Author's response to reviews

Title: The effect of transcutaneous electrical acupoint stimulation on pregnancy rates in women undergoing in vitro fertilization: a study protocol for a randomized controlled trial

Authors:

Cui Hong Zheng (chzheng2008@qq.com)
Juan Zhang (1264298243@qq.com)
Jing Wu (wujingrlh@163.com)
Ming Min Zhang (mmzhang@tjh.tjmu.edu.cn)

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Author's response to reviews:

Dear editors and reviewers,

We are very grateful for your elaborate suggestions. We have addressed the comments in the revised manuscript. Now we are giving the response to the concerns point by point.

a) The English is awkward in places. The manuscript should be edited by a native English speaker.

Answer: A native English speakers have reviewed and edited our manuscript.

b) The word "improve" in the title suggests we already know the outcome of the trial. It might be reworded to something like, "The effect of transcutaneous electrical acupoint stimulation on pregnancy rates in women undergoing in vitro fertilization: a study protocol for a randomized controlled trial."

Answer: Thank you very much for your suggestion. We have reworded the title.

c) The background should explain why, if electro-acupuncture plus IVF has been shown to be superior to IVF alone, it is ethical to use a control group of IVF alone.

Answer: Although the latest comprehensive meta-analysis demonstrated that acupuncture improves CPR among women undergoing IVF, most IVF centers do not attach great importance to that. They do not add acupuncture as conventional auxiliary treatment, only use IVF alone. So, the group of IVF alone is mainly as a control group for providing a baseline pregnancy rate and we can further demonstrate the effects of acupuncture and TEAS.

d) There are two references to different Figure 1's (pages 6 and 11). That should be corrected (presumably, page 11 should refer to Figure 2) and the Figure 1 referenced on page 6 was not included. The figure included in the text (presumably a new figure 2) should have a title.

Answer: Thank you for your reminding. We have deleted the first Figure 1. It is
unnecessary. The new Figure 1’s title is “acupoint locations”.

e) In the sample size section, it seems (though it is not explicitly stated) that the study is powered to detect a difference between TEAS plus IVF and the control (IVF alone). Is this correct? If so, since one of the main goals is to compare TEAS plus IVF against EA plus IVF (page 5, bottom says "...whether if brings the same or better effects as compared with real acupuncture."), is there any power for that comparison?

Answer: Thank you for your query. We have discussed and confirmed the calculation again. The primary purpose of this study is to explore whether there are any differences between EA and TEAS in increasing pregnancy rates in women undergoing IVF compared with conventional IVF. Based on the previous studies, we estimated a 7% increase for the EA group and a 15% increase for the TEAS group compared with the control group. The possible proportion of women with a clinical pregnancy for women with two or more cycle failures in the control group was 20%. To detect differences using a pairwise comparison method, the sample size should be 1850 according to optimum allocation (700 for the TEAS group, 700 for the EA group, and 450 for the control group) using the Shieh-O’Brien approximation method assuming that alpha (two-sided) is 0.05, the overall power is 0.90, the power between the TEAS and EA groups is 0.80, and the power between the EA and control group is also 0.80. A total sample size of 2220 women (840 for the TEAS group, 840 for the EA group, and 540 for the control group) is required allowing for a 20% loss due to canceled cycles or no ET.

f) In the Statistical Analysis section, how will missing data, withdrawals, etc. be handled in the intention-to-treat analysis?

Answer: All of the analyses will be based on both an intention-to-treat analysis (ITT#with all randomized patients) and a treated-per-protocol analysis (TPP#with all randomized patients subtracting withdrawals). Missing patient data for those that dropped out of the study will be analyzed using the last observation carried forward method. Patients with complete data missing of primary outcomes will be considered as a negative ITT pregnancy result and eliminated in the TPP analysis.

g) In the Trial Status section, when did (or when will) enrollment begin and when is it expected to be completed?

Answer: The enrollment will begin on 1 May 2014 and is expected to be completed before 1 May 2016.

Editorial requests:
1. Please reformat your Abstract. This should not exceed 350 words and should be structured into separate sections headed Background, Methods/Design, Discussion (if appropriate). Please do not use abbreviations or references in the abstract. Trial Registration, if your Study protocol is a protocol of a controlled health care intervention, please list the trial registry, along with the unique identifying number.
Answer: We have reformatted the abstract as you suggested. We used abbreviations for the repeated words after the first full name.

2. Please modify your Authors' Contributions section to demonstrate that each author meets all three of the following criteria to qualify for authorship:
- Substantial contributions to: the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published

Any author who does not meet all of the above requirements should be removed from the author list. We suggest the following kind of format for this section:

EP: conception and design, data collection and analysis, manuscript writing and final approval of the manuscript. SP: data collection and analysis, critical revision and final approval of the manuscript. MG: data collection and analysis, critical revision and final approval of the manuscript. AP: data collection and analysis and final approval of the manuscript. LS: data collection and analysis and final approval of the manuscript. MCL: data collection and analysis and final approval of the manuscript. FB: conception and design, financial support, manuscript writing, final approval of manuscript. XH: conception and design, data collection and analysis, manuscript writing, final approval of the manuscript. All authors read and approved the final manuscript?

It has come to our attention that there are two additional authors in your Authors' Contributions section. Can you please confirm why they are not on your author list?

Answer: We are so sorry for the negligence in this section. We have deleted the two additional authors in the section of “Authors' Contributions” in the revised manuscript.

3. please remove the attached ethics and funding documentation.

Answer: We will remove the attached ethics and funding documentation when uploading the revised manuscript.

With best wishes,

Cuihong Zheng

Institute of Integrated Traditional Chinese and Western Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei 430030, China