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Keywords:	electroacupuncture, low back pain, back surgery, postoperative pain, integrative medicine, pilot trial

Electroacupuncture as a complement to usual care for patients with non-acute low back pain after back surgery: A pilot randomisedcontrolled trial

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ABSTRACT

Objectives

The aim of this pilot study was to test the feasibility of a large pragmatic study of the comparative effectiveness of electroacupuncture (EA) for low back pain (LBP) after back surgery.

Design

Randomised, active-controlled, assessor-blinded.

Participants

Patients with recurrent or persistent LBP, defined as a visual analogue scale (VAS) score ≥50 mm, with or without leg pain after back surgery.

Interventions

Patients were randomised to an EA plus usual care (UC) group or to a UC alone group in a1:1 ratio. Patients assigned to each group received UC, including drug therapy, physical therapy and back pain education, twice a week for 4weeks; those assigned to the EA plus UC group also received EA.

Outcome measures

The primary outcome was severity of LBP measured on the VAS. Secondary outcomes were back pain-related disability, assessed using the Oswestry Disability Index (ODI), and quality of life, assessed using the EuroQol five dimensions (EQ-5D) questionnaire. The statistical analysis was performed using paired and independent *t*-tests. A p-value <0.05 was considered to be statistically significant.

Results

Thirty-nine patients were allocated to receive EA plus UC (n=18) or UC alone (n=21). There was no statistically significant difference in VAS or EQ-5D score between the two groups, but there was a significant decrease in the ODI score (p=0.0081).Using G*Power, it was calculated that 40 participants per group would be needed for a future trial according to VAS score. Considering for a 25% dropout rate, 108 participants (54 per group) would be needed.

Conclusions

A future trial addressing the risk of bias and including the estimated sample size would allow better clinical assessment of the benefits of EA plus UC in the treatment of patients with non-acute pain after back surgery.

Trial registration

ClinicalTrials.gov (Identifier: NCT01966250, 11 Oct, 2013)

Keywords: electroacupuncture, low back pain, back surgery, postoperative pain, integrative medicine, pilot trial

Strengths and limitations of this study

1. This trial is designed to be a feasible, comparative effectiveness trial design that is similar to common clinical situations.

2. Individualised acupuncture points according to patients' symptoms during the delivery of acupuncture treatment reflect the real clinical practice of acupuncture.

3. We expect that this pilot study will provide the clinical basis and information that is required to assess the feasibility of a future large-scale trial.

4. The size of the study sample limits the power of the observations.

INTRODUCTION

Low back pain (LBP) afflicts approximately 10% of people worldwide and is a source of considerable social and economic burden.[1] Although there are a number of surgical options available to treat LBP,[2] many people develop complications after lumbar spine surgery and some report that their symptoms are worse after surgery than before.[3] The most common complication is LBP, which occurs in about 40% of patients after back surgery.[4] Therefore, management of postoperative pain is a very important component of patient care,[5] and a wide range of treatments, including physical and/or cognitive-behavioural modalities, systemic or local pharmacological therapies, and neuraxial treatments are used.[6] Opioids, in particular morphine, hydromorphine, and meperidine, are commonly used in the management of postoperative pain,[7] but have significant side effects, including sedation, nausea and vomiting, and itching.[8] Therefore, a safe and effective method for management of pain after back surgery is required.

Several studies have shown that acupuncture is a safer[9,10] and more cost-effective[11] treatment than usual care (UC), which comprises drug treatment and physical therapy,[12,13] and that electroacupuncture (EA) is one of the most common strategies used for pain management.[14-16] Therefore, EA could be a good method for treating pain after back surgery. There has been a systematic review of the evidence for acupuncture as a non-pharmacological strategy in the treatment of acute postoperative pain after back surgery.[17] However, very few clinical trials[18,19] have assessed the effectiveness of EA for non-acute pain after back surgery, and the quality of the relevant research is too poor to reach any valid conclusions.

We have conducted a pilot feasibility study to compare the effectiveness of EA in

combination with UC with that of UC alone in controlling non-acute pain and improving function at ≥3 weeks[20] after back surgery. The primary purpose of this study was to explore whether EA in combination with UC is beneficial in patients with non-acute pain and dysfunction after back surgery. A further aim was to assess the feasibility of such research and to estimate the appropriate sample size needed for a future confirmative, pragmatic, comparative randomised controlled trial (RCT) to determine the effectiveness of EA in combination with UC when compared with UC alone in relieving non-acute pain and dysfunction after back surgery. This research adhered to STRICTA[21] and CONSORT[22]guidelines.

METHODS

Study design

This randomised, active-controlled, assessor-blinded, parallel-group pilot trial was conducted at the Pusan National University Korean Medicine Hospital (PNUKH) in Yangsan, Korea between 26 September, 2013 and 30 June, 2015. Patients were recruited for the trial between 29 October, 2013 and 18 September, 2014. A detailed study protocol has already been published.[23] The protocol was approved by the institutional review board at PNUKH in September2013 (approval number 2013012) and is registered with ClinicalTrials.gov (Identifier: NCT01966250, 11 Oct, 2013).

Participants

As already mentioned in the published protocol, the study investigators screened patients with LBP after back surgery for eligibility. Patients were eligible if they were aged 19–70 years and had LBP that recurred or persisted for at least 3 weeks (non-acute) after back surgery, with or without leg pain, and required intermittent medical treatment. LBP was defined as a visual analogue scale (VAS) score ≥50 mm. Patients found to be eligible and willing to participate voluntarily in this study were guided through the consent process and signed informed consent forms. The exclusion criteria were as follows: serious disease that could cause LBP (e.g., cancer, vertebral fracture, spinal infection, inflammatory spondylitis, cauda equina compression); chronic disease that could influence the effects or results of treatment (e.g., severe cardiovascular disease, diabetic neuropathy, dementia, or epilepsy); progressive neurological deficit or severe neurological symptoms; conditions inappropriate or unsafe for EA (e.g., because of haemorrhagic disease, a clotting disorder, history of having received anticoagulant therapy within the preceding 3weeks, severe diabetes with a risk of infection, or severe cardiovascular disease); pain not caused by spinal or soft tissue disease, such as ankylosing spondylitis, fibromyalgia, rheumatoid arthritis, or gout; pregnancy or planning to become pregnant; psychiatric disease; participation in another clinical trial; inability to provide written informed consent; and ineligibility for inclusion in the study in the opinion of the investigators.

Interventions

Patients randomised to either treatment group received UC for 4 weeks. UC included drug therapy, physiotherapy, and an educational program about management of LBP.[20]Conventional drug treatment or therapies (e.g., pain medication, injections, but not surgical procedures) for LBP after back surgery were allowed and monitored. Physiotherapy

and an educational program about back care were undertaken twice a week for 4 weeks. Interferential current therapy (OG Giken Co., Okayama, Japan) was administered for 15 minutes with application of a hot (or ice) pack for 10 minutes. The structured education program explained the physiology, pathology, and epidemiology of pain after back surgery and was delivered in brochure format. Korean medical doctors also demonstrated postures and exercises suitable for management of LBP in a 15-min face-to-face education session.

Patients randomised to the EA plus UC group received EA in addition to UC. In this group, the acupuncture point prescriptions used were fixed point plus personalised to each patient and at the discretion of the practitioner. Differentiating the acupuncture point is an important part of traditional Korean medical theory and for reflecting the actual clinical situation, and was used to select acupuncture points according to each patient's symptoms. Detailed information on EA is summarised in Appendix 1of the published protocol[23] and is based on the revised STRICTA statement.[21] EA treatment procedures were designed to reflect the feasibility afforded in the actual clinical setting by a consensus of 5experts on acupuncture and spinal disorders. EA was performed by licensed Korean medical doctors using disposable stainless steel needles 0.25 mm in diameter and 0.40 mm in length (Dongbang Acupuncture Inc., Seongnam, Korea). Acupuncture points included Jia-ji (Ex-B2, L3-L5; bilaterally) as fixed points, and other reasonable points could be chosen as accessory points by the practitioner. Between 6 and 15 access points were used by the physicians according to the clinical features of each individual patient. Electric stimulation was applied using an ES-160 electronic stimulator (ITO Co. Ltd, Tokyo, Japan) twice a week for 4 weeks. Stimulation was applied with a biphasic waveform current, which is a compressional wave that combines an interrupted wave and a continuous wave, in triangular form at a frequency of 50 Hz,[24]and was delivered via alligator clips connected to Jia-ji (Ex-B2, L3/L5;

bilaterally). Each EA session lasted 15 minutes. Patients in both groups received 8 treatment sessions in the course of 4 weeks.

Outcome measures

At the initial screening visit, a clinical research coordinator asked all patients to complete a questionnaire regarding their sociodemographic characteristics, including age, sex, height, and weight, and recorded their vital signs. Before the start of treatment at each visit, each patient was assessed to record the outcomes of the previous treatment session. All patients were followed up at 4 and 8 weeks after the 4-week treatment period.

The primary outcome of back pain intensity was assessed using a 100 mm pain visual analogue scale (VAS), on which 0 indicates absence of pain and 100 indicates unbearable pain.[25,26] Each patient was asked to rate his or her degree of back pain during the previous 3days on the VAS. Back pain was measured at baseline (assessment 1) prior to each of the 8treatment sessions (assessments 2–9), and at the2 follow-up visits (assessments 10 and 11). The primary endpoint was assessment 10, which marked the end of the 8 active treatment sessions. A responder was defined as a study participant with ≥50% pain relief using the 100mm VAS for pain intensity and a non-responder was defined as having pain relief of <50% at assessments 9–11.

The secondary outcome measures were back pain-related disability, assessed using the Oswestry Disability Index (ODI),and quality of life, assessed by the EuroQol five dimensions (EQ-5D) questionnaire.[27] The ODI contains 10 questions about daily life and includes measures of pain intensity, personal care, lifting, walking, sitting, standing, sleeping, social

life, and travelling. Each question is rated on a scale of 0 to 5, with a higher score indicating more severe pain-related disability. The validated Korean version of the ODI[28] was administered before treatment at assessments 2, 5, 9,10, and 11.The validated Korean version of the EQ-5D[29, 30] includes generic questions about personal health-related quality of life and consists of five dimensions pertaining to mobility, self-care, usual daily activities, pain and discomfort, and anxiety/depression. Each dimension is scored on a scale of 1 to 3, with a lower score indicating a better state of health. The EQ-5D was administered before treatment assessments 2, 5, 9, 10, and 11.

Randomisation

Before the first treatment session, a statistician assigned patients to one of the 2 groups by a central telephone randomisation procedure according to a computer-generated randomisation sequence using SPSS version 22.0 software (IBM Corp., Armonk, NY, USA).The randomisation was performed by a trial coordinator who has no contact with the patients. The clinical research coordinator obtained the codes for the trial (A or B) from the central telephone service and informed the EA practitioner. The practitioner used these codes to assign patients to one of the two groups and to deliver the appropriate treatment.

The National Clinical Research Centre for Korean Medicine at PNUKH stored the random numbers. The allocation sequence was concealed from the researchers responsible for enrolling, treating, and assessing patients by dividing their roles and contact with the study participants.

Blinding

It was impossible to blind either the patients or treating clinicians in this trial because the study design was pragmatic and comparative and not placebo-controlled. However, the risk of detection bias was minimal because all treatments and assessments were conducted independently and the treating clinicians were not involved in assessment of the outcomes.[31] The assessors, who received standardized training, always performed the outcome assessments in a separate room and were blinded to treatment assignment. However, there was provision in the study protocol for unblinding in exceptional circumstances when knowledge of the actual treatment would be essential for further management of the patient (e.g., a serious adverse event).

Statistical analysis

The statistical analysis was performed on both an intention-to-treat(ITT) and a per-protocol basis. For the ITT analysis, we applied the last-observation-carried-forward rule for missing data. The statistical significance of differences in the data for each group was analysed using the paired *t*-test, and the statistical significance of differences between the groups was analysed using the independent *t*-test. Analysis of covariance was used to analyse and adjust the baseline characteristics if there were statistically significant differences and there was a possibility of covariance of baseline characteristics. The chi-square test or Fisher's exact test was used to analyse categorical data, such as responses/responders recorded and described as frequencies(%). We did not perform an interim analysis because we expected EA and UC to be associated with a minimal risk of harm in this small pilot trial. All statistical analyses were performed by a statistician using SPSS for Windows version 22.0 software. The significance level was set at 5%.The sample size required for a future trial was estimated using the free G*Power version 3.1.7 program (Franz Faul, Christian-Albrechts-Universität zu Kiel, Kiel,

Germany).

The sample size for this pilot trial was estimated according to a previously published protocol.[23] When a two-tailed test with a power of 80% and a significance level of 5% (α error) was applied to the formula shown in the protocol, the number of subjects required for each group was 16. Considering a dropout rate of 20% and a 1:1 allocation ratio, the total sample size was calculated to be 20.

RESULTS

Participants

Forty-seven eligible patients agreed to participate in the trial after screening. Eight participants withdrew their informed consent before the start of treatment, leaving 39 patients who were randomly allocated to the two groups (18 in the EA plus UC group and 21 in the UC alone group). Eight further patients dropped out during the treatment period because of withdrawal of informed consent or protocol violation (6 in the EA plus UC group and 2 in the UC alone group). A further patient dropped out after treatment because of protocol deviation, leaving 30 patients (12 in the EA plus UC group and 18 in the UC alone group) for the per-protocol analysis (Fig. 1).

The mean (standard deviation) age of the 39 treated patients was 57.6 (9.52) years and 19 patients were men (48.7%). There were no statistically significant differences between the 2 groups with regard to baseline demographic characteristics (Table 1), mean scores on the VAS for non-acute back pain after surgery, or scores on the ODI and EQ-5D at the first

weekly evaluation (Table 2).

Table 1. Patient demographic characteristics at baseline

Variables	Total	Group		p-value*
		EA+UC (n=18)	UC alone (n=21)	
Sex, n(%)				.882
Male	19 (48.7)	9 (50.0)	10 (47.6)	
Female	20 (51.3)	9 (50.0)	11 (52.4)	
Age (y)				
Mean±SD	57.6±9.5	58.9±9.8	56.5±9.4	.773
Range	37–70	40–70	37–70	
Height (cm)				
Mean±SD	164.1±9.8	163.0±9.0	165.1±10.6	.734
Range	145–187	145–179	150–187	
Weight (kg)				
Mean±SD	66.9±9.8	67.1±9.5	67.1±9.5	.837
Range	53–88	53–88	55–83	

*t-test or chi-square test. EA, electroacupuncture; UC, usual care; SD, standard deviation.

Table 2. Difference in primary and secondary results of electroacupuncture (EA) in combination with usual care (UC) group and UC alone group between each evaluation and baseline

Variables	Group		p-value*
	EA+UC (n=18) mean [95% CI], n(%)	UC alone (n=21) mean [95% CI],n(%)	
VAS (mm)			
Week 1	64.61 [57.19, 72.03]	67.33 [62.63, 72.04]	.5069
Week 4	41.50 [29.19, 53.81]	58.24 [48.76, 67.72]	
Difference	-23.11 [-36.60, -9.62]	-14.33 [-23.29, -5.38]	.0675
p-value**	.0021	.0216	
Responder	6(33.3)	2(9.5)	.1123†
ODI (%point)			
Week 1	44.7 [37.04, 52.37]	38.23 [31.63, 44.83]	.1854
Week 4	31.95 [22.72, 41.19]	32.47 [25.16, 39.77]	
Difference	-12.75 [-17.23, -8.28]	-5.77 [-8.75, -2.79]	.0081
p-value**	<.0001	.0006	
EQ-5D (point)			
Week 1	0.65 [0.58, 0.71]	0.66 [0.59, 0.73]	.7234
Week 4	0.73 [0.65, 0.81]	0.74 [0.68, 0.8]	
Difference	0.09 [0.02, 0.16]	0.06 [0.02, 0.11]	.5151
p-value**	.0178	.0083	

*t-test for comparison of difference between groups; **paired t-test for comparison of difference from baseline;†Fisher's exact test for comparison of difference between groups. EA, electroacupuncture; UC, usual care; CI, confidence interval; VAS, visual analogue scale; ODI, Oswestry Disability Index; EQ-5D,EuroQol five dimensions questionnaire.

