend a more appropriate term: "efficacy".
   
   Answer: In accordance with the reviewer’s suggestion, we have now used "efficacy" instead of "effectiveness" in the revised version.

3. Who enrolled participants, and who assigned participants to interventions?
   
   Answer: We are very sorry for our negligence of the missing items. We have added this information into the "Patient population and setting" and "Randomization and blinding" sections.

4. **Not Germany, but German.**
   
   Answer: Correction has been made in the revised version.

5. **Not dates, but data.**
   
   Answer: The spelling error has been revised.

6. **Not intervention, but intention.**
   
   Answer: We are very sorry for our incorrect writing. This correction has been made in the revised version.

7. As you are aware, sham acupuncture may not be inert as it evokes
peripheral and central neural effects.

Answer: We agree with the reviewer that sham acupuncture may not be inert. Therefore, we have deleted the statement of no therapeutic effect, and have revised the sentence. Also, we have added three new references to support our point of view. Changes can be found in the last paragraph of the "Discussion" section.

Special thanks to you for your constructive comments.

Replies to Reviewer #2:

Major compulsory revision

1. Abstract Background. You need to include the control in the primary objective statement.

Answer: We have re-written this part according to the reviewer’s suggestion.

2. Abstract Methods. Trial design should include a descriptor for type of trial (ie. parallel group, cross-over, factorial) and framework (ie. Superiority, equivalence, noninferiority or exploratory).

Answer: Thanks for the reviewer’s suggestion. We have now added the descriptor in our revised manuscript.

3. Please include a statement that all groups were given routine ondansetron 8mg before skin closure, and the route of administration of ondansetron.

Answer: In accordance with the reviewer’s suggestion, we have added the statement in the "Abstract Methods" section. Also, we have used "intravenous" to state the route of administration of ondansetron in the revised version.

4. Methods. Design, first paragraph. Delete statements on intervention and outcomes as this is covered in a later section. Move your hypothesis and study objectives to last paragraph of Background and give full details of type and framework of trial (see point #2 above).

Answer: According to the reviewer’s comment, we have re-written the "Design" section and have moved our hypothesis and study objectives to last paragraph of the "Background" section. Also, the full details of type
and framework for our trial have been provided in the revised version.

5. Methods. Exclusion criteria. Specify which phase of the menstrual cycle is an exclusion criterion and clarify what you mean by “poorly controlled diabetes mellitus, bleeding disorders and serious systemic disease”.

Answer: As the reviewer suggested, we have specified the phase of the menstrual cycle in the “Exclusion criteria” section. Meanwhile, a few words have been added to clarify items (14), (15) and (16) in this part.

6. Methods. Specify if dexamethasone or droperidol are used in this clinical setting as these are potential confounders to the outcome.

Answer: We have added a statement into the first paragraph of the “Interventions” section.

7. Methods. Include a statement about what demographic and clinical data you are collecting that will be included in a table of baseline data in the final report when the study is completed.

Answer: The statements have been added into the first paragraph of the “Outcome measurement” section.

8. Methods. Allocation generation. Please state if stratification was used, and list any factors used for stratification.

Answer: Based upon the reviewer’s suggestion, we have added a statement into the "Randomization and blinding" section.

9. Methods. State who generated the allocation sequence, who will recruit subjects and who will assign patients to the intervention groups.

Answer: We are very sorry for our negligence of the missing items. Now, we have added them into the "Patient population and setting" and "Randomization and blinding" sections.

10. Methods. Outcomes. Please define PONV. Are you reporting incidence of postoperative nausea, incidence of vomiting, or incidence of nausea and/or vomiting?

Answer: Thanks for the reviewer’s suggestion. PONV is defined as vomiting and/or nausea occurring within 24 h after surgery (McCracken G, Houston P, Lefebvre G: Guideline for the management of postoperative nausea and vomiting. J Obstet Gynaecol Can 2008, 30:600-607, 608-616). In our study, the primary endpoint is the incidence of postoperative
vomiting. Therefore, we have changed the improper term "incidence of PONV" into "incidence of postoperative vomiting" in the "Outcome measurement" section.

11. Methods. Outcomes. Please state how you will measure patient’s satisfaction with PONV management. Did you use a valid and reliable questionnaire as patient’s satisfaction is multidomain specific?

Answer: Several sentences have been added in the "Outcome measurement" section to address this issue.

12. Methods. Statistical analysis. Please describe how you will compare patient satisfaction levels between the five intervention groups.

Answer: In our study, patient satisfaction will be measured by a 0 (very dissatisfied) to 10 (very satisfied) scale. Therefore, each patient’s satisfaction level will be presented with different numbers (satisfaction score). After acquiring all the data, a Kruskal-Wallis test will be used to compare patient satisfaction levels between the five intervention groups.

13. Methods. Statistical analysis. Please describe how you will analyze noninvasive versus invasive methods to answer the second objective stated in the Abstract.

Answer: In order to answer the second objective, different statistical methods will be used. As for postoperative vomiting rate and complete response rate, Chi-square test will be used to examine the differences between the five groups, and the Scheffe test will be used for multiple comparisons within the five groups. As for nausea score, satisfaction score and antiemetic dosage, the differences among the five groups will be examined by the Kruskal-Wallis test, and the Nemenyi test will be used for multiple comparisons within the five groups.

Minor essential revision

1. Methods. Design. Insert a subheading “Patient population and setting”.

Answer: We have now added the subheading according to the reviewer’s suggestion.


Answer: The typographical error has been corrected in the revised version.

3. Methods. Interventions. State route of ondansetron 8mg and
**Metoclopramide 10mg.**

Answer: Thanks for the reviewer’s suggestion. We have used “intravenous” to state the route of administration of ondansetron, and used “intramuscular” to state the route of administration of metoclopramide in the revised manuscript.

4. **Methods. Sample size.** Correct typographically error “β=0.01 (power 90%).”

Answer: Correction has been made in the revised version.

5. **Methods. Statistical analysis.** “….quantitative data is presented as mean…” should be replaced with “continuous data is presented as mean....”

Answer: We have made this correction according to the reviewer’s comments.

6. **Methods. Statistical analysis.** “Chi-square test is used to compare….other qualitative data” should be replaced with “Chi-square test is used to compare…. other nominal data.”

Answer: As the reviewer suggested that, we have replaced this word in the revised version.

Special thanks to you for your constructive feedback.

**Replies to editorial request:**

Answer: We have added the statement into the "Methods Design" section.

Additionally, we have invited two native English speakers to help us improve the quality of written English and help us revise the paper. Those corrections are also in highlighted text. In order to express our thanks for their contribution, we have added the "Acknowledgments" section at the end of the paper. We hope that these revisions are satisfactory and that the revised version will be approved.

Once again, thank you very much for your comments and suggestions.

With best wishes,

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