PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Electroacupuncture as a complement to usual care for patients with non-acute pain after back surgery: a study protocol for a pilot randomised controlled trial
AUTHORS	HWANG, MAN-SUK; Heo, Kwang-Ho; Cho, Hyun-Woo; Shin, Byung-Cheul; Lee, Hyeon-Yeop; Heo, In; Kim, Nam-Kwen; Choi, Byung-Kwan; Son, Dong-Wuk; Hwang, Eui-Hyoung

VERSION 1 - REVIEW

REVIEWER	Jun-Hwan Lee Korea Institute of Oriental Medicine, South Korea
REVIEW RETURNED	10-Dec-2014

GENERAL COMMENTS	1. This pilot study will determine the feasibility of running a study of electroacupuncture as a complement to usual care on non-acute pain after surgery. In spite of pilot study, sample size calculation was well-performed and the whole protocol was well-designed. 2. The major weakness of this study is that the authors haven't mentioned about the kind of surgery that participant had. According to the kind of surgery, some factors including causes of pain, recurrence rate, and prognosis may differ. Taking the purpose of this study (the feasibility) into consideration, detailed data about back surgery (i.e. fusion, decompression or discectomy, and which level was and how many levels were involved) would have been collected. I would ask the authors to include this point as limitation of the study. 3. Details about manufacturer of stainless-steel needles is not consistent in interventions section and appendix 1. 4. Before the start of treatment at each point, patients will be assessed to record the outcomes of the previous treatments. If the primary endpoint is really assessment 9(prior to 8th treatment session), does this mean the outcome of seven previous treatment sessions?

REVIEWER	HYANGSOOK LEE KYUNG HEE UNIVERSITY, SOUTH KOREA
REVIEW RETURNED	15-Dec-2014

GENERAL COMMENTS	This study protocol is well-written and I hope the following comments can be of help for conducting and analysing the upcoming results. 1. The authors claim that it is a pilot study for a large-scale pragmatic trial. However, both the terms 'pilot' and 'pragmatic' are used for this study. This is far from the pragmatic trial and the term pragmatic should be deleted throughout the manuscript if it was used for this study, not for a future trial. 2. The sample size calculation is based on Tsukayama's study where electroacupuncture and TENS were compared. In my view, Tsukayama's study is quite different from the present study in terms of participants (LBP without leg pain vs. LBP with or without leg pain after back surgery), intervention (4 sessions of EA vs. 8 sessions of EA and manual acupuncture? on top of standard care), control group (TENS vs. standard care including medication, ICT, and education leaflet, but obviously without TENS), and outcomes (pain relief on VAS where one end indicates pain severity at the beginning of the study and the other no pain at all vs. pain intensity on VAS). The values used in sample size calculation, i.e. 21 mm of intergroup difference, 86 mm – 65 mm, are different from what we usually expect from a 100-mm VAS for pain intensity. 86 mm in Tsukayama's study demonstrates 14% of pain relief relative to 100% previous pain at the start of the study. Additionally, as this study will have only 20 per group, the data are highly likely to be skewed. This is problematic as the mean values can be misleading, potentially giving unreliable and inaccurate estimates of efficacy (McQuay et al. 1996). The authors said, non-parametric test will be used when the data are skewed, but I suggest, instead, that the authors use a responder vs. non-responder approach. The responder can be defined as e.g. a participant with 50% pain relief, using a 100-mm VAS for pain intensity, which is a more reliable and reasonable approach. The sample size calculation is not quite necessary for a pilot study and rather, it can be determined only after a pilot study. I suggest that the sample size calculation and statistical analysis should be revised in this context. 3. The VAS should be administered with a clear wording. In the manuscript, the VAS is given to check degree of back pain 'during recent days'. This can be confusing to the participants and should be clarified how it is administered and exactly what pain (e.g. pain right now? pain for the previous 3 days?) the authors are measuring. 4. The surgery can be diverse and in the inclusion criteria, the participants should have persisting pain for at least 3 weeks after 'recent' back surgery. The term 'recent' can be interpreted differently. How recent is recent? Without clarification of postoperative period, the participants can be a very heterogeneous group. 5. I cannot get a clear understanding of how subgroup analysis is going to be performed in this study. 6. The EA intervention is described in detail. Nevertheless, how alligator clips are connected is not clear and I suspect that manual acupuncture needling is also given when I examined the acupoints' locations and numbers. All in all, this study is interesting and generally well written, provided the comments above are addressed properly. [References]