Effects of EA

In both treatment groups, there was a statistically significant improvement in VAS back pain scores and in the ODI and EQ-5D score at 4 weeks when compared with baseline (Table 2). However, there were no statistically significant differences in the VAS score for back pain(p=0.0675) or in the EQ-5D score between the 2 treatment groups after 4 weeks (Table 2). There was a statistically significant decrease in the ODI after 4 weeks in the EA plus UC group when compared with the UC alone group (p=0.0081; Table 2). In the ITT analysis(n=39), the proportion of responders, defined as participants with ≥50% pain relief on the 100mm VAS for pain intensity, was 6% (n=6) in the EA plus UC group and 2% (n=2) in the UC alone group; the difference between the groups was not statistically significant (p=0.1123; Table 2). And no adverse events were reported in this study.

Estimating sample size of a future trial

On completion of this pilot study, we calculated an appropriately powered sample size that would be suitable for a larger RCT, based on the difference in changes in VAS score between the groups, with consideration of a 5% significant level, a two-tailed test, 80% power, and a *t*-test for comparison between groups. The mean (standard deviation) difference in the VAS score for back pain between the EA plus UC group and the UC alone group was 14.02 (22.12) mm after treatment based on ITT analysis. On this basis, the sample size calculated by G*Power would be 40 participants per group. Considering a 25% dropout rate, a total of 108 participants (54 per group) would need to be recruited for the future trial.

DISCUSSION

Many people suffer from LBP after back surgery and experience the side effects of opioids used to relieve their pain. Previous research has shown that patients treated with acupuncture or related techniques have less pain and use less opioid analgesia.[32] Therefore, EA could be a good alternative as a non-pharmacological treatment to avoid the side effects of opioids. EA is often used for management of postoperative pain.[33-36] Therefore, we undertook this pilot RCT to guide the design of a full-scale randomised trial. The purpose of the pilot study was to confirm the feasibility of such a study rather than to determine the effectiveness of EA. Therefore, although the number of samples used in the analysis was insufficient for the number of roughly estimated samples in advance, we focused on analysing the approximate validity and calculating the sample size needed for a future trial.

From the results of this pilot study, we can put the case that EA in combination with UC is more effective than UC alone for management of patients with non-acute pain after back surgery. First, there was no statistically significant difference between the two groups in this regard, but the changes in VAS score in the EA plus UC group (mean-23.11, 95% confidence interval -36.60, -9.62) was still different from that in the UC alone group (mean-14.13, 95% confidence interval -23.29, -5.38).Further, the reason for our contention is the significant ($p=0.0081$) between-group difference in changes in ODI, which assesses back pain-related disability and in this study favoured EA plus UC therapy in terms of functional improvement in the lumbar spine. Given the clinical reality that it is difficult to expect improvement of function without relief of pain, our supposition seems reasonable. This preliminary finding confirms that we should proceed in the future to a pragmatic RCT comparing the effectiveness of EA with UC with that of UC alone in the treatment of non-acute pain after back surgery.

There are several considerations to be taken into account before proceeding to a larger RCT. First, for cultural reasons, most participants in such a study would already have had experience with acupuncture in Korea, which would make a factor limiting the efficacy of treatment using acupuncture and the reason why many clinical trials using acupuncture, or related techniques such as EA, are often considered to have a high risk of bias.[37, 38] Therefore, treatment and assessment would need to be performed independently in a follow-up trial to prevent detection bias. Further, there were many dropouts in this pilot trial, and it would be necessary to find an appropriate method of overcoming this problem Inclusion of a patient satisfaction survey in a future trial may help to shed light on this high dropout rate.

A future trial that addresses the above-mentioned concerns and includes the estimated sample size will allow better clinical assessment of the benefits of EA in combination with UC in the treatment of patients with non-acute pain after back surgery. In addition, cost data will be collected using a structured survey for economic evaluation of EA plus UC treatment in a future trial. The results of a follow-up trial can be expected to establish a new clinical basis for acupuncture combined with electrical stimulation in these patients.

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Competing interests

The authors declare that they have no competing interests.

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Author contributions

All authors conceived and designed the trial by discussion. IH wrote the manuscript. MSH, EHH, JHC, and IHH helped to conceive and design the trial. BCS as the principal investigator conceived the trial and revised the manuscript. IH and MSH recruited the patients and conducted the trial.NKK acted as an economic evaluation expert and clinical trial expert. DWS was involved as a neurosurgical expert. KMS and JHL supervised the trial. All authors read and approved the final manuscript.

Data sharing statement

Data may be requested from the corresponding author and made available to researchers who meet the criteria for access to confidential patient data according to the Institutional Review Board of Pusan National University Korean Medicine Hospital.

REFERENCES

1 Hoy D, March L, Brooks P, et al. Measuring the global burden of low back pain. *Best Pract Res ClinRheumatol*2010;24:155–65.

2 Sarrazin JL. Imaging of postoperative lumbar spine. *J Radiol* 2003;84(2 Pt 2):241–52.

3 Herrera Herrera I, Moreno de la Presa R, Gonzalez Gutierrez R, et al. Evaluation of the postoperative lumbar spine. *Radiologia* 2013;55:12–23.

4 Aghion D, Chopra P, Oyelese AA. Failed back syndrome. *Med Health R I* 2012;95:391–3.

5 SkolaskyRL, Wegener ST, Maggard AM, et al. The impact of reduction of pain after lumbar spine surgery: the relationship between changes in pain and physical function and disability. *Spine* 2014;39:1426–32.

6 Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain* 2016;17:131–57.

7 Hutchison RW, Chon EH, Tucker Jr. WF, et al. A comparison of a fentanyl, morphine, and hydromorphone patient-controlled intravenous delivery for acute postoperative analgesia: a multicenter study of opioid-induced adverse reactions. *Hosp Pharm* 2006;41:659–63.

8 Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. *Pain Physician* 2008;11(2 Suppl):S105–20.

9 White A, Hayhoe S, Hart A, et al. Survey of adverse events following acupuncture (SAFA): a prospective study of 32,000 consultations. *Acupunct Med* 2001;19:84–92.

10 Wheway J, Agbabiaka TB, Ernst E. Patient safety incidents from acupuncture treatments:

a review of reports to the National Patient Safety Agency. *Int J Risk Saf Med*2012;24:163–9.

11 Lin CW, Haas M, Maher CG, et al. Cost-effectiveness of guideline-endorsed treatments for low back pain: a systematic review. *Eur Spine J*2011;20:1024–38.

12 Lee JH, Choi TY, Lee MS, et al. Acupuncture for acute low back pain: a systematic review. *Clin J Pain* 2013;29:172–85.

13 Shin JS, Ha IH, Lee J, et al. Effects of motion style acupuncture treatment in acute low back pain patients with severe disability: a multicenter, randomized, controlled, comparative effectiveness trial. *Pain* 2013;154:1030–7.

14 Casimiro L, Barnsley L, Brosseau L, et al. Acupuncture and electroacupuncture for the treatment of rheumatoid arthritis. *Cochrane Database Syst Rev*2005;4:CD003788.

15 Zhao XB, Xing QZ, Han XC. [Observation on electroacupuncture at neimadian (extra) and neiguan (PC 6) for analgesia after thoracic surgery]. *Zhongguo Zhen Jiu*2013;33:829–32. Article in Chinese.

16 Chia KL. Electroacupuncture treatment of acute low back pain: unlikely to be a placebo response. *Acupunct Med* 2014;32:354–5.

17 Cho YH, Kim CK, HeoKH, et al. Acupuncture for acute postoperative pain after back surgery: a systematic review and meta-analysis of randomized controlled trials.*Pain Pract*2015;15:279–91.

18 Huang HT, ZhengSH, Feng J, et al. Thin's abdominal acupuncture for treatment of failed back surgery syndrome in 20 cases of clinical observation. *Guid J Trad Chin Med Pharm* 2012;18:63–5.

19 ZhengSH, Wu YT, Liao JR, et al. [Abdominal acupuncture treatment of failed back surgery syndrome clinical observation]. *J EmergTrad Chin Med* 2010;19:1497–8. Article in Chinese.

20 National Guideline Clearinghouse. Low Back Disorders. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2011. Available from: http://www.guideline.gov/content.aspx?id=38438.

21 MacPherson H, Altman DG, Hammerschlag R, et al. Revised STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): Extending the CONSORT statement. *J Evid Based Med* 2010;3:140–55.

22 Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Int J Surg* 2012;10:28–55.

23 Hwang MS, HeoKH, ChoHW, et al. 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. *BMJ Open*2015;5:e007031.

24 Jung YP, Jung HK, Chiang SY, et al. The clinical study of electroacupuncture treatment at Hua-Tuo-Jia-Ji-Xue on spondylolisthesis. *The Journal of Korean Acupuncture &Moxibustion Society* 2008;25:221–32.

25 Revill SI, Robinson JO, Rosen M, et al. The reliability of a linear analogue for evaluating pain. *Anaesthesia* 1976;31:1191–8.

26 Carlsson AM. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. *Pain* 1983;16:87–101.

27 Fairbank JC, PynsentPB. The Oswestry Disability Index. *Spine* 2000;25:2940–52.

28 Jeon CH, Kim DJ, Kim SK, et al. Validation in the cross-cultural adaptation of the Korean version of the Oswestry Disability Index. *J Korean Med Sci* 2006;21:1092–7.

29 Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001;33:337–43.

30 Kang EJ, Shin SH, Park HJ, et al. A validation of health status using EQ-5D. *The Korean*

Journal of Health Economics and Policy 2006;12:19–43.

31 Higgins J, Green S, Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions. Chichester, UK; Wiley-Blackwell; 2008.

32 Wu MS, Chen KH, Chen IF, et al. The efficacy of acupuncture in post-operative pain management: a systematic review and meta-analysis. *PLoS One*2016;11:e0150367.

33 Chi H, Zhou WX, Wu YY, et al. [Electroacupuncture intervention combined with general anesthesia for 80 cases of heart valve replacement surgery under cardiopulmonary bypass]. *Zhen Ci Yan Jiu* 2014;39:1–6. Article in Chinese.

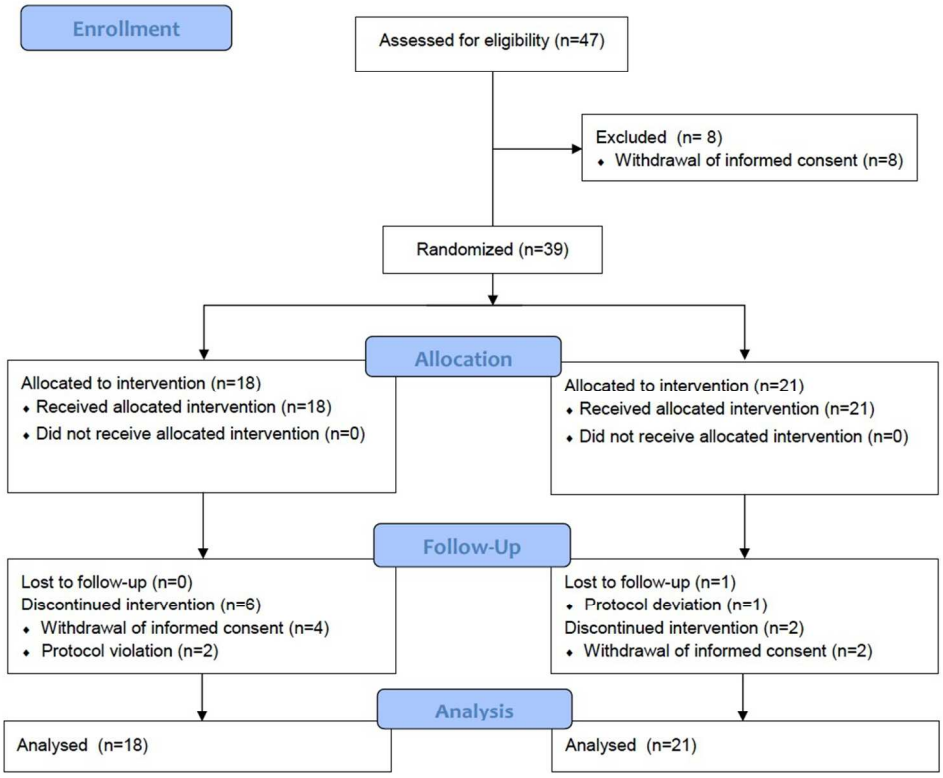
34 Wu J, Zhao Y, Yang CM, et al. [Effects of electroacupuncture preemptive intervention on postoperative pain of mixed hemorrhoids]. *Zhongguo Zhen Jiu*2014;34:279–83. Article in Chinese.

35 Zhang H, Wang L, Zhang M, et al. [Effects of electroacupuncture on postoperative functional recovery in patients with gynaecological laparoscopic surgery]. *Zhongguo Zhen Jiu*2014;34:273–8. Article in Chinese.

36 Zhang Z, Wang C, Li Q, et al. Electroacupuncture at ST36 accelerates the recovery of gastrointestinal motility after colorectal surgery: a randomised controlled trial. *Acupunct Med* 2014;32:223–6.

37 Kim SI, Lee KB, Lee HS, et al. Acupuncture experience in patients with chronic low back pain(2): a qualitative study - focused on participants in randomized controlled trial. *Korean J Acupunct* 2012;29:581–97.

38 Lee H, Bang H, Kim Y, et al. Non-penetrating sham needle, is it an adequate sham control in acupuncture research? Complement Ther Med 2011;19Suppl1:S41–8.



CONSORT 2010 Flow Diagram

290x247mm (96 x 96 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3~5
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	6
	2b	Specific objectives or hypotheses	6~7
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	7
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8~9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	10~11
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	12~13
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	11
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	11
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	11
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	11
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	12

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	12
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	13
	13b	For each group, losses and exclusions after randomisation, together with reasons	13
Recruitment	14a	Dates defining the periods of recruitment and follow-up	15
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	14
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	15
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	15
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	15
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	16~17
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	16
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	7
Protocol	24	Where the full trial protocol can be accessed, if available	7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	18

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

BMJ Open

Electroacupuncture as a complement to usual care for patients with non-acute low back pain after back surgery: A pilot randomised controlled trial

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Electroacupuncture as a complement to usual care for patients with non-acute low back pain after back surgery: A pilot randomised controlled trial

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ABSTRACT

Objectives

The aim of this pilot study was to estimate sample size of a large pragmatic study of the comparative effectiveness of electroacupuncture (EA) for low back pain (LBP) after back surgery.

Design

Randomised, active-controlled, assessor-blinded.

Participants

Patients with recurrent or persistent LBP, defined as a visual analogue scale (VAS) score ≥50 mm, with or without leg pain after back surgery.

Interventions

Patients were randomised to an EA plus usual care (UC) group or to a UC alone group in a1:1 ratio. Patients assigned to each group received UC, including drug therapy, physical therapy and back pain education, twice a week for 4weeks; those assigned to the EA plus UC group also received EA.

Outcome measures

The primary outcome was severity of LBP measured on the VAS. Secondary outcomes were back pain-related disability, assessed using the Oswestry Disability Index (ODI), and quality of life, assessed using the EuroQol five dimensions (EQ-5D) questionnaire. The statistical analysis was performed using paired and independent *t*-tests. A p-value <0.05 was considered to be statistically significant.

Results

Thirty-nine patients were allocated to receive EA plus UC (n=18) or UC alone (n=21). There was no statistically significant difference in VAS or EQ-5D score between the two groups, but there was a significant decrease in the ODI score (p=0.0081). Using G*Power, it was calculated that 40 participants per group would be needed for a future trial according to VAS score. Considering for a 25% dropout rate, 108 participants (54 per group) would be needed.

Conclusions

A future trial addressing the risk of bias and including the estimated sample size would allow better clinical assessment of the benefits of EA plus UC in the treatment of patients with non-acute pain after back surgery.

Trial registration

ClinicalTrials.gov (Identifier: NCT01966250, 11 Oct, 2013)

Keywords: electroacupuncture, low back pain, back surgery, postoperative pain, integrative medicine, pilot trial

Strengths and limitations of this study

1. This trial is designed to be a feasible, comparative effectiveness trial design that is similar to common clinical situations.

