Author’s response to reviews

Title: Efficacy and safety of combined treatment of miniscalpel acupuncture and non-steroidal anti-inflammatory drugs: study protocol for a randomized controlled trial.

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1. Considering your manuscript is a protocol article, the title should illustrate it. Besides, I read the objective of the manuscript is to evaluate the efficacy and safety of the combined treatment in patients with chronic neck pain, but the title gave the expression to evaluate the efficacy and safety of the three interventions (miniscalpel acupuncture, non-steroidal anti-inflammatory drugs and combined treatment). Please clarify your final objective.

-Answer: Thank you for your advice. The objective of this study is focused on the combined treatment of miniscalpel acupuncture and NSAIDs. Therefore the title has been changed to “Efficacy and safety of combined treatment of miniscalpel acupuncture and non-steroidal anti-inflammatory drugs: an assessor-blinded randomized controlled pilot study”
2. There is few words about the safety of the interventions in the main body of your manuscript, which looks contradiction with the title.

-Answer: The information about how to assess the safety of this treatment is in the ‘safety’ section. It is as follows: ‘The safety of this trial will be assessed by the red blood cell count, hemoglobin level, hematocrit, total white blood cell count, differential count, erythrocyte sedimentation rate, platelet count, aspartate aminotransferase level, alanine aminotransferase level, blood urea nitrogen level, prothrombin time, partial thromboplastin time, C-reactive protein and creatinine levels, serum sodium level, serum potassium level, and serum chloride level. All participants will undergo blood tests twice during the study, once at screening and once at the fourth follow-up visit. Nexina (potassium bismuth citrate 100 mg/Tab, ranitidine hydrochloride 84 mg/Tab, sucralfate hydrate 300 mg/Tab) will be prescribed if the participants complain of dyspepsia symptoms such as nausea, abdominal discomfort, and diarrhea.

All adverse effects and vital signs will be observed at every visit. Serious adverse effects will be reported to the IRB. The subjects will be asked to voluntarily report information about adverse effects, and the researchers will confirm the occurrence of adverse events through methods such as medical interviews. Details about adverse effects, such as the date of occurrence, degree of severity, causal relationship with the treatment, other treatments or medications that are suspected to cause the adverse effect, and treatment of the adverse effect, will be reported in detail.’

Based on above information, we will determine the safety of the interventions.

3. The sample size looks so small, and you expect a 20% drop out rate. Please, do as much as you can in order to prevent them. Besides, please provide the evidence of the minimum number recommended for pilot studies.

-Answer: We inserted some sentences to justify the sample size of the study in the Participants section as followings.

“One of the main objectives of this study is to provide an estimate of the sample size required for the full-scale randomized controlled clinical trial."

A reference for this sample size for a pilot study is as follows; Julious, Steven A. Sample size of 12 per group rule of thumb for a pilot study. Pharmaceutical Statistics, 2005, 4.4: 287-291.

According to this reference, we decided to recruit total of 36 participants.
4. The exclusion criteria did not illustrate the patients who were taking the NSAIDs.

-Answer: We inserted some phrases in the exclusion criteria.

“There are those using aspirin or anticoagulant medications; those using NSAIDs; those with abnormal findings in blood tests for renal or hepatic function; and those deemed ineligible by the recruiting researcher will be excluded.”

5. Endpoint evaluations included in the article are almost subjective ones, and some objective ones should be used to increase the strength of the results.

-Answer: We understand that this can be a limitation of this study. However, because this study is based on the pain, it is difficult to have objective evaluation measurement system. Objective measurement such as range of motion, radiography, computed tomography and magnetic resonance imaging cannot be used as measurement methods in this study. In addition, the study is currently finished and it is difficult to change measurement methods.

6. I understand that your primary outcome is the difference of VAS value of the nice pain before and after the treatment. I suggest give the computational formula.

-Answer: In this question, we had difficulty understanding what the computational formula of VAS means. In case you mean to describe how we measure VAS score, we inserted “10-cm line will be drawn using computer” in ‘Primary outcome measurement’ section. In addition, we described how the VAS measurement will work in ‘primary outcome measurement’ section. “VAS is a 10-cm measurement instrument to determine the severity of pain. 10-cm line will be drawn using computer. The subjects rates his or her pain on a scale of 0 to 10, where 0 indicates the absence of pain and 10 indicates the worst pain imaginable”

If what we answered is not what you intended, please give us more specific advice and we will give appropriate answer.