	McQuay HJ, Carroll D, Moore RA. Variation in the placebo effect in randomised controlled trials of analgesics: all is as blind as it seems. Pain 1996;64:331–5.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1;Jun-Hwan Lee (Korea Institute of Oriental Medicine, South Korea)

Q1. This pilot study will determine the feasibility of running a study of electroacupuncture as a complement to usual care on non-acute pain after surgery. In spite of pilot study, sample size calculation was well-performed and the whole protocol was well-designed.
Answer) Thank you for your positive comment on this manuscript. In accordance with the recommendation of another reviewer (reviewer 2) on sample size calculation, we supplemented more details about how our sample size was made. We added reviewer's point in 'Sample size' in page 14.

Q2.The major weakness of this study is that the authors haven't mentioned about the kind of surgery that participant had. According to the kind of surgery, some factors including causes of pain, recurrence rate, and prognosis may differ. Taking the purpose of this study (the feasibility) into consideration, detailed data about back surgery (i.e. fusion, decompression or discectomy, and which level was and how many levels were involved) would have been collected. I would ask the authors to include this point as limitation of the study.
Answer) Thank you. We added this point in the 'Statistical methods and analysis' as a subgroup analysis by the type of back surgeryand surgically involved spine(s) (level and numbers) in page 15. Also we supplemented this comment in the 'Discussion' section in page 17.

Q3.Details about manufacturer of stainless-steel needles is not consistent in interventions section and appendix 1.
Answer) Sorry. We matched the information of manufacturer of stainless-steel needles between interventions section in page 11 and appendix 1.

Q4.Before the start of treatment at each point, patients will be assessed to record the outcomes of the previous treatments. If the primary endpoint is really assessment 9(prior to 8th treatment session), does this mean the outcome of seven previous treatment sessions?
Answer) Sorry. It is our mistake. As you pointed out, the primary endpoint is assessment 10(right after to 8th treatment session). We changed this point in Method in page 13.

Reviewer 2: HYANGSOOK LEE (KYUNG HEE UNIVERSITY, SOUTH KOREA)

This study protocol is well-written and I hope the following comments can be of help for conducting and analysing the upcoming results.
Answer) Thank you for your evaluation. Through your suggestions, indeed, our manuscript was much upgraded by valuable comments from you. Actually, we missed very important points.

Q1. The authors claim that it is a pilot study for a large-scale pragmatic trial. However, both the terms 'pilot' and 'pragmatic' are used for this study. This is far from the pragmatic trial and the term pragmatic should be deleted throughout the manuscript if it was used for this study, not for a future trial.
Answer) Thank you for your comment. As you suggested, we deleted the term 'pragmatic' throughout the manuscript.

Q2. The sample size calculation is based on Tsukayama's study where electroacupuncture and TENS were compared. In my view, Tsukayama's study is quite different from the present study in terms of participants (LBP without leg pain vs. LBP with or without leg pain after back surgery), intervention (4 sessions of EA vs. 8 sessions of EA and manual acupuncture? on top of standard care), control group (TENS vs. standard care including medication, ICT, and education leaflet, but obviously without TENS), and outcomes (pain relief on VAS where one end indicates pain severity at the beginning of the study and the other no pain at all vs. pain intensity on VAS). The values used in sample size calculation, i.e. 21 mm of intergroup difference, 86 mm – 65 mm, are different from what we usually expect from a 100-mm VAS for pain intensity. 86 mm in Tsukayama's study demonstrates 14% of pain relief relative to 100% previous pain at the start of the study. Additionally, as this study will have only 20 per group, the data are highly likely to be skewed. This is problematic as the mean values can be misleading, potentially giving unreliable and inaccurate estimates of efficacy (McQuay et al. 1996). The authors said, non-parametric test will be used when the data are skewed, but I suggest, instead, that the authors use a responder vs. non-responder approach. The responder can be defined as e.g. a participant with 50% pain relief, using a 100-mm VAS for pain intensity, which is a more reliable and reasonable approach.
Answer) Thank you for your important comment. As you suggested, we revised the sample size calculation and statistical analysis through the manuscript by discussing with a biomedical statistician. We changed Tsukayama's study to more reliable references. Also we added 'responder vs. non-responder' approach in the 'secondary outcomes measurements' in page 14 and in the 'statistical analysis' in page 15.