2. Individualised acupuncture points according to patients' symptoms during the delivery of acupuncture treatment reflect the real clinical practice of acupuncture.

3. We expect that this pilot study will provide the clinical basis and information that is required to assess the feasibility of a future large-scale trial.

4. The size of the study sample limits the power of the observations.

INTRODUCTION

Low back pain (LBP) afflicts approximately10% of people worldwide and is a source of considerable social and economic burden.[1] Although there are a number of surgical options available to treat LBP,[2]many people develop complications after lumbar spine surgery and some report that their symptoms are worse after surgery than before.[3] The most common complication is LBP, which occurs in about 40% of patients after back surgery.[4]Therefore, management of postoperative pain is a very important component of patient care,[5]and a wide range of treatments, including physical and/or cognitive-behavioural modalities, systemic or local pharmacological therapies, and neuraxial treatments are used.[6] Opioids, in particular morphine, hydromorphine, and meperidine, are commonly used in the management of postoperative pain,[7]but have significant side effects, including sedation, nausea and vomiting, and itching.[8]Therefore, a safe and effective method for management of pain after back surgery is required.

Several studies have shown that acupuncture is a safer[9,10] and cost-effective[11] treatment than usual care (UC), which comprises drug treatment and physical therapy,[12,13]and that electroacupuncture (EA) is one of the most common strategies used for pain management.[14-16]Therefore, EA could be a good method for treating pain after back surgery. There has been a systematic review of the evidence for acupuncture as a non-pharmacological strategy in the treatment of acute postoperative pain after back surgery.[17] However, very few clinical trials[18,19] have assessed the effectiveness of EA for non-acute pain after back surgery, and the quality of the relevant research is too poor to reach any valid conclusions.

We have conducted a pilot study to compare the effectiveness of EA in combination with UC

with that of UC alone in controlling non-acute pain and improving function at ≥3 weeks[20]after back surgery. The primary purpose of this study was to estimate the appropriate sample size needed for a future confirmative, pragmatic, comparative randomised controlled trial (RCT) to determine the effectiveness of EA in combination with UC when compared with UC alone in relieving non-acute pain and dysfunction after back surgery. This research adhered to STRICTA[21] and CONSORT[22]guidelines.

METHODS

Study design

This randomised, active-controlled, assessor-blinded, parallel-group pilot trial was conducted at the Pusan National University Korean Medicine Hospital (PNUKH) in Yangsan, Korea between 26September, 2013 and 30 June,2015. Patients were recruited for the trial between 29 October, 2013 and 18 September, 2014.A detailed study protocol has already been published.[23] The protocol was approved by the institutional review board at PNUKH in September2013 (approval number 2013012) and is registered with ClinicalTrials.gov (Identifier: NCT01966250, 11 Oct, 2013).In addition to this trial on the effectiveness of the EA for LBP after surgery, the qualitative research and the economic evaluation conducted by other researcher were conducted concurrently. Because the statistical analysis was performed after all data collection was completed, our reporting have been postponed unfortunately.

Participants

As already mentioned in the published protocol, the study investigators screened patients with LBP after back surgery for eligibility. Patients were eligible if they were aged 19–70 years and had LBP that recurred or persisted for at least 3 weeks (non-acute) after back surgery, with or without leg pain, and required intermittent medical treatment. LBP was defined as a visual analogue scale (VAS) score ≥50 mm. Patients found to be eligible and willing to participate voluntarily in this study were guided through the consent process and signed informed consent forms. The exclusion criteria were as follows: serious disease that could cause LBP (e.g., cancer, vertebral fracture, spinal infection, inflammatory spondylitis, cauda equina compression); chronic disease that could influence the effects or results of treatment (e.g., severe cardiovascular disease, diabetic neuropathy, dementia, or epilepsy); progressive neurological deficit or severe neurological symptoms; conditions inappropriate or unsafe for EA (e.g., because of haemorrhagic disease, a clotting disorder, history of having received anticoagulant therapy within the preceding 3weeks, severe diabetes with a risk of infection, or severe cardiovascular disease); pain not caused by spinal or soft tissue disease, such as ankylosing spondylitis, fibromyalgia, rheumatoid arthritis, or gout; pregnancy or planning to become pregnant; psychiatric disease; participation in another clinical trial; inability to provide written informed consent; and ineligibility for inclusion in the study in the opinion of the investigators.

Interventions

Patients randomised to either treatment group received UC for 4 weeks. UC included drug therapy, physiotherapy, and an educational program about management of LBP, not Korean medicine treatment such as acupunture, moxibustion, cupping and so on.[20]Conventional drug treatment or therapies (e.g., pain medication, injections, but not surgical procedures) for

LBP after back surgery were allowed and monitored. Physiotherapy and an educational program about back care were undertaken twice a week for 4 weeks. Interferential current therapy (OG Giken Co., Okayama, Japan) was administered for 15 minutes with application of a hot (or ice) pack for 10 minutes. The structured education program explained the physiology, pathology, and epidemiology of pain after back surgery and was delivered in brochure format. Korean medical doctors also demonstrated postures and exercises suitable for management of LBP in a 15-min face-to-face education session.

Patients randomised to the EA plus UC group received EA in addition to UC. In this group, the acupuncture point prescriptions used were fixed point plus personalised to each patient and at the discretion of the practitioner. Differentiating the acupuncture point is an important part of traditional Korean medical theory and for reflecting the actual clinical situation, and was used to select acupuncture points according to each patient's symptoms. Detailed information on EA is summarised in the published protocol[23]and is based on the revised STRICTA statement.[21] EA treatment procedures were designed to reflect the feasibility afforded in the actual clinical setting by a consensus of 5experts on acupuncture and spinal disorders. EA was performed by licensed Korean medical doctors using disposable stainless steel needles 0.25 mm in diameter and 0.40 mm in length (Dongbang Acupuncture Inc., Seongnam, Korea). Acupuncture points included Jia-ji (Ex-B2, L3-L5; bilaterally) as fixed points, and other reasonable points could be chosen as accessory points by the practitioner. Between 6 and 15 access points were used by the physicians according to the clinical features of each individual patient. Electric stimulation was applied using an ES-160 electronic stimulator (ITO Co. Ltd, Tokyo, Japan) twice a week for 4 weeks. Stimulation was applied with a biphasic waveform current, which is a compressional wave that combines an interrupted wave and a continuous wave, in triangular form at a frequency of 50 Hz,[24]and

was delivered via alligator clips connected to Jia-ji (Ex-B2, L3/L5; bilaterally). Each EA session lasted 15 minutes. Patients in both groups received 8 treatment sessions in the course of 4 weeks.

Outcome measures

At the initial screening visit, a clinical research coordinator asked all patients to complete a questionnaire regarding their sociodemographic characteristics, including age, sex, height, and weight, and recorded their vital signs. Before the start of treatment at each visit, each patient was assessed to record the outcomes of the previous treatment session. All patients were followed up at 4 and 8 weeks after the 4-week treatment period.

The primary outcome of back pain intensity was assessed using a 100 mm pain visual analogue scale (VAS), on which 0 indicates absence of pain and 100 indicates unbearable pain.[25,26]Each patient was asked to rate his or her degree of back pain during the previous 3days on the VAS. Back pain was measured at baseline (assessment 1, week 0) prior to each of the 8 treatment sessions (assessments 2–9, week 1-4), and at the2 follow-up visits (assessments 10 and 11, week 8 and 12). The primary endpoint was assessment 10 (week 8), which marked the end of the 8 active treatment sessions. A responder was defined as a study participant with ≥50% pain relief using the 100mm VAS for pain intensity and a non-responder was defined as having pain relief of <50% at assessments 9, 10 and 11 (week 4, 8 and 12).

The secondary outcome measures were back pain-related disability, assessed using the Oswestry Disability Index (ODI),and quality of life, assessed by the EuroQol five dimensions (EQ-5D) questionnaire.[27] The ODI contains 10 questions about daily life and includes

measures of pain intensity, personal care, lifting, walking, sitting, standing, sleeping, social life, and travelling. Each question is rated on a scale of 0 to 5, with a higher score indicating more severe pain-related disability. The validated Korean version of the ODI[28] was administered before treatment at assessments 2, 5, 9,10, and 11 (week 1, 2, 4, 8, and 12). The validated Korean version of the EQ-5D[29, 30] includes generic questions about personal health-related quality of life and consists of five dimensions pertaining to mobility, self-care, usual daily activities, pain and discomfort, and anxiety/depression. Each dimension is scored on a scale of 1 to 3, with a lower score indicating a better state of health. The EQ-5D was administered before treatment assessments 2, 5, 9, 10, and 11 (week 1, 2, 4, 8, and 12).

Randomisation

Before the first treatment session, a statistician assigned patients to one of the 2 groups by a central telephone randomisation procedure according to a computer-generated randomisation sequence using SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). The randomisation was performed by a trial coordinator who has no contact with the patients. The clinical research coordinator obtained the codes for the trial (A or B) from the central telephone service and informed the EA practitioner. The practitioner used these codes to assign patients to one of the two groups and to deliver the appropriate treatment.

The National Clinical Research Centre for Korean Medicine at PNUKH stored the random numbers. The allocation sequence was concealed from the researchers responsible for enrolling, treating, and assessing patients by dividing their roles and contact with the study participants.

Blinding

It was impossible to blind either the patients or treating clinicians in this trial because the study design was pragmatic and comparative and not placebo-controlled. However, the risk of detection bias was minimal because all treatments and assessments were conducted independently and the treating clinicians were not involved in assessment of the outcomes.[31] The assessors, who received standardized training, always performed the outcome assessments in a separate room and were blinded to treatment assignment. However, there was provision in the study protocol for unblinding in exceptional circumstances when knowledge of the actual treatment would be essential for further management of the patient (e.g., a serious adverse event).

Statistical analysis

The statistical analysis was performed on both an intention-to-treat(ITT) and a per-protocol basis. For the ITT analysis, we applied the last-observation-carried-forward (LOCF) rule for missing data. The statistical significance of differences in the data for each group was analysed using the paired *t*-test, and the statistical significance of differences between the groups was analysed using the independent *t*-test. Analysis of covariance was used to analyse and adjust the baseline characteristics if there were statistically significant differences and there was a possibility of covariance of baseline characteristics. The chi-square test or Fisher's exact test was used to analyse categorical data, such as responses/responders recorded and described as frequencies(%). We did not perform an interim analysis because we expected EA and UC to be associated with a minimal risk of harm in this small pilot trial. All statistical analyses were performed by a statistician using SPSS for Windows version 22.0

software. The significance level was set at 5%.

The sample size for this pilot trial was estimated according to a previously published protocol.[23] When a two-tailed test with a power of 80% and a significance level of 5% (α error) was applied to the following formula shown in the protocol, the number of subjects required for each group was 16. Considering a dropout rate of 20% and a 1:1 allocation ratio, the total sample size was calculated to be 20.

Sample size $n = \frac{2(Z_{\alpha/2} + Z_{1-\beta})^2 \delta^2}{(\mu t - \mu c)^2}$

n=the number of participants required in each group
$Z_{\alpha/2}=Z_{0.05/2}=1.96$
$Z_{1-\beta}=Z_{0.8}=0.84$
$\delta=19$
$\mu_t-\mu_c=20$

The sample size required for a future trial will be estimated using the free G*Power version 3.1.7 program (Franz Faul, Christian-Albrechts-Universität zu Kiel, Kiel, Germany), which calculates the sample size on the same principle as the above formula using mean difference and standard deviation.

RESULTS

Participants

Forty-seven eligible patients agreed to participate in the trial after screening. Eight participants withdrew their informed consent before the start of treatment, leaving 39 patients who were randomly allocated to the two groups (18 in the EA plus UC group and 21 in the UC alone group). Eight of 39 patients dropped out during the treatment period because of

withdrawal of informed consent or protocol violation (6 in the EA plus UC group and 2 in the UC alone group). A further patient in UC alone group dropped out after treatment because of protocol deviation, leaving 30 patients (12 in the EA plus UC group and 18 in the UC alone group) for the per-protocol analysis (Fig. 1).

The mean (standard deviation) age of the 39 treated patients was 57.6 (9.52) years and 19 patients were men (48.7%). Detailed baseline demographic characteristics were provided in Table 1. The mean scores on the VAS for non-acute back pain after surgery, or scores on the ODI and EQ-5D at the baseline evaluation were in the Table 2.

Table 1. Patient demographic characteristics at baseline

Variables	Total	Group		p-value*
		EA+UC (n=18)	UC alone (n=21)	
Sex, n(%)				.882
Male	19 (48.7)	9 (50.0)	10 (47.6)	
Female	20 (51.3)	9 (50.0)	11 (52.4)	
Age (y)				
Mean±SD	57.6±9.5	58.9±9.8	56.5±9.4	.773
Range	37–70	40–70	37–70	
Height (cm)				
Mean±SD	164.1±9.8	163.0±9.0	165.1±10.6	.734
Range	145–187	145–179	150–187	
Weight (kg)				
Mean±SD	66.9±9.8	67.1±9.5	67.1±9.5	.837
Range	53–88	53–88	55–83	

*t-test or chi-square test. EA, electroacupuncture; UC, usual care; SD, standard deviation.

Table 2. Difference in primary and secondary results of electroacupuncture (EA) in combination with usual care (UC) group and UC alone group between each evaluation and baseline

Variables	Group		p-value*
	EA+UC (n=18) mean [95% CI], p-value**	UC alone(n=21) mean [95% CI], p-value**	

VAS [mm]			
baseline	64.61 [57.19, 72.03]	67.33 [62.63, 72.04]	.5069
After 4 weeks	51.78 [41.52, 62.03]	60.24 [51.48, 69.00]	
difference	-12.83 [-25.27, -0.39], p=.0439	-7.10 [-13.22, -0.97], p=.0253	.3919
After 8 weeks	41.50 [29.19, 53.81]	58.24 [48.76, 67.72]	
difference	-23.11 [-36.60, -9.62], p=.0021	-9.10 [-16.71, -1.48], p=.0216	.0675
After 12 weeks	41.78 [29.53, 54.02]	53.00 [43.26, 62.74]	
difference	-22.83 [-35.86, -9.81], p=.0018	-14.33 [-23.29, -5.38], p=.0033	.2553
Responder[%(n)]			
After 4 weeks	22.2 (4)	4.8 (1)	.1618†
After 8 weeks	33.3 (6)	9.5 (2)	.1123†
After 12 weeks	38.9 (7)	19.1 (4)	.1698‡
ODI [%point]			
baseline	44.7 [37.04, 52.37]	38.23 [31.63, 44.83]	.1854
After 4 weeks	33.78 [25.1, 42.45]	34.19 [26.41, 41.97]	
difference	-10.93 [-15.92, -5.94], p=.0002	-4.04 [-7.59, -0.5], p=.0274	.0210
After 8 weeks	31.95 [22.72, 41.19]	32.47 [25.16, 39.77]	
difference	-12.75 [-17.23, -8.28], p<.0001	-5.77 [-8.75, -2.79], p=.0006	.0081
After 12 weeks	29.67 [20.49, 38.85]	28.6 [21.01, 36.2]	
difference	-15.04 [-20.16, -9.91], p<.0001	-9.63 [-14.39, -4.87], p=.0004	.1137
EQ-5D [point]			
baseline	0.65 [0.58, 0.71]	0.66 [0.59, 0.73]	.7234
After 4 weeks	0.71 [0.65, 0.76]	0.72 [0.65, 0.78]	
difference	0.06 [0.01-0.12], p=.0298	0.05 [0.02-0.09], p=.0043	.7698
After 8 weeks	0.73 [0.65, 0.81]	0.74 [0.68, 0.8]	
difference	0.09 [0.02, 0.16], p=.0178	0.06 [0.02, 0.11], p=.0083	.5151
After 12 weeks	0.73 [0.65, 0.81]	0.74 [0.68, 0.8]	
difference	0.08 [0, 0.17], p=.0481	0.08 [0.04, 0.12], p=.0007	.9441

*t-test for comparison of difference between groups; **paired t-test for comparison of difference from baseline;†Fisher's exact test for comparison of difference between groups; ‡Chi-square test for comparison of difference between groups.EA, electroacupuncture; UC, usual care; CI, confidence interval; VAS, visual analogue scale; ODI, Oswestry Disability Index; EQ-5D,EuroQol five dimensions questionnaire.

Effects of EA

In both treatment groups, there was a statistically significant improvement in VAS back pain scores , ODI score and EQ-5D score at 8 weeks when compared with baseline (Table 2). However, there were no statistically significant differences in the VAS score for back pain (p=0.0675) and in the EQ-5D (p=0.5151) score between the 2 treatment groups after 8 weeks (Table 2). There was a statistically significant decrease in the ODI after 8 weeks in the EA plus UC group when compared with the UC alone group (p=0.0081; Table 2). In the ITT analysis (n=39), the proportion of responders, defined as participants with ≥50% pain relief

on the 100mm VAS for pain intensity, was 33.3% (n=6) in the EA plus UC group (n=18) and 9.5% (n=2) in the UC alone group (n=21); the difference between the groups was not statistically significant (p=0.1123; Table 2). No adverse events were reported in this study.

Estimating sample size of a future trial

On completion of this pilot study, we calculated an appropriately powered sample size that would be suitable for a larger RCT, based on the difference in changes in VAS score between the groups, with consideration of a 5% significant level, a two-tailed test, 80% power, and a *t*-test for comparison between groups. The mean difference(standard deviation) in the VAS score for back pain between the EA plus UC group and the UC alone group was 14.02 (22.12) mm at the primary endpoint, 8 weeks after treatment start, based on ITT analysis. On this basis, the sample size calculated by G*Power would be 40 participants per group. Considering a 25% dropout rate, a total of 108 participants (54 per group) would need to be recruited for the future trial.

DISCUSSION

Many people suffer from LBP after back surgery and experience the side effects of opioids used to relieve their pain. Previous research has shown that patients treated with acupuncture or related techniques have less pain and use less opioid analgesia.[32] Therefore EA, is a part of acupuncture treatment from the viewpoint of Korean medicine doctors, could be a good alternative as a non-pharmacological treatment to avoid the side effects of opioids.

Electroacupuncture is known to alleviate sensory and affective components of pain through specific neuroscientific mechanisms and may be used to decrease pain medication dosages.[33]Also EA is often used for management of postoperative pain.[34-37]Therefore, we believe that large-scale study is necessary to confirm the effectiveness of EA combined with UC, western conventional treatment, as the treatment of postoperative pain reflecting clinical reality.So we undertook this pilot RCT to estimate sample size of a full-scale randomised trial. Although the number of samples used in the analysis was insufficient for the number of roughly estimated samples in advance, we focused on analysing the approximate validity and calculating the sample size needed for a future trial.

From the results of this pilot study, we can have the basis for carrying out the full scale RCT. Although there was no statistically significant difference between the two groups in VAS, the reason for our insistence is the significant (p=0.0081) between-group difference in changes in ODI, which assesses back pain-related disability and in this study favoured EA plus UC therapy in terms of functional improvement in the lumbar spine. Given the clinical reality that it is difficult to expect improvement of function without relief of pain, our basis seems reasonable. The mean difference of VAS in EA plus UC group (23.11) is over the minimum clinically important difference (MCID) values (22.50 in low back pain) found in the other study,[38]and the effect size by the mean difference (14.02) and standard deviation (22.12) of the two groups means medium-sized effect. Considering a small number of samples in this pilot study, following large-scaled trial can expect a mean difference much over MCID and a larger effect size. These preliminary findings, although which had several limitation as mentioned above, confirm that we need to proceed in the future to a pragmatic RCT comparing the effectiveness of EA with UC with that of UC alone in the treatment of non-acute pain after back surgery.

There are several considerations to be taken into account before proceeding to a larger RCT. First, for cultural reasons, most participants in such a study would already have had experience with acupuncture in Korea, which would make a factor limiting the efficacy of treatment using acupuncture and the reason why many clinical trials using acupuncture, or related techniques such as EA, are often considered to have a high risk of bias.[39, 40] Also our three main outcome measures were all patients reported. This can serve as a limitation from the outcomes used, although using assessor blinding as possible as we could. Therefore, treatment, assessment and statistical analysis will have to be performed independently in a follow-up trial to prevent detection bias.

Further, there were many dropouts in this pilot trial, and it would be necessary to find an appropriate method of overcoming this problem. Especially in order to overcome the possible problems related to withdrawal of consent before the treatment progress, a method of adjusting the timing of randomisation or initiation of treatment may be considered in the following trial. In addition to LOCF rule, it is also necessary to consider an appropriate method for handling missing data such as multiple imputation. Also inclusion of a patient satisfaction survey in a future trial may help to shed light on this high dropout rate.

As a result of considering the clinical reality, western medical treatment such as drug treatment excluding surgery or injection therapy was allowed during the treatment period. In many professional conferences, it was difficult to completely rule out medication when considering the realistic aspects of pain management. As also this pilot trial was pragmatic comparative effectiveness RCT, therefore, we reflected real world condition in clinical current status. Therefore we permitted drug therapy in UC for reflecting current use of medication. In addition, the subgroup analysis based on the type of diagnosis, type of surgery, and duration of pain, which could not be confirmed due to the limitation of data collection,

should be conducted in a following trial through a structured questionnaire.

A future trial that addresses the above-mentioned concerns and includes the estimated sample size will allow better clinical assessment of the benefits of EA in combination with UC in the treatment of patients with non-acute pain after back surgery. In addition, the qualitative research and the economic evaluation will be conducted using a supplemented with results of pilot study in a future trial. The results of a follow-up trial can be expected to establish a new clinical basis for acupuncture combined with electrical stimulation in these patients.

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Competing interests

The authors declare that they have no competing interests.

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Author contributions

All authors conceived and designed the trial by discussion. IH wrote the manuscript. MSH, EHH, JHC, and IHH helped to conceive and design the trial. BCS as the principal investigator conceived the trial and revised the manuscript. IH and MSH recruited the patients and conducted the trial.NKK acted as an economic evaluation expert and clinical trial expert.DWS was involved as a neurosurgical expert. KMS and JHL supervised the trial. All authors read and approved the final manuscript.

Data sharing statement

Data may be requested from the corresponding author and made available to researchers who meet the criteria for access to confidential patient data according to the Institutional Review Board of Pusan National University Korean Medicine Hospital.

REFERENCES

1 Hoy D, March L, Brooks P, et al. Measuring the global burden of low back pain. *Best Pract Res ClinRheumatol*2010;24:155–65.

2Sarrazin JL. Imaging of postoperative lumbar spine. *J Radiol* 2003;84(2 Pt 2):241–52.

3Herrera Herrera I, Moreno de la Presa R, Gonzalez Gutierrez R, et al. Evaluation of the postoperative lumbar spine. *Radiologia* 2013;55:12–23.

4Aghion D, Chopra P, Oyelese AA. Failed back syndrome. *Med Health R I* 2012;95:391–3.

5SkolaskyRL, Wegener ST, Maggard AM, et al. The impact of reduction of pain after lumbar spine surgery: the relationship between changes in pain and physical function and disability. *Spine* 2014;39:1426–32.

6 Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain* 2016;17:131–57.

7 Hutchison RW, Chon EH, Tucker Jr. WF, et al. A comparison of a fentanyl, morphine, and hydromorphone patient-controlled intravenous delivery for acute postoperative analgesia: a multicenter study of opioid-induced adverse reactions. *Hosp Pharm* 2006;41:659–63.

8 Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. *Pain Physician* 2008;11(2 Suppl):S105–20.

9 White A, Hayhoe S, Hart A, et al. Survey of adverse events following acupuncture (SAFA): a prospective study of 32,000 consultations. *Acupunct Med* 2001;19:84–92.

10Wheway J, Agbabiaka TB, Ernst E. Patient safety incidents from acupuncture treatments: a

review of reports to the National Patient Safety Agency. *Int J Risk Saf Med*2012;24:163–9.

11 Lin CW, Haas M, Maher CG, et al. Cost-effectiveness of guideline-endorsed treatments for low back pain: a systematic review. *Eur Spine J*2011;20:1024–38.

12 Lee JH, Choi TY, Lee MS, et al. Acupuncture for acute low back pain: a systematic review. *Clin J Pain* 2013;29:172–85.

13 Shin JS, Ha IH, Lee J, et al. Effects of motion style acupuncture treatment in acute low back pain patients with severe disability: a multicenter, randomized, controlled, comparative effectiveness trial. *Pain* 2013;154:1030–7.

14Casimiro L, Barnsley L, Brosseau L, et al. Acupuncture and electroacupuncture for the treatment of rheumatoid arthritis. *Cochrane Database Syst Rev*2005;4:CD003788.

15 Zhao XB, Xing QZ, Han XC. [Observation on electroacupuncture at neimadian (extra) and neiguan (PC 6) for analgesia after thoracic surgery]. *Zhongguo Zhen Jiu*2013;33:829–32. Article in Chinese.

16 Chia KL. Electroacupuncture treatment of acute low back pain: unlikely to be a placebo response. *Acupunct Med* 2014;32:354–5.

17 Cho YH, Kim CK, HeoKH, et al. Acupuncture for acute postoperative pain after back surgery: a systematic review and meta-analysis of randomized controlled trials.*Pain Pract*2015;15:279–91.

18 Huang HT, ZhengSH, Feng J, et al. Thin's abdominal acupuncture for treatment of failed back surgery syndrome in 20 cases of clinical observation. *Guid J Trad Chin Med Pharm* 2012;18:63–5.

19ZhengSH, Wu YT, Liao JR, et al. [Abdominal acupuncture treatment of failed back surgery syndrome clinical observation]. *J EmergTrad Chin Med* 2010;19:1497–8. Article in Chinese.

20 National Guideline Clearinghouse. Low Back Disorders. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2011. Available from: http://www.guideline.gov/content.aspx?id=38438.

21 MacPherson H, Altman DG, Hammerschlag R, et al. Revised STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): Extending the CONSORT statement. *J Evid Based Med* 2010;3:140–55.

22Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Int J Surg* 2012;10:28–55.

23 Hwang MS, HeoKH, ChoHW, et al. 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. *BMJ Open*2015;5:e007031.

24 Jung YP, Jung HK, Chiang SY, et al. The clinical study of electroacupuncture treatment at Hua-Tuo-Jia-Ji-Xue on spondylolisthesis. *The Journal of Korean Acupuncture &Moxibustion Society* 2008;25:221–32.

25Revill SI, Robinson JO, Rosen M, et al. The reliability of a linear analogue for evaluating pain. *Anaesthesia* 1976;31:1191–8.

26Carlsson AM. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. *Pain* 1983;16:87–101.

27 Fairbank JC, PynsentPB. The Oswestry Disability Index. *Spine* 2000;25:2940–52.

28 Jeon CH, Kim DJ, Kim SK, et al. Validation in the cross-cultural adaptation of the Korean version of the Oswestry Disability Index. *J Korean Med Sci* 2006;21:1092–7.

29 Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001;33:337–43.

30 Kang EJ, Shin SH, Park HJ, et al. A validation of health status using EQ-5D. *The Korean*

Journal of Health Economics and Policy 2006;12:19–43.

31Higgins J, Green S, Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions. Chichester, UK; Wiley-Blackwell; 2008.

32 Wu MS, Chen KH, Chen IF, et al. The efficacy of acupuncture in post-operative pain management: a systematic review and meta-analysis. *PLoS One*2016;11:e0150367.

33Zhang R, Lao L, Ren K, et al.Mechanisms of acupuncture-electroacupuncture on persistent pain.*Anesthesiology* 2014;120:482-503.

34Chi H, Zhou WX, Wu YY, et al. [Electroacupuncture intervention combined with general anesthesia for 80 cases of heart valve replacement surgery under cardiopulmonary bypass]. *Zhen Ci Yan Jiu* 2014;39:1–6. Article in Chinese.

35Wu J, Zhao Y, Yang CM, et al. [Effects of electroacupuncture preemptive intervention on postoperative pain of mixed hemorrhoids]. *Zhongguo Zhen Jiu*2014;34:279–83. Article in Chinese.

36Zhang H, Wang L, Zhang M, et al. [Effects of electroacupuncture on postoperative functional recovery in patients with gynaecological laparoscopic surgery]. *Zhongguo Zhen Jiu*2014;34:273–8. Article in Chinese.

37Zhang Z, Wang C, Li Q, et al. Electroacupuncture at ST36 accelerates the recovery of gastrointestinal motility after colorectal surgery: a randomised controlled trial. *Acupunct Med* 2014;32:223–6.

38ParkKB, ShinJS, LeeJ,etal.MinimumClinicallyImportantDifferenceandSubstantialClinical BenefitinPain,Functional,andQualityofLifeScalesinFailedBackSurgerySyndromePatients.*Spine*2017;42:E474-81

39Kim SI, Lee KB, Lee HS, et al. Acupuncture experience in patients with chronic low back pain(2): a qualitative study - focused on participants in randomized controlled trial. *Korean J Acupunct* 2012;29:581–97.

40Lee H, Bang H, Kim Y, et al. Non-penetrating sham needle, is it an adequate sham controlin acupuncture research?*Complement Ther Med*2011;19Suppl1:S41–8.

Figure 1. CONSORT trial flow diagram. EA, electroacupuncture; UC, usual care.

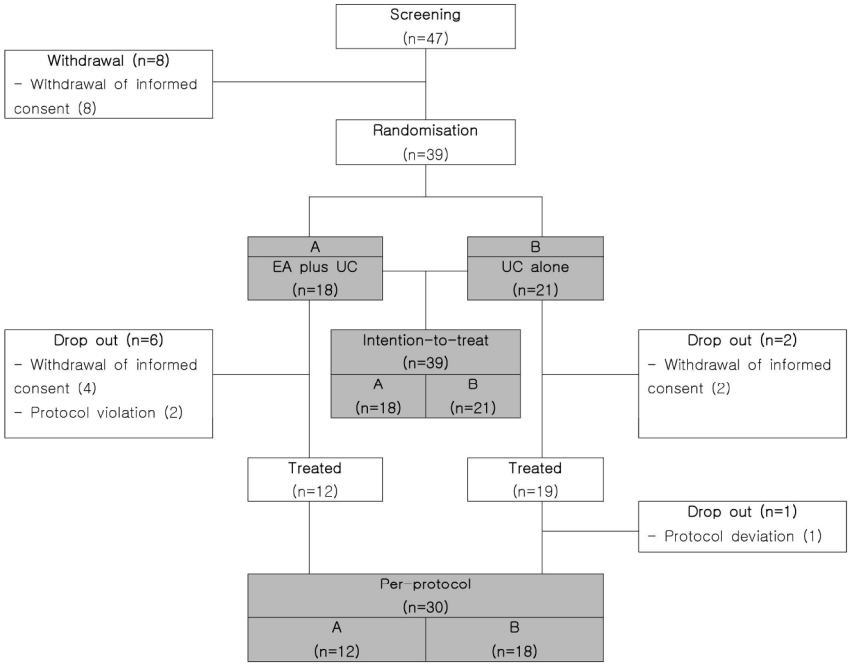

Figure 1. CONSORT trial flow diagram. EA, electroacupuncture; UC, usual care.

209x189mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	3~4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	6
	2b	Specific objectives or research questions for pilot trial	6~7
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	7
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	-
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	7
	4c	How participants were identified and consented	8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8~10
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	10~11
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	-
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	-
Sample size	7a	Rationale for numbers in the pilot trial	13
	7b	When applicable, explanation of any interim analyses and stopping guidelines	-
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	11
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	11
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	11

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	11
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	12
	11b	If relevant, description of the similarity of interventions	-
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	12~13
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	13~14
	13b	For each group, losses and exclusions after randomisation, together with reasons	13~14
Recruitment	14a	Dates defining the periods of recruitment and follow-up	7
	14b	Why the pilot trial ended or was stopped	-
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	14~15
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	13~14
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	14~16
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	-
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	16
	19a	If relevant, other important unintended consequences	-
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	18~19
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	17
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	16~17
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	17~19
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	7
Protocol	24	Where the pilot trial protocol can be accessed, if available	7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	9
	26	Ethical approval or approval by research review committee, confirmed with reference number	7

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*We strongly recommend reading this statement in conjunction with the CONSORT 2010, extension to randomised pilot and feasibility trials, Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

BMJ Open

Electroacupuncture as a complement to usual care for patients with non-acute low back pain after back surgery: A pilot randomised controlled trial

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Electroacupuncture as a complement to usual care for patients with non-acute low back pain after back surgery: A pilot randomised controlled trial

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ABSTRACT

Objectives

The aim of this pilot study was to estimate the sample size for a large pragmatic study of the comparative effectiveness of electroacupuncture (EA) for low back pain (LBP) after back surgery.

Design

A randomised, active-controlled, assessor-blinded trial.

Participants

Patients with recurrent or persistent LBP, defined as a visual analogue scale (VAS) score of≥50 mm, with or without leg pain after back surgery.

Interventions

Patients were randomised to an EA plus usual care (UC) group or to a UC alone groupata1:1 ratio. Patients assigned to each group received UC, including drug therapy, physical therapy and back pain education, twice a week for 4weeks; those assigned to the EA plus UC group additionally received EA.

Outcome measures

The primary outcome was severity of LBP as measured by VAS. Secondary outcomes included back pain-related disability, assessed using the Oswestry Disability Index (ODI), and quality of life, assessed using the EuroQolfive dimensions (EQ-5D) questionnaire. Statistical analysis was performed using paired and independent *t*-tests. A p-value of <0.05 was considered statistically significant.

Results

Thirty-nine patients were allocated to receive EA plus UC (n=18) or UC alone (n=21). There was no statistically significant difference in VAS or EQ-5D score between the two groups, but there was a significant decrease in ODI scores (p=0.0081). Using G*Power, it was calculated that 40 participants per group would be needed for a future trial according to VAS scores. Considering for a 25% dropout rate, 108 participants (54 per group) would be needed.

Conclusions

A future trial addressing the risk of bias and including the estimated sample size would allow for better clinical assessment of the benefits of EA plus UC in treatment of patients with non-acute pain after back surgery.

Trial registration

ClinicalTrials.gov (Identifier: NCT01966250, 11 Oct, 2013)

Keywords: electroacupuncture, low back pain, back surgery, postoperative pain, integrative medicine, pilot trial

Strengths and limitations of this study

1. This trial was designed as a feasible, comparative effectiveness trial which reflects common clinical situations.

2. Individualised acupuncture points according to patients' symptoms during the delivery of acupuncture treatment reflect real-world clinical practice of acupuncture.

3. We expect that this pilot study will provide the clinical basis and information that is required to assess the feasibility of a future large-scale trial.

4. The size of the study sample of the current study limits the power of the observations.

INTRODUCTION

Low back pain (LBP) afflicts approximately10% of people worldwide and is a source of considerable social and economic burden.[1] Although there are a number of surgical options available to treat LBP,[2] many people develop complications after lumbar spine surgery and some report that their symptoms are worse after surgery.[3] The most common complication is LBP, which occurs in about 40% of patients after back surgery.[4] Therefore, management of postoperative pain is a very important component ofpatient care,[5] and a wide range of treatments, including physical and/or cognitive-behavioural modalities, systemic or local pharmacological therapies, and neuraxial treatments are used.[6] Opioids, in particular morphine, hydromorphine, and meperidine, are commonly used in the management of postoperative pain,[7] but have significant side effects, including sedation, nausea, vomiting, and itching.[8] Therefore, a safe and effective method for management of pain after back surgery is required.

Several studies have shown that acupuncture is a safer[9,10] and cost-effective[11] treatment compared to usual care (UC), which comprises drug treatment and physical therapy,[12,13] and that electroacupuncture (EA) is one of the most common strategies used for pain management.[14-16] Therefore, EA could be a good method for treating pain after back surgery. There has been a systematic review of the evidence for acupuncture as a non-pharmacological strategy in treatment of acute postoperative pain after back surgery.[17] However, very few clinical trials[18,19] have assessed the effectiveness of EA for non-acute pain after back surgery, and the quality of the relevant research is too poor to reach any valid conclusions.

We have conducted a pilot study to compare the effectiveness of EA in combination with UC

with that of UC alone in controlling non-acute pain and improving function at ≥3 weeks[20] after back surgery. The primary purpose of this study was to estimate the appropriate sample size needed for a future confirmative, pragmatic, comparative randomised controlled trial (RCT) to determine the effectiveness of EA in combination with UC when compared with UC alone in relieving non-acute pain and dysfunction after back surgery. This research adhered to STRICTA[21] and CONSORT[22] guidelines.

METHODS

Study design

This randomised, active-controlled, assessor-blinded, parallel-group pilot trial was conducted at Pusan National University Korean Medicine Hospital (PNUKH)in Yangsan, Korea between 26 September, 2013 and 30 June,2015. Patients were recruited for the trial between 29 October, 2013 and 18 September, 2014.Thedetails have been published in the study protocol.[23] The protocol was approved by the institutional review board at PNUKH in September 2013 (approval number 2013012) and is registered at ClinicalTrials.gov (Identifier: NCT01966250, 11 Oct, 2013). In addition to this trial on the effectiveness of EA for LBP after surgery, qualitative research and economic evaluations as conducted by other researchers were performed concurrently.

Participants

In accordance to the published protocol, the study investigators screened patients with LBP after back surgery for eligibility. Patients were eligible if they were aged 19–70 years and had LBP that had recurred or persisted for at least 3 weeks (non-acute) after back surgery, with or without leg pain, and required medical treatment. LBP was defined as a visual analogue scale (VAS) score of ≥50 mm. Patients found to be eligible and willing to participate voluntarily in this study were guided through the consent process and signed informed consent forms. The exclusion criteria were as follows: serious disease that could cause LBP (e.g., cancer, vertebral fracture, spinal infection, inflammatory spondylitis, cauda equina compression); chronic disease that could influence the effects or results of treatment (e.g., severe cardiovascular disease, diabetic neuropathy, dementia, or epilepsy); progressive neurological deficit or severe neurological symptoms; conditions inappropriate or unsafe for EA (e.g., due to haemorrhagic disease, clotting disorder, history of having received anticoagulant therapy within the preceding 3weeks, severe diabetes with risk of infection, or severe cardiovascular disease); pain not caused by spinal or soft tissue disease, such as ankylosing spondylitis, fibromyalgia, rheumatoid arthritis, or gout; pregnancy or planning to become pregnant; psychiatric disease; participation in another clinical trial; inability to provide written informed consent; and ineligibility for inclusion in the study in the opinion of the investigators.

Sample size

We calculated the sample size of this pilot study, which was estimated according to a previously published protocol,[23] using the mean difference (20) and standard deviation (19) derived from other similar studies. The number of subjects required for each group was 16. Considering a dropout rate of 20% and a 1:1 allocation ratio, the sample size was 40 in total

(20 per arm).

Interventions

Patients randomised to both treatment groups received UC for 4 weeks. UC included drug therapy, physiotherapy, and an educational program on management of LBP, and excluded such Korean medicine treatments as acupuncture, moxibustion, and cupping.[20] Conventional drug treatment or therapies (e.g., pain medication, injections; excluding surgical procedures) for LBP after back surgery were allowed and monitored. Physiotherapy and an educational program on back care were undertaken twice a week for 4 weeks. Interferential current therapy (OG Giken Co., Okayama, Japan) was administered for 15 minutes with application of a hot (or ice) pack for 10 minutes. The structured education program explaining the physiology, pathology, and epidemiology of pain after back surgery was delivered in brochure format. Korean medical doctors also demonstrated postures and exercises suitable for management of LBP in a 15-min face-to-face education session.

Patients randomised to the EA plus UC group received EA in addition to UC. In this group, the acupuncture point prescriptions used were fixed acupuncture points plus points personalised to each patient and at the discretion of the practitioner. Differentiating the acupuncture point is an important part of traditional Korean medical theory and for reflecting actual clinical situation, and was used to select acupuncture points according to each patient's symptoms. Detailed information on the method of EA administration is summarised in the published protocol[23] and is based on the revised STRICTA statement.[21] EA treatment procedures were designed to reflect the feasibility afforded in the actual clinical setting by consensus of 5experts on acupuncture and spinal disorders. EA was performed by licensed

Korean medical doctors using disposable stainless steel needles 0.25 mm in diameter and 0.40 mm in length (Dongbang Acupuncture Inc., Seongnam, Korea). Acupuncture points included Jia-ji (Ex-B2, L3-L5; bilaterally) as fixed points, and other reasonable points could be chosen as accessory points by the practitioner. Between 6 and 15 access points were used by the physicians according to the clinical features of each individual patient. Electric stimulation was applied using an ES-160 electronic stimulator (ITO Co. Ltd, Tokyo, Japan) twice a week for 4 weeks. Stimulation was applied with a biphasic waveform current, which is a compressional wave that combines an interrupted wave and a continuous wave, in triangular form at a frequency of 50 Hz,[24] and was delivered via alligator clips connected to acupuncture needles inserted at Jia-ji (Ex-B2, L3/L5; bilaterally). Each EA session lasted 15 minutes. Patients in both groups received 8 treatment sessions over the course of 4 weeks.

Outcome measures

At the initial screening visit, a clinical research coordinator asked all patients to complete a questionnaire regarding their sociodemographic characteristics, including age, sex, height, and weight, and recorded their vital signs. Before the start of treatment at each visit, each patient was assessed to record the outcomes of the previous treatment session. All patients were followed up at 4 and 8 weeks after the 4-week treatment period.

The primary outcome of back pain intensity was assessed using a 100 mm pain visual analogue scale (VAS), on which 0 indicates absence of pain and 100 indicates unbearable pain.[25,26] Each patient was asked to rate his or her degree of back pain during the previous 3days on the VAS. Back pain was measured at baseline (assessment 1 at week 0) prior to each of the 8treatment sessions (assessments 2–9atweeks 1-4), and at the2 follow-up visits

(assessments 10 and 11 at weeks 8 and 12). The primary endpoint was assessment 10(week 8), which marked the end of the 8 active treatment sessions. A responder was defined as a study participant with ≥50% pain relief using the 100mm VAS for pain intensity at assessments 9, 10 and 11, and a non-responder as having pain relief of <50%, respectively (weeks 4, 8 and 12).

The secondary outcome measures were back pain-related disability, assessed using the Oswestry Disability Index (ODI), and quality of life, assessed by the EuroQol five dimensions (EQ-5D) questionnaire.[27] The ODI contains 10 questions about daily life and includes measures of pain intensity, personal care, lifting, walking, sitting, standing, sleeping, social life, and travelling. Each question is rated on a scale of 0 to 5, with a higher score indicating more severe pain-related disability. The validated Korean version of the ODI[28] was administered before treatment at assessments 2, 5, 9,10, and 11(weeks 1, 2, 4, 8, and 12).The validated Korean version of the EQ-5D[29, 30] includes generic questions about personal health-related quality of life and consists of five dimensions pertaining to mobility, self-care, usual daily activities, pain and discomfort, and anxiety/depression. Each dimension is scored on a scale of 1 to 3, with a lower score indicating a better state of health. The EQ-5D was administered before treatment assessments 2, 5, 9, 10, and 11(weeks 1, 2, 4, 8, and 12).

Randomisation

Before the first treatment session, a statistician assigned patients to one of 2 groups by a central telephone randomisation procedure according to a computer-generated randomisation sequence using SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Randomisation

was performed by a trial coordinator who had no contact with the patients. The clinical research coordinator obtained the codes for the trial (A or B) from the central telephone service and informed the EA practitioner. The practitioner used these codes to assign patients to one of the two groups and to deliver the appropriate treatment.

The National Clinical Research Center for Korean Medicine at PNUKH stored the random numbers. The allocation sequence was concealed from the researchers responsible for enrolling, treating, and assessing patients by dividing their roles and contact with the study participants.

Blinding

It was impossible to blind either the patients or treating clinicians in this trial as the study design was pragmatic and comparative and not placebo-controlled. However, the risk of detection bias was minimal because all treatments and assessments were conducted independently and the treating clinicians were not involved in assessment of outcomes.[31] The assessors, who received standardized training, always performed the outcome assessments in a separate room and were blinded to treatment assignment. However, there was provision in the study protocol for unblinding in exceptional circumstances where knowledge of the actual treatment would be essential for further management of the patient (e.g., serious adverse event).

Statistical analysis

The statistical analysis was performed on both an intention-to-treat (ITT) and a per-protocol

basis. For the ITT analysis, we applied the last-observation-carried-forward (LOCF) rule for missing data. The statistical significance of differences in the data for each group was analysed using the paired *t*-test, and the statistical significance of differences between groups was analysed using the independent *t*-test. Analysis of covariance was used to analyse and adjust the baseline characteristics if there were statistically significant differences and possibility of covariance of baseline characteristics. The chi-square test or Fisher's exact test was used to analyse categorical data, such as responses/responders, and were recorded and described as frequencies (%). We did not perform an interim analysis as we expected EA and UC to be associated with a minimal risk of harm. All statistical analyses were performed by a statistician using SPSS for Windows version 22.0 software. The significance level was set at 5%.

The sample size required for a future trial will be estimated using the free G*Power version 3.1.7 program (Franz Faul, Christian-Albrechts-Universitätzu Kiel, Kiel, Germany), which calculates the sample size using mean difference and standard deviation.

Patient and Public Involvement

The aim of this pilot study was to estimate the sample size for a large pragmatic study of the comparative effectiveness of EA with usual care for LBP after back surgery. Therefore, patients and the public sector were not directly involved in the design of, recruitment to, and conduct of this pilot study. We developed the research question, study design, outcome measures, patient recruitment and trial conduct methodology in light of the general Korean medical environment created as a result of its dual medical system of conventional and Korean medicine. As the choice of intervention reflects this medical environment, we did not

view the intervention as burdensome and the burden of the intervention was not assessed by the patients themselves. The results of the qualitative research and economic evaluation which was conducted concurrently with this pilot study will be considered along with patient and public involvement in study design in the development process of a future trial. The results of this confirmative, pragmatic, comparative RCT will be disseminated in peer-reviewed journals and at academic conferences.

RESULTS

Participants

Forty-seven eligible patients agreed to participate in the trial after screening. Eight participants withdrew their informed consent before the start of treatment, leaving 39 patients who were randomly allocated to the two groups (18 in the EA plus UC group, and 21 in the UC alone group). Eight of 39 patients dropped out during the treatment period due to withdrawal of informed consent or protocol violation (6 in the EA plus UC group, and 2 in the UC alone group). One more patient in UC alone group dropped out after treatment because of protocol deviation, leaving 30 patients (12 in the EA plus UC group, and 18 in the UC alone group) for the per-protocol analysis (Fig. 1).

The mean (standard deviation) age of the 39 treated patients was 57.6 (9.52) years and 19 participants were men (48.7%). The detailed baseline demographic characteristics are provided in Table 1. The mean scores on the VAS for non-acute back pain after surgery, and scores on the ODI and EQ-5D at the baseline evaluation are presented in Table 2.

Table 1. Demographic features of the participants at baseline

Variables	Total	Group	
		EA+UC (n=18)	UC alone (n=21)
Gender, n(%)			
Male	19 (48.7)	9 (50.0)	10 (47.6)
Female	20 (51.3)	9 (50.0)	11 (52.4)
Age (yrs)			
Mean±SD	57.6±9.5	58.9±9.8	56.5±9.4
Range	37-70	40-70	37-70
Height (cm)			
Mean±SD	164.1±9.8	163.0±9.0	165.1±10.6
Range	145-187	145-179	150-187
Weight (kg)			
Mean±SD	66.9±9.8	67.1±9.5	67.1±9.5
Range	53-88	53-88	55-83

EA; electroacupuncture, UC; usual care, SD; standard deviation

Table 2. Difference in primary and secondary results in theelectroacupuncture (EA) in combination with usual care (UC) group and UC alone group between each evaluation and baseline

Variables	Group		p-value*
	EA+UC (n=18) mean±SD mean [95% CI]	UC alone(n=21) mean±SD mean [95% CI]	
VAS [mm]			
Baseline	64.61±14.92	67.33±10.33	
After 4 weeks	51.78±20.62	60.24±19.25	
Difference	-12.83 [-25.27, -0.39]	-7.10 [-13.22, -0.97]	.3919
After 8 weeks	41.50±24.75	58.24±20.83	
Difference	-23.11 [-36.60, -9.62]	-9.10 [-16.71, -1.48]	.0675
After 12 weeks	41.78±24.62	53.00±21.39	
Difference	-22.83 [-35.86, -9.81]	-14.33 [-23.29, -5.38]	.2553
Responder [%(n)]			
After 4 weeks	22.2 (4)	4.8 (1)	.1618**
After 8 weeks	33.3 (6)	9.5 (2)	.1123**
After 12 weeks	38.9 (7)	19.1 (4)	.1698†
ODI [%point]			
Baseline	44.70±15.42	38.23±14.5	
After 4 weeks	33.78±17.45	34.19±17.09	
Difference	-10.93 [-15.92, -5.94]	-4.04 [-7.59, -0.5]	.0210
After 8 weeks	31.95±18.57	32.47±16.04	
Difference	-12.75 [-17.23, -8.28]	-5.77 [-8.75, -2.79]	.0081
After 12 weeks	29.67±18.46	28.60±16.69	
Difference	-15.04 [-20.16, -9.91]	-9.63 [-14.39, -4.87]	.1137
EQ-5D [point]			
Baseline	0.65±0.13	0.66±0.15	
After 4 weeks	0.71±0.11	0.72±0.14	
Difference	0.06 [0.01-0.12]	0.05 [0.02-0.09]	.7698
After 8 weeks	0.74±0.15	0.73±0.13	
Difference	0.09 [0.02, 0.16]	0.06 [0.02, 0.11]	.5151
After 12 weeks	0.73±0.17	0.74±0.13	
Difference	0.08 [0, 0.17]	0.08 [0.04, 0.12]	.9441

EA; electroacupuncture, UC; usual care, CI; confidence interval, VAS; visual analogue scale, ODI; Oswestry

disability index, EQ-5D; EuroQol five dimensions questionnaire
*t-test for comparison of difference between groups
** Fisher's exact test for comparison of difference between groups
†Chi-square test for comparison of difference between groups

Effects of EA

In both treatment groups, there were statistically significant improvements in VAS scores for back pain, and ODI and EQ-5D scores at 8 weeks compared to baseline (Table 2). However, there were no statistically significant differences in the VAS score for back pain (p=0.0675) and in the EQ-5D (p=0.5151) score between the 2 treatment groups at 8 weeks (Table 2). There was a statistically significant decrease in the ODI after 8 weeks in the EA plus UC group when compared with the UC alone group (p=0.0081; Table 2). In the ITT analysis (n=39), the proportion of responders, defined as participants with ≥50% pain relief on the 100mm VAS for pain intensity, was 33.3% (n=6) in the EA plus UC group (n=18) and9. 5% (n=2) in the UC alone group (n=21); the difference between the groups was not statistically significant (p=0.1123; Table 2). No adverse events were reported in this study.

Estimating sample size of a future trial

On completion of this pilot study, we calculated an appropriately powered sample size that would be suitable for a larger RCT, based on the difference in change in VAS score between groups, with consideration of a 5% significance level, two-tailed, 80% powered test, and *t*-test for comparison between groups. The mean difference (standard deviation) in the VAS score for back pain between the EA plus UC group and the UC alone group was 14.02 (22.12) mm at the primary endpoint, which was 8 weeks post-treatment initiation, based on ITT analysis. On this basis, the sample size calculated by the following formula, the number of

subjects required for each group was 40.

Sample size n = $$\frac{2(Z_{\alpha/2} + Z_{1-\beta})^2 \delta^2}{(\mu t - \mu c)^2}$$

n=the number of participants required in each group
$Z_{\alpha/2}=Z_{0.05/2}=1.96$
$Z_{1-\beta}=Z_{0.8}=0.84$
δ (standard deviation) = 22.12
$\mu_t-\mu_c$(mean difference) = 14.02

Also using G*Power program on the same basis, the results would be 40 participants per group. Therefore, considering a 25% dropout rate, a total of 108 participants (54 per group) would need to be recruited for a future trial.

DISCUSSION

Many people suffer from LBP after back surgery and experience side effects from the opioids used to relieve their pain. Previous research has shown that patients treated with acupuncture or related techniques experience less pain and consequently use less opioids for pain control.[32] Therefore, it may be carefully conjectured that EA, a type of acupuncture treatment commonly used by Korean medicine doctors, maybe a good alternative as a non-pharmacological treatment without the risk of opioid-related side effects. Electroacupuncture is known to alleviate sensory symptoms and regulate components of pain through specific neuroscientific mechanisms and is thus used to decrease pain medication dosages.[33] Also, as EA is often used for management of postoperative pain,[34-37] we propose that a large-scale study is necessary to confirm the effectiveness of EA combined with UC, western conventional medicine treatment, as these treatments for postoperative pain reflect real-world circumstances and settings. We therefore undertook this pilot RCT to estimate the sample size

for a full-scale randomised trial. Although the number of samples included in the analysis was insufficient to confirm the effect of treatment as it was roughly estimated a priori, we focused on analysing the approximate validity and calculating the sample size needed for a future trial.

From the results of this pilot study, we determined the basis needed in carrying out a full scale RCT. Although there was no statistically significant difference between the two groups in VAS, between-group difference in changes in ODI, which assesses back pain-related disability, was significant (p=0.0081) and favoured EA plus UC therapy in terms of functional improvement in the lumbar spine. Given the clinical reality that it is difficult to expect functional improvement without relief of pain, our basis for a full scale RCT seems reasonable.

The change in VAS scores in the EA plus UC group (23.11) is over the minimum clinically important difference (MCID) values (22.50 in low back pain)as reported in a previous study,[38]and the effect size by the mean difference (14.02) and standard deviation (22.12) of the two groups indicates a medium-sized effect. Considering the small number of samples in this pilot study, the following large-scale trial is expected to show a greater change in VAS higher than MCID and larger effect size.

Also, as there were no previous trials comparable to this study regarding RCT design, we calculated the sample size of this pilot study using the mean difference (20) and standard deviation (19) derived from other similar studies. However, as those studies were dissimilar from our trial in terms of patients, methods of treatment and study design, they differed in mean difference (14.02) and standard deviation (22.12) of this pilot study. These differences may be attributed to the underpowered results of this pilot study, and act as a further reason that a large-scale follow-up study is needed.

These preliminary findings, albeit limited with several limitations as mentioned above, confirm the need to proceed with future pragmatic RCTs comparing the effectiveness of EA with UC with that of UC alone for treatment of non-acute pain after back surgery. However, there are several considerations to be taken into account before proceeding with larger RCTs. First, for cultural reasons, most participants in such studies would have had acupuncture experience in countries such as Korea, which would act as a limiting factor in efficacy of acupuncture-related treatment, and the reason why many clinical trials using acupuncture, or related techniques such as EA, are often considered to have high risk of bias.[39, 40] Also, the three main outcome measures were all patient-reported outcomes. This can serve as a limitation regarding subjective outcome measurement, although we used assessor blinding to offset this limitation as much as possible. Therefore, treatment, assessment and statistical analysis should be performed independently in future trials to prevent detection bias.

Further, there were many dropouts in this pilot trial, and it is necessary to find an appropriate method of overcoming this problem. Especially in order to overcome potential problems related to withdrawal of consent before the start of treatment, such methods as adjusting the timing of randomisation or initiation of treatment may be considered in following trials. In addition to the LOCF rule, it is also necessary to consider an appropriate method for handling missing data such as multiple imputation. Also, inclusion of a patient satisfaction survey in future trials may help shed light on this high dropout rate.

In an effort to reflect real-world situations, only western medical treatments such as drug treatment excluding surgery or injection therapy were allowed during the treatment period. In many professional conferences, it was difficult to completely rule out medication when considering the realistic aspects of pain management. Also, as this pilot trial was a pragmatic comparative effectiveness RCT, we tried to reflect real-world conditions in current clinical

status too. We therefore permitted drug therapy in UC to reflect current use of medication. In addition, subgroup analyses based on diagnosis, type of surgery, and duration of pain, which could not be confirmed in the present study due to limitations in data collection, should be conducted in future trials by means of structured questionnaires.

A future trial that addresses the above-mentioned concerns and covers the estimated sample size will be better equipped for clinical assessment of the benefits of EA in combination with UC in treatment of patients with non-acute pain after back surgery. In addition, qualitative research and economic evaluation will be conducted in future trials using evaluation tools supplemented through pilot study results. The results of a follow-up trial are expected to establish a robust clinical basis for the effects of acupuncture combined with electrical stimulation in this patient population.

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Competing interests

The authors declare that they have no competing interests.

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Author contributions

All authors conceived and designed the trial by discussion. IH wrote the manuscript. MSH, EHH, JHC, and IHH helped to conceive and design the trial. BCS as the principal investigator conceived the trial and revised the manuscript. IH and MSH recruited the patients and conducted the trial.NKK acted as an economic evaluation expert and clinical trial expert.DWS was involved as a neurosurgical expert. KMS and JHL supervised the trial. All authors read and approved the final manuscript.

Data sharing statement

Data may be requested from the corresponding author and made available to researchers who meet the criteria for access to confidential patient data according to the Institutional Review Board of Pusan National University Korean Medicine Hospital.

REFERENCES

1 Hoy D, March L, Brooks P, et al. Measuring the global burden of low back pain. *Best Pract Res ClinRheumatol*2010;24:155–65.

2 Sarrazin JL. Imaging of postoperative lumbar spine. *J Radiol* 2003;84(2 Pt 2):241–52.

3 Herrera Herrera I, Moreno de la Presa R, Gonzalez Gutierrez R, et al. Evaluation of the postoperative lumbar spine. *Radiologia* 2013;55:12–23.

4 Aghion D, Chopra P, Oyelese AA. Failed back syndrome. *Med Health R I* 2012;95:391–3.

5 SkolaskyRL, Wegener ST, Maggard AM, et al. The impact of reduction of pain after lumbar spine surgery: the relationship between changes in pain and physical function and disability. *Spine* 2014;39:1426–32.

6 Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain* 2016;17:131–57.

7 Hutchison RW, Chon EH, Tucker Jr. WF, et al. A comparison of a fentanyl, morphine, and hydromorphone patient-controlled intravenous delivery for acute postoperative analgesia: a multicenter study of opioid-induced adverse reactions. *Hosp Pharm* 2006;41:659–63.

8 Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. *Pain Physician* 2008;11(2 Suppl):S105–20.

9 White A, Hayhoe S, Hart A, et al. Survey of adverse events following acupuncture (SAFA): a prospective study of 32,000 consultations. *Acupunct Med* 2001;19:84–92.

10 Wheway J, Agbabiaka TB, Ernst E. Patient safety incidents from acupuncture treatments:

a review of reports to the National Patient Safety Agency. *Int J Risk Saf Med*2012;24:163–9.

11 Lin CW, Haas M, Maher CG, et al. Cost-effectiveness of guideline-endorsed treatments for low back pain: a systematic review. *Eur Spine J*2011;20:1024–38.

12 Lee JH, Choi TY, Lee MS, et al. Acupuncture for acute low back pain: a systematic review. *Clin J Pain* 2013;29:172–85.

13 Shin JS, Ha IH, Lee J, et al. Effects of motion style acupuncture treatment in acute low back pain patients with severe disability: a multicenter, randomized, controlled, comparative effectiveness trial. *Pain* 2013;154:1030–7.

14 Casimiro L, Barnsley L, Brosseau L, et al. Acupuncture and electroacupuncture for the treatment of rheumatoid arthritis. *Cochrane Database Syst Rev*2005;4:CD003788.

15 Zhao XB, Xing QZ, Han XC. [Observation on electroacupuncture at neimadian (extra) and neiguan (PC 6) for analgesia after thoracic surgery]. *Zhongguo Zhen Jiu*2013;33:829–32. Article in Chinese.

16 Chia KL. Electroacupuncture treatment of acute low back pain: unlikely to be a placebo response. *Acupunct Med* 2014;32:354–5.

17 Cho YH, Kim CK, HeoKH, et al. Acupuncture for acute postoperative pain after back surgery: a systematic review and meta-analysis of randomized controlled trials.*Pain Pract*2015;15:279–91.

18 Huang HT, ZhengSH, Feng J, et al. Thin's abdominal acupuncture for treatment of failed back surgery syndrome in 20 cases of clinical observation. *Guid J Trad Chin Med Pharm* 2012;18:63–5.

19 ZhengSH, Wu YT, Liao JR, et al. [Abdominal acupuncture treatment of failed back surgery syndrome clinical observation]. *J EmergTrad Chin Med* 2010;19:1497–8. Article in Chinese.

20 National Guideline Clearinghouse. Low Back Disorders. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2011. Available from: http://www.guideline.gov/content.aspx?id=38438.

21 MacPherson H, Altman DG, Hammerschlag R, et al. Revised STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): Extending the CONSORT statement. *J Evid Based Med* 2010;3:140–55.

22 Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Int J Surg* 2012;10:28–55.

23 Hwang MS, HeoKH, ChoHW, et al. 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. *BMJ Open*2015;5:e007031.

24 Jung YP, Jung HK, Chiang SY, et al. The clinical study of electroacupuncture treatment at Hua-Tuo-Jia-Ji-Xue on spondylolisthesis. *The Journal of Korean Acupuncture &Moxibustion Society* 2008;25:221–32.

25 Revill SI, Robinson JO, Rosen M, et al. The reliability of a linear analogue for evaluating pain. *Anaesthesia* 1976;31:1191–8.

26 Carlsson AM. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. *Pain* 1983;16:87–101.

27 Fairbank JC, PynsentPB. The Oswestry Disability Index. *Spine* 2000;25:2940–52.

28 Jeon CH, Kim DJ, Kim SK, et al. Validation in the cross-cultural adaptation of the Korean version of the Oswestry Disability Index. *J Korean Med Sci* 2006;21:1092–7.

29 Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001;33:337–43.

30 Kang EJ, Shin SH, Park HJ, et al. A validation of health status using EQ-5D. *The Korean*

Journal of Health Economics and Policy 2006;12:19–43.

31 Higgins J, Green S, Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions. Chichester, UK; Wiley-Blackwell; 2008.

32 Wu MS, Chen KH, Chen IF, et al. The efficacy of acupuncture in post-operative pain management: a systematic review and meta-analysis. *PLoS One*2016;11:e0150367.

33 Zhang R, Lao L, Ren K, et al.Mechanisms of acupuncture-electroacupuncture on persistent pain.*Anesthesiology* 2014;120:482-503.

34 Chi H, Zhou WX, Wu YY, et al. [Electroacupuncture intervention combined with general anesthesia for 80 cases of heart valve replacement surgery under cardiopulmonary bypass]. *Zhen Ci Yan Jiu* 2014;39:1–6. Article in Chinese.

35 Wu J, Zhao Y, Yang CM, et al. [Effects of electroacupuncturepreemptive intervention on postoperative pain of mixed hemorrhoids]. *Zhongguo Zhen Jiu*2014;34:279–83. Article in Chinese.

36 Zhang H, Wang L, Zhang M, et al. [Effects of electroacupuncture on postoperative functional recovery in patients with gynaecological laparoscopic surgery]. *Zhongguo Zhen Jiu*2014;34:273–8. Article in Chinese.

37 Zhang Z, Wang C, Li Q, et al. Electroacupuncture at ST36 accelerates the recovery of gastrointestinal motility after colorectal surgery: a randomised controlled trial. *Acupunct Med* 2014;32:223–6.

38 Park KB, Shin JS, Lee J, et al. Minimum Clinically Important Difference and Substantial Clinical Benefit in Pain, Functional, and Quality of Life Scales in Failed Back Surgery Syndrome Patients.*Spine*2017;42:E474-81

39 Kim SI, Lee KB, Lee HS, et al. Acupuncture experience in patients with chronic low back pain(2): a qualitative study - focused on participants in randomized controlled trial. *Korean J Acupunct* 2012;29:581–97.

40 Lee H, Bang H, Kim Y, et al. Non-penetrating sham needle, is it an adequate sham controlin acupuncture research?*Complement Ther Med*2011;19Suppl1:S41–8.

Figure 1. CONSORT trial flow diagram. EA, electroacupuncture; UC, usual care.

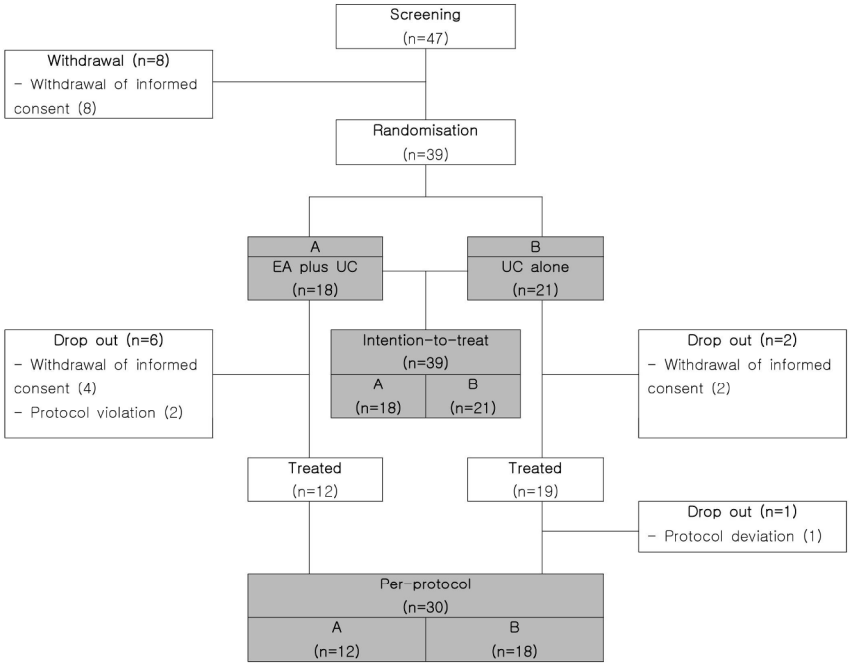

Figure 1. CONSORT trial flow diagram. EA, electroacupuncture; UC, usual care.

209x189mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	3~4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	6
	2b	Specific objectives or research questions for pilot trial	6~7
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	7
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	-
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	7
	4c	How participants were identified and consented	8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8~10
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	10~11
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	-
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	-
Sample size	7a	Rationale for numbers in the pilot trial	13
	7b	When applicable, explanation of any interim analyses and stopping guidelines	-
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	11
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	11
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	11

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	11
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	12
	11b	If relevant, description of the similarity of interventions	-
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	12~13
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	13~14
	13b	For each group, losses and exclusions after randomisation, together with reasons	13~14
Recruitment	14a	Dates defining the periods of recruitment and follow-up	7
	14b	Why the pilot trial ended or was stopped	-
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	14~15
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	13~14
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	14~16
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	-
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	16
	19a	If relevant, other important unintended consequences	-
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	18~19
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	17
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	16~17
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	17~19
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	7
Protocol	24	Where the pilot trial protocol can be accessed, if available	7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	9
	26	Ethical approval or approval by research review committee, confirmed with reference number	7

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*We strongly recommend reading this statement in conjunction with the CONSORT 2010, extension to randomised pilot and feasibility trials, Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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Electroacupuncture as a complement to usual care for patients with non-acute low back pain after back surgery: A pilot randomised controlled trial

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Electroacupuncture as a complement to usual care for patients with non-acute low back pain after back surgery: A pilot randomised controlled trial

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ABSTRACT

Objectives

The aim of this pilot study was to estimate the sample size for a large pragmatic study of the comparative effectiveness of electroacupuncture (EA) for low back pain (LBP) after back surgery.

Design

A randomised, active-controlled, assessor-blinded trial.

Participants

Patients with recurrent or persistent LBP, defined as a visual analogue scale (VAS) score of≥50 mm, with or without leg pain after back surgery.

Interventions

Patients were randomised to an EA plus usual care (UC) group or to a UC alone group at a 1:1 ratio. Patients assigned to each group received UC, including drug therapy, physical therapy and back pain education, twice a week for 4 weeks; those assigned to the EA plus UC group additionally received EA.

Outcome measures

The primary outcome was severity of LBP as measured by VAS. Secondary outcomes included back pain-related disability, assessed using the Oswestry Disability Index (ODI), and quality of life, assessed using the EuroQolfive dimensions (EQ-5D) questionnaire. Statistical analysis was performed using paired and independent *t*-tests. A p-value of <0.05 was considered statistically significant.

Results

Thirty-nine patients were allocated to receive EA plus UC (n=18) or UC alone (n=21). There was no statistically significant difference in VAS or EQ-5D score between the two groups, but there was a significant decrease in ODI scores (p=0.0081). Using G*Power, it was calculated that 40 participants per group would be needed for a future trial according to VAS scores. Considering for a 25% dropout rate, 108 participants (54 per group) would be needed.

Conclusions

A future trial addressing the risk of bias and including the estimated sample size would allow for better clinical assessment of the benefits of EA plus UC in treatment of patients with non-acute pain after back surgery.

Trial registration

ClinicalTrials.gov (Identifier: NCT01966250, 11 Oct, 2013)

Keywords: electroacupuncture, low back pain, back surgery, postoperative pain, integrative medicine, pilot trial

Strengths and limitations of this study

1. This trial was designed as a feasible, comparative effectiveness trial which reflects common clinical situations.

2. Individualised acupuncture points according to patients' symptoms during the delivery of acupuncture treatment reflect real-world clinical practice of acupuncture.

3. We expect that this pilot study will provide the clinical basis and information that is required to assess the feasibility of a future large-scale trial.

4. The size of the study sample of the current study limits the power of the observations.

INTRODUCTION

Low back pain (LBP) afflicts approximately 10% of people worldwide and is a source of considerable social and economic burden.[1] Although there are a number of surgical options available to treat LBP,[2] many people develop complications after lumbar spine surgery and some report that their symptoms are worse after surgery.[3] The most common complication is LBP, which occurs in about 40% of patients after back surgery.[4] Therefore, management of postoperative pain is a very important component of patient care,[5] and a wide range of treatments, including physical and/or cognitive-behavioural modalities, systemic or local pharmacological therapies, and neuraxial treatments are used.[6] Opioids, in particular morphine, hydromorphine, and meperidine, are commonly used in the management of postoperative pain,[7] but have significant side effects, including sedation, nausea, vomiting, and itching.[8] Therefore, a safe and effective method for management of pain after back surgery is required.

Several studies have shown that acupuncture is a safer[9,10] and cost-effective[11] treatment compared to usual care (UC), which comprises drug treatment and physical therapy,[12,13] and that electroacupuncture (EA) is one of the most common strategies used for pain management.[14-16] Therefore, EA could be a good method for treating pain after back surgery. There has been a systematic review of the evidence for acupuncture as a non-pharmacological strategy in treatment of acute postoperative pain after back surgery.[17] However, very few clinical trials[18,19] have assessed the effectiveness of EA for non-acute pain after back surgery, and the quality of the relevant research is too poor to reach any valid conclusions.

We have conducted a pilot study to compare the effectiveness of EA in combination with UC

with that of UC alone in controlling non-acute pain and improving function at ≥3 weeks[20] after back surgery. The primary purpose of this study was to estimate the appropriate sample size needed for a future confirmative, pragmatic, comparative randomised controlled trial (RCT) to determine the effectiveness of EA in combination with UC when compared with UC alone in relieving non-acute pain and dysfunction after back surgery. This research adhered to STRICTA[21] and CONSORT[22] guidelines.

METHODS

Study design

This randomised, active-controlled, assessor-blinded, parallel-group pilot trial was conducted at Pusan National University Korean Medicine Hospital (PNUKH)in Yangsan, Korea between 26 September, 2013 and 30 June, 2015. Patients were recruited for the trial between 29 October, 2013 and 18 September, 2014. The details have been published in the study protocol.[23] The protocol was approved by the institutional review board at PNUKH in September 2013 (approval number 2013012) and is registered at ClinicalTrials.gov (Identifier: NCT01966250, 11 Oct, 2013). In addition to this trial on the effectiveness of EA for LBP after surgery, qualitative research and economic evaluations as conducted by other researchers were performed concurrently.

Participants

In accordance to the published protocol, the study investigators screened patients with LBP after back surgery for eligibility. Patients were eligible if they were aged 19–70 years and had LBP that had recurred or persisted for at least 3 weeks (non-acute) after back surgery, with or without leg pain, and required medical treatment. LBP was defined as a visual analogue scale (VAS) score of ≥50 mm. Patients found to be eligible and willing to participate voluntarily in this study were guided through the consent process and signed informed consent forms. The exclusion criteria were as follows: serious disease that could cause LBP (e.g., cancer, vertebral fracture, spinal infection, inflammatory spondylitis, cauda equina compression); chronic disease that could influence the effects or results of treatment (e.g., severe cardiovascular disease, diabetic neuropathy, dementia, or epilepsy); progressive neurological deficit or severe neurological symptoms; conditions inappropriate or unsafe for EA (e.g., due to haemorrhagic disease, clotting disorder, history of having received anticoagulant therapy within the preceding 3weeks, severe diabetes with risk of infection, or severe cardiovascular disease); pain not caused by spinal or soft tissue disease, such as ankylosing spondylitis, fibromyalgia, rheumatoid arthritis, or gout; pregnancy or planning to become pregnant; psychiatric disease; participation in another clinical trial; inability to provide written informed consent; and ineligibility for inclusion in the study in the opinion of the investigators.

Sample size

We calculated the sample size of this pilot study, which was estimated according to a previously published protocol.[23] using the mean difference (20) and standard deviation (19) derived from other similar studies. The number of subjects required for each group was 16. Considering a dropout rate of 20% and a 1:1 allocation ratio, the sample size was 40 in total

(20 per arm).

Interventions

Patients randomised to both treatment groups received UC for 4 weeks. UC included drug therapy, physiotherapy, and an educational program on management of LBP, and excluded such Korean medicine treatments as acupuncture, moxibustion, and cupping.[20] Conventional drug treatment or therapies (e.g., pain medication, injections; excluding surgical procedures) for LBP after back surgery were allowed and monitored. Physiotherapy and an educational program on back care were undertaken twice a week for 4 weeks. Interferential current therapy (OG Giken Co., Okayama, Japan) was administered for 15 minutes with application of a hot (or ice) pack for 10 minutes. The structured education program explaining the physiology, pathology, and epidemiology of pain after back surgery was delivered in brochure format. Korean medical doctors also demonstrated postures and exercises suitable for management of LBP in a 15-min face-to-face education session.

Patients randomised to the EA plus UC group received EA in addition to UC. In this group, the acupuncture point prescriptions used were fixed acupuncture points plus points personalised to each patient and at the discretion of the practitioner. Differentiating the acupuncture point is an important part of traditional Korean medical theory and for reflecting actual clinical situation, and was used to select acupuncture points according to each patient's symptoms. Detailed information on the method of EA administration is summarised in the published protocol[23] and is based on the revised STRICTA statement.[21] EA treatment procedures were designed to reflect the feasibility afforded in the actual clinical setting by consensus of 5 experts on acupuncture and spinal disorders. EA was performed by licensed

Korean medical doctors using disposable stainless steel needles 0.25 mm in diameter and 0.40 mm in length (Dongbang Acupuncture Inc., Seongnam, Korea). Acupuncture points included Jia-ji (Ex-B2, L3-L5; bilaterally) as fixed points, and other reasonable points could be chosen as accessory points by the practitioner. Between 6 and 15 access points were used by the physicians according to the clinical features of each individual patient. Electric stimulation was applied using an ES-160 electronic stimulator (ITO Co. Ltd, Tokyo, Japan) twice a week for 4 weeks. Stimulation was applied with a biphasic waveform current, which is a compressional wave that combines an interrupted wave and a continuous wave, in triangular form at a frequency of 50 Hz,[24] and was delivered via alligator clips connected to acupuncture needles inserted at Jia-ji (Ex-B2, L3/L5; bilaterally). Each EA session lasted 15 minutes. Patients in both groups received 8 treatment sessions over the course of 4 weeks.

Outcome measures

At the initial screening visit, a clinical research coordinator asked all patients to complete a questionnaire regarding their sociodemographic characteristics, including age, sex, height, and weight, and recorded their vital signs. Before the start of treatment at each visit, each patient was assessed to record the outcomes of the previous treatment session. All patients were followed up at 4 and 8 weeks after the 4-week treatment period.

The primary outcome of back pain intensity was assessed using a 100 mm pain visual analogue scale (VAS), on which 0 indicates absence of pain and 100 indicates unbearable pain.[25,26] Each patient was asked to rate his or her degree of back pain during the previous 3 days on the VAS. Back pain was measured at baseline (assessment 1 at week 0) prior to each of the 8 treatment sessions (assessments 2–9 at weeks 1-4), and at the 2 follow-up visits

(assessments 10 and 11 at weeks 8 and 12). The primary endpoint was assessment 10(week 8), which marked the end of the 8 active treatment sessions. A responder was defined as a study participant with ≥50% pain relief using the 100mm VAS for pain intensity at assessments 9, 10 and 11, and a non-responder as having pain relief of <50%, respectively (weeks 4, 8 and 12).

The secondary outcome measures were back pain-related disability, assessed using the Oswestry Disability Index (ODI), and quality of life, assessed by the EuroQol five dimensions (EQ-5D) questionnaire.[27] The ODI contains 10 questions about daily life and includes measures of pain intensity, personal care, lifting, walking, sitting, standing, sleeping, social life, and travelling. Each question is rated on a scale of 0 to 5, with a higher score indicating more severe pain-related disability. The validated Korean version of the ODI[28] was administered before treatment at assessments 2, 5, 9,10, and 11(weeks 1, 2, 4, 8, and 12).The validated Korean version of the EQ-5D[29, 30] includes generic questions about personal health-related quality of life and consists of five dimensions pertaining to mobility, self-care, usual daily activities, pain and discomfort, and anxiety/depression. Each dimension is scored on a scale of 1 to 3, with a lower score indicating a better state of health. The EQ-5D was administered before treatment assessments 2, 5, 9, 10, and 11(weeks 1, 2, 4, 8, and 12).

Randomisation

Before the first treatment session, a statistician assigned patients to one of 2 groups by a central telephone randomisation procedure according to a computer-generated randomisation sequence using SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Randomisation

was performed by a trial coordinator who had no contact with the patients. The clinical research coordinator obtained the codes for the trial (A or B) from the central telephone service and informed the EA practitioner. The practitioner used these codes to assign patients to one of the two groups and to deliver the appropriate treatment.

The National Clinical Research Center for Korean Medicine at PNUKH stored the random numbers. The allocation sequence was concealed from the researchers responsible for enrolling, treating, and assessing patients by dividing their roles and contact with the study participants.

Blinding

It was impossible to blind either the patients or treating clinicians in this trial as the study design was pragmatic and comparative and not placebo-controlled. However, the risk of detection bias was minimal because all treatments and assessments were conducted independently and the treating clinicians were not involved in assessment of outcomes.[31] The assessors, who received standardized training, always performed the outcome assessments in a separate room and were blinded to treatment assignment. However, there was provision in the study protocol for unblinding in exceptional circumstances where knowledge of the actual treatment would be essential for further management of the patient (e.g., serious adverse event).

Statistical analysis

The statistical analysis was performed on both an intention-to-treat (ITT) and a per-protocol

basis. For the ITT analysis, we applied the last-observation-carried-forward (LOCF) rule for missing data. The statistical significance of differences in the data for each group was analysed using the paired *t*-test, and the statistical significance of differences between groups was analysed using the independent *t*-test. Analysis of covariance was used to analyse and adjust the baseline characteristics if there were statistically significant differences and possibility of covariance of baseline characteristics. The chi-square test or Fisher's exact test was used to analyse categorical data, such as responses/responders, and were recorded and described as frequencies (%). We did not perform an interim analysis as we expected EA and UC to be associated with a minimal risk of harm. All statistical analyses were performed by a statistician using SPSS for Windows version 22.0 software. The significance level was set at 5%.

The sample size required for a future trial will be estimated using the free G*Power version 3.1.7 program (Franz Faul, Christian-Albrechts-Universitätzu Kiel, Kiel, Germany), which calculates the sample size using mean difference and standard deviation.

Patient and Public Involvement

The aim of this pilot study was to estimate the sample size for a large pragmatic study of the comparative effectiveness of EA with usual care for LBP after back surgery. Therefore, patients and the public sector were not directly involved in the design of, recruitment to, and conduct of this pilot study. We developed the research question, study design, outcome measures, patient recruitment and trial conduct methodology in light of the general Korean medical environment created as a result of its dual medical system of conventional and Korean medicine. As the choice of intervention reflects this medical environment, we did not

view the intervention as burdensome and the burden of the intervention was not assessed by the patients themselves. The results of the qualitative research and economic evaluation which was conducted concurrently with this pilot study will be considered along with patient and public involvement in study design in the development process of a future trial. The results of this confirmative, pragmatic, comparative RCT will be disseminated in peer-reviewed journals and at academic conferences.

RESULTS

Participants

Forty-seven eligible patients agreed to participate in the trial after screening. Eight participants withdrew their informed consent before the start of treatment, leaving 39 patients who were randomly allocated to the two groups (18 in the EA plus UC group, and 21 in the UC alone group). Eight of 39 patients dropped out during the treatment period due to withdrawal of informed consent or protocol violation (6 in the EA plus UC group, and 2 in the UC alone group). One more patient in UC alone group dropped out after treatment because of protocol deviation, leaving 30 patients (12 in the EA plus UC group, and 18 in the UC alone group) for the per-protocol analysis (Fig. 1).

The mean (standard deviation) age of the 39 treated patients was 57.6 (9.52) years and 19 participants were men (48.7%). The detailed baseline demographic characteristics are provided in Table 1. The mean scores on the VAS for non-acute back pain after surgery, and scores on the ODI and EQ-5D at the baseline evaluation are presented in Table 2.

Table 1. Demographic features of the participants at baseline

Variables	Total	Group	
		EA+UC (n=18)	UC alone (n=21)
Gender, n(%)			
Male	19 (48.7)	9 (50.0)	10 (47.6)
Female	20 (51.3)	9 (50.0)	11 (52.4)
Age (yrs)			
Mean±SD	57.6±9.5	58.9±9.8	56.5±9.4
Range	37-70	40-70	37-70
Height (cm)			
Mean±SD	164.1±9.8	163.0±9.0	165.1±10.6
Range	145-187	145-179	150-187
Weight (kg)			
Mean±SD	66.9±9.8	67.1±9.5	67.1±9.5
Range	53-88	53-88	55-83

EA; electroacupuncture, UC; usual care, SD; standard deviation

Table 2. Difference in primary and secondary results in theelectroacupuncture (EA) in combination with usual care (UC) group and UC alone group between each evaluation and baseline

Variables	Group		p-value*
	EA+UC (n=18) mean±SD mean [95% CI]	UC alone(n=21) mean±SD mean [95% CI]	
VAS [mm]			
Baseline	64.61±14.92	67.33±10.33	
After 4 weeks	51.78±20.62	60.24±19.25	
Difference	-12.83 [-25.27, -0.39]	-7.10 [-13.22, -0.97]	.3919
After 8 weeks	41.50±24.75	58.24±20.83	
Difference	-23.11 [-36.60, -9.62]	-9.10 [-16.71, -1.48]	.0675
After 12 weeks	41.78±24.62	53.00±21.39	
Difference	-22.83 [-35.86, -9.81]	-14.33 [-23.29, -5.38]	.2553
Responder [%(n)]			
After 4 weeks	22.2 (4)	4.8 (1)	.1618**
After 8 weeks	33.3 (6)	9.5 (2)	.1123**
After 12 weeks	38.9 (7)	19.1 (4)	.1698†
ODI [%point]			
Baseline	44.70±15.42	38.23±14.5	
After 4 weeks	33.78±17.45	34.19±17.09	
Difference	-10.93 [-15.92, -5.94]	-4.04 [-7.59, -0.5]	.0210
After 8 weeks	31.95±18.57	32.47±16.04	
Difference	-12.75 [-17.23, -8.28]	-5.77 [-8.75, -2.79]	.0081
After 12 weeks	29.67±18.46	28.60±16.69	
Difference	-15.04 [-20.16, -9.91]	-9.63 [-14.39, -4.87]	.1137
EQ-5D [point]			
Baseline	0.65±0.13	0.66±0.15	
After 4 weeks	0.71±0.11	0.72±0.14	
Difference	0.06 [0.01-0.12]	0.05 [0.02-0.09]	.7698
After 8 weeks	0.74±0.15	0.73±0.13	
Difference	0.09 [0.02, 0.16]	0.06 [0.02, 0.11]	.5151
After 12 weeks	0.73±0.17	0.74±0.13	
Difference	0.08 [0, 0.17]	0.08 [0.04, 0.12]	.9441

EA; electroacupuncture, UC; usual care, CI; confidence interval, VAS; visual analogue scale, ODI; Oswestry

disability index, EQ-5D; EuroQol five dimensions questionnaire
*t-test for comparison of difference between groups
** Fisher's exact test for comparison of difference between groups
†Chi-square test for comparison of difference between groups

Effects of EA

In both treatment groups, there were statistically significant improvements in VAS scores for back pain, and ODI and EQ-5D scores at 8 weeks compared to baseline (Table 2). However, there were no statistically significant differences in the VAS score for back pain (p=0.0675) and in the EQ-5D (p=0.5151) score between the 2 treatment groups at 8 weeks (Table 2). There was a statistically significant decrease in the ODI after 8 weeks in the EA plus UC group when compared with the UC alone group (p=0.0081; Table 2). In the ITT analysis (n=39), the proportion of responders, defined as participants with ≥50% pain relief on the 100mm VAS for pain intensity, was 33.3% (n=6) in the EA plus UC group (n=18) and9. 5% (n=2) in the UC alone group (n=21); the difference between the groups was not statistically significant (p=0.1123; Table 2). No adverse events were reported in this study.

Estimating sample size of a future trial

On completion of this pilot study, we calculated an appropriately powered sample size that would be suitable for a larger RCT, based on the difference in change in VAS score between groups, with consideration of a 5% significance level, two-tailed, 80% powered test, and *t*-test for comparison between groups. The mean difference (standard deviation) in the VAS score for back pain between the EA plus UC group and the UC alone group was 14.02 (22.12) mm at the primary endpoint, which was 8 weeks post-treatment initiation, based on ITT analysis. On this basis, using the G*Power program, 40 participants per group would be

required. Allowing for a dropout rate of 25%, a total of 108 participants (54 per group) would need to be recruited.

DISCUSSION

Many people suffer from LBP after back surgery and experience side effects from the opioids used to relieve their pain. Previous research has shown that patients treated with acupuncture or related techniques experience less pain and consequently use less opioids for pain control.[32] Therefore, it may be carefully conjectured that EA, a type of acupuncture treatment commonly used by Korean medicine doctors, maybe a good alternative as a non-pharmacological treatment without the risk of opioid-related side effects. Electroacupuncture is known to alleviate sensory symptoms and regulate components of pain through specific neuroscientific mechanisms and is thus used to decrease pain medication dosages.[33] Also, as EA is often used for management of postoperative pain,[34-37] we propose that a large-scale study is necessary to confirm the effectiveness of EA combined with UC, western conventional medicine treatment, as these treatments for postoperative pain reflect real-world circumstances and settings. We therefore undertook this pilot RCT to estimate the sample size for a full-scale randomised trial. Although the number of samples included in the analysis was insufficient to confirm the effect of treatment as it was roughly estimated a priori, we focused on analysing the approximate validity and calculating the sample size needed for a future trial.

From the results of this pilot study, we determined the basis needed in carrying out a full scale RCT. Although there was no statistically significant difference between the two groups

in VAS, between-group difference in changes in ODI, which assesses back pain-related disability, was significant (p=0.0081) and favoured EA plus UC therapy in terms of functional improvement in the lumbar spine. Given the clinical reality that it is difficult to expect functional improvement without relief of pain, our basis for a full scale RCT seems reasonable.

The observed change in VAS scores in the EA plus UC group (23.11) is greater than the minimum clinically important difference (MCID) value (22.50 in low back pain) reported in a previous study, [38] and the mean difference (14.02) and standard deviation (22.12) of the two groups indicates a medium-sized effect, justifying the need for a larger scale follow-up study.

The pilot study was underpowered, the sample size being based on the mean difference (20) and standard deviation (19) derived from other similar studies. However, those studies differed from our trial in terms of patients, methods of treatment and study design. It follows that the sample size for our future RCT based on a similar protocol to the pilot study should be calculated using our observed parameters so that a future study would be conservatively powered for a meaningful effect.

These preliminary findings, albeit limited with several limitations as mentioned above, confirm the need to proceed with future pragmatic RCTs comparing the effectiveness of EA with UC with that of UC alone for treatment of non-acute pain after back surgery. However, there are several considerations to be taken into account before proceeding with larger RCTs. First, for cultural reasons, most participants in such studies would have had acupuncture experience in countries such as Korea, which would act as a limiting factor in efficacy of acupuncture-related treatment, and the reason why many clinical trials using acupuncture, or related techniques such as EA, are often considered to have high risk of bias.[39, 40] Also,

the three main outcome measures were all patient-reported outcomes. This can serve as a limitation regarding subjective outcome measurement, although we used assessor blinding to offset this limitation as much as possible. Therefore, treatment, assessment and statistical analysis should be performed independently in future trials to prevent detection bias.

Further, there were many dropouts in this pilot trial, and it is necessary to find an appropriate method of overcoming this problem. Especially in order to overcome potential problems related to withdrawal of consent before the start of treatment, such methods as adjusting the timing of randomisation or initiation of treatment may be considered in following trials. In addition to the LOCF rule, it is also necessary to consider an appropriate method for handling missing data such as multiple imputation. Also, inclusion of a patient satisfaction survey in future trials may help shed light on this high dropout rate.

In an effort to reflect real-world situations, only western medical treatments such as drug treatment excluding surgery or injection therapy were allowed during the treatment period. In many professional conferences, it was difficult to completely rule out medication when considering the realistic aspects of pain management. Also, as this pilot trial was a pragmatic comparative effectiveness RCT, we tried to reflect real-world conditions in current clinical status too. We therefore permitted drug therapy in UC to reflect current use of medication. In addition, subgroup analyses based on diagnosis, type of surgery, and duration of pain, which could not be confirmed in the present study due to limitations in data collection, should be conducted in future trials by means of structured questionnaires.

A future trial that addresses the above-mentioned concerns and covers the estimated sample size will be better equipped for clinical assessment of the benefits of EA in combination with UC in treatment of patients with non-acute pain after back surgery. In addition, qualitative research and economic evaluation will be conducted in future trials using evaluation tools

supplemented through pilot study results. The results of a follow-up trial are expected to establish a robust clinical basis for the effects of acupuncture combined with electrical stimulation in this patient population.

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Competing interests

The authors declare that they have no competing interests.

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Author contributions

All authors conceived and designed the trial by discussion. IH wrote the manuscript. MSH, EHH, JHC, and IHH helped to conceive and design the trial. BCS as the principal investigator conceived the trial and revised the manuscript. IH and MSH recruited the

patients and conducted the trial. NKK acted as an economic evaluation expert and clinical trial expert. DWS was involved as a neurosurgical expert. KMS and JHL supervised the trial. All authors read and approved the final manuscript.

Data sharing statement

Data may be requested from the corresponding author and made available to researchers who meet the criteria for access to confidential patient data according to the Institutional Review Board of Pusan National University Korean Medicine Hospital.

REFERENCES

1 Hoy D, March L, Brooks P, et al. Measuring the global burden of low back pain. *Best Pract Res Clin Rheumatol* 2010;24:155–65.

2 Sarrazin JL. Imaging of postoperative lumbar spine. *J Radiol* 2003;84(2 Pt 2):241–52.

3 Herrera Herrera I, Moreno de la Presa R, Gonzalez Gutierrez R, et al. Evaluation of the postoperative lumbar spine. *Radiologia* 2013;55:12–23.

4 Aghion D, Chopra P, Oyelese AA. Failed back syndrome. *Med Health R I* 2012;95:391–3.

5 Skolasky RL, Wegener ST, Maggard AM, et al. The impact of reduction of pain after lumbar spine surgery: the relationship between changes in pain and physical function and disability. *Spine* 2014;39:1426–32.

6 Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain* 2016;17:131–57.

7 Hutchison RW, Chon EH, Tucker Jr. WF, et al. A comparison of a fentanyl, morphine, and hydromorphone patient-controlled intravenous delivery for acute postoperative analgesia: a multicenter study of opioid-induced adverse reactions. *Hosp Pharm* 2006;41:659–63.

8 Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. *Pain Physician* 2008;11(2 Suppl):S105–20.

9 White A, Hayhoe S, Hart A, et al. Survey of adverse events following acupuncture (SAFA): a prospective study of 32,000 consultations. *Acupunct Med* 2001;19:84–92.

10 Wheway J, Agbabiaka TB, Ernst E. Patient safety incidents from acupuncture treatments:

a review of reports to the National Patient Safety Agency. *Int J Risk Saf Med* 2012;24:163–9.

11 Lin CW, Haas M, Maher CG, et al. Cost-effectiveness of guideline-endorsed treatments for low back pain: a systematic review. *Eur Spine J* 2011;20:1024–38.

12 Lee JH, Choi TY, Lee MS, et al. Acupuncture for acute low back pain: a systematic review. *Clin J Pain* 2013;29:172–85.

13 Shin JS, Ha IH, Lee J, et al. Effects of motion style acupuncture treatment in acute low back pain patients with severe disability: a multicenter, randomized, controlled, comparative effectiveness trial. *Pain* 2013;154:1030–7.

14 Casimiro L, Barnsley L, Brosseau L, et al. Acupuncture and electroacupuncture for the treatment of rheumatoid arthritis. *Cochrane Database Syst Rev* 2005;4:CD003788.

15 Zhao XB, Xing QZ, Han XC. [Observation on electroacupuncture at neimadian (extra) and neiguan (PC 6) for analgesia after thoracic surgery]. *Zhongguo Zhen Jiu* 2013;33:829–32. Article in Chinese.

16 Chia KL. Electroacupuncture treatment of acute low back pain: unlikely to be a placebo response. *Acupunct Med* 2014;32:354–5.

17 Cho YH, Kim CK, Heo KH, et al. Acupuncture for acute postoperative pain after back surgery: a systematic review and meta-analysis of randomized controlled trials. *Pain Pract* 2015;15:279–91.

18 Huang HT, Zheng SH, Feng J, et al. Thin's abdominal acupuncture for treatment of failed back surgery syndrome in 20 cases of clinical observation. *Guid J Trad Chin Med Pharm* 2012;18:63–5.

19 Zheng SH, Wu YT, Liao JR, et al. [Abdominal acupuncture treatment of failed back surgery syndrome clinical observation]. *J EmergTrad Chin Med* 2010;19:1497–8. Article in Chinese.

20 National Guideline Clearinghouse. Low Back Disorders. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2011. Available from: http://www.guideline.gov/content.aspx?id=38438.

21 MacPherson H, Altman DG, Hammerschlag R, et al. Revised STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): Extending the CONSORT statement. *J Evid Based Med* 2010;3:140–55.

22 Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Int J Surg* 2012;10:28–55.

23 Hwang MS, Heo KH, Cho HW, et al. 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. *BMJ Open* 2015;5:e007031.

24 Jung YP, Jung HK, Chiang SY, et al. The clinical study of electroacupuncture treatment at Hua-Tuo-Jia-Ji-Xue on spondylolisthesis. *The Journal of Korean Acupuncture & Moxibustion Society* 2008;25:221–32.

25 Revill SI, Robinson JO, Rosen M, et al. The reliability of a linear analogue for evaluating pain. *Anaesthesia* 1976;31:1191–8.

26 Carlsson AM. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. *Pain* 1983;16:87–101.

27 Fairbank JC, Pynsent PB. The Oswestry Disability Index. *Spine* 2000;25:2940–52.

28 Jeon CH, Kim DJ, Kim SK, et al. Validation in the cross-cultural adaptation of the Korean version of the Oswestry Disability Index. *J Korean Med Sci* 2006;21:1092–7.

29 Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001;33:337–43.

30 Kang EJ, Shin SH, Park HJ, et al. A validation of health status using EQ-5D. *The Korean*

Journal of Health Economics and Policy 2006;12:19–43.

31 Higgins J, Green S, Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions. Chichester, UK; Wiley-Blackwell; 2008.

32 Wu MS, Chen KH, Chen IF