Author's response to reviews

Title: Acupuncture for post anaesthetic recovery and postoperative pain: study protocol for a randomized controlled trial

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Author's response to reviews: see over
Dear Editors-in-Chief,

Thank you for your valuable revision considering our manuscript entitled: “Acupuncture for post anaesthetic recovery and postoperative pain: study protocol for a randomized controlled trial” possible for publication in Trials.

Enclosed you will find a point-by-point response to the concerns such as the revised version of the manuscript. All changes made within the manuscript have been highlighted with yellow colour.

Reviewer’s report

Major Compulsory Revisions:

Revision: The protocol of AcuARP trial was designed to investigate the effectiveness of an acupuncture therapy in the perioperative period on post anaesthetic recovery and postoperative pain. The clinical trial is interested in the field of acupuncture-assisted anesthesia because the results of this study will provide evidence whether acupuncture may improve patients post anaesthetic recovery. In general, the patients inclusion/exclusion criteria, randomization, blinding, Interventions and statistical analysis was suitable, but my main consideration is sample size estimation. The main outcome measure is the time from extubation to “ready for discharge” from the post-anesthesia care unit, the sample size can be estimated by the mean time and anticipated percent decrease in the primary outcome measure. An example from Anaesthesia proof as attachment. For the primary outcome measure of time to achieve recovery room discharge eligibility, the mean (SD) time to achieve recovery room discharge eligibility was 50 (20) min in a pilot study. To capture an anticipated 30% decrease in the primary outcome measure to 35 (15) min, a sample of 46 patients (23 per group) would provide a two-sided unpaired Student’s t-test with 80% power at an alpha of 0.05. To account for potential
loss to follow-up and enable greater statistical power for secondary analyses, the sample size was increased to 72 patients (36 per group).

Answer: We appreciate the recognition of the methodological details we are using in our study. We agree that sample size is an important factor in the development of clinical trials. We would like to point out that our trial was designed as an exploratory trial, in order to provide the basis for following confirmative trials, consequently also data for more profound sample size calculations. At the time point of designing the study there were no other data available to estimate sample sizes. Therefore we estimated the sample size on the basis of an a-priori analysis using G*Power (Version 3.1.3, University of Düsseldorf, Germany). From a conservative point of view we assumed the effect to be small to medium (d = 0.4), according to Jacob Cohen (1988, *Statistical power analysis for the behavioral sciences*: Psychology Press). Taking the three group trial design into account, setting the α-error to 0.05 and the β-error to 0.8, we calculated a total sample size of 66. An adjustment for a 15% drop-out rate resulted in a total sample size of 75 patients. We added a detailed description of the sample size estimation including the following table to our manuscript (page 10):

| F tests – ANOVA: Fixed effects, omnibus, one-way Analysis: A priori: Compute required sample size |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| **Input:**                      | **Output:**                     | **Input:**                      | **Output:**                     |
| Effect size f                  | Noncentrality parameter λ       | α err prob                      | Critical F                      |
| = 0.4                           | = 10.5600000                    | = 0.05                          | = 3.1428085                     |
| Power (1–β err prob)            | Numerator df                    | Power (1–β err prob)            | Denominator df                  |
| = 0.8                           | = 2                             | = 0.8                           | = 63                            |
| Number of groups               | Total sample size               | Actual power                    |                                  |
| = 3                             | = 66                            | = 0.8180744                     |                                  |

Regarding possible bias, a retrospective modification of the sample size estimation process is methodologically critical: For randomisation a computer-based algorithm was used and had been pre-set before the inclusion of the first patient (Randoulette®) by the Institute for Medical Informatics, Biometry and Epidemiology (IBE), Ludwig-Maximilians-University Munich, Germany.

In conclusion we agree with the reviewers opinion on the importance of appropriate sample size estimation, but think that we could demonstrate that in this trial protocol we properly addressed the raised concerns.

Revision: Quality of written English: Needs some language corrections before being published.

Answer: We revised the manuscript in this regard.
Editorial requests:

1. Please include the date your study was registered with your trial registration number at the end of you Abstract.

   Answer: The study was received first October 28, 2012 by ClinicalTrials.gov and information was added to the manuscript (abstract p.2)

2. Please include a trial status section after your Discussion. This should state the status of the trial at the time of manuscript submission. The journal considers study protocol articles for proposed or ongoing trials provided they have not completed patient recruitment at the time of submission.

   Answer: The section was added on page 16 following the discussion.

3. Please move your list of abbreviations below your trial status.

   Answer: We moved the list of abbreviations to page 16.

Dear reviewer, dear editors,
We addressed all of your questions and could hopefully clarify all of your requests. Thank your for carefully reviewing our manuscript and considering it as possible for publication in TRIALS.

Sincerely yours,

Dr. Johannes Fleckenstein