Q3. The sample size calculation is not quite necessary for a pilot study and rather, it can be determined only after a pilot study. I suggest that the sample size calculation and statistical analysis should be revised in this context.
Answer) For the sample size calculation, we discussed this point with a biomedical statistician when we designed our RCT. We know the fact that general pilot trial may be conducted to explore the feasibility of future full size of trial, therefore, there is no need to conduct sample size calculation. But from the pilot study, we are able to estimate enough sample size preventing under powered in future large effectiveness trial. However reviewer 1 supported sample size calculation and we want to estimate more exact sample size for preventing under powered, also we want to retrospectively re-calculate power from the results of our pilot trial for comparing our estimation (assumption: 80% power) and real results. Then we want to know the gap between the sample size from our prospective statistical estimation (estimated power is 80%) and the one from retrospectively calculated power to find factors related to influence the effectiveness of EA if exist. Details about how our sample size was made are described in 'Statistical methods and analysis' in page 16 and 'Sample size' in page 14.
Q4. The VAS should be administered with a clear wording. In the manuscript, the VAS is given to check degree of back pain 'during recent days'. This can be confusing to the participants and should be clarified how it is administered and exactly what pain (e.g. pain right now? pain for the previous 3 days?) the authors are measuring.
Answer) We missed this points. We changed this point in 'OUTCOME ASSESSMENT' in page 12 as 'degree of back pain for the previous 3 days'.

Q5. The surgery can be diverse and in the inclusion criteria, the participants should have persisting pain for at least 3 weeks after 'recent' back surgery. The term 'recent' can be interpreted differently. How recent is recent? Without clarification of postoperative period, the participants can be a very heterogeneous group.
Answer) Thank you. Instead, we erased the term 'recent' for preventing confusion of readers in page 7 and added subgroup analysis according to the postoperative period for knowing the existence of clinical heterogeneity in Statistical methods and analysis in page 15. As our aim of inclusion of postoperative period is non-acute, therefore, we included subacute (3 weeks to 3 months) or chronic (over 3 months) period.

Q6. I cannot get a clear understanding of how subgroup analysis is going to be performed in this study.
Answer) Thank you. As you suggested, we changed that sentence clearer. We added the details of subgroup analysis in Statistical methods and analysis in page 15.

Q7. The EA intervention is described in detail. Nevertheless, how alligator clips are connected is not clear and I suspect that manual acupuncture needling is also given when I examined the acupoints' locations and numbers.
Answer) We thoughtfully agreed with you. As you suggested, we described details of how alligator clips were applied. We added this point in Method in page 11. It wasn't connected to the EA on all points, and manual acupuncture needling was also given. We added this point in the section of 'interventions' in page 11 and appendix 1 (STRICTA guideline).

All in all, this study is interesting and generally well written, provided the comments above are addressed properly.
Answer) Thank you for your valuable comments.

VERSION 2 – REVIEW

REVIEWER	Jun-Hwan Lee Korea Institute of Oriental Medicine, South Korea
REVIEW RETURNED	02-Jan-2015

GENERAL COMMENTS	The revised manuscript is satisfactory. I would recommend acceptance of the manuscript for publication in BMJ open.

REVIEWER	HYANGSOOK LEE KYUNG HEE UNIVERSITY, KOREA
REVIEW RETURNED	09-Jan-2015

GENERAL COMMENTS	My comments and suggestions are well addressed and for me, no further revisions appear necessary. Thank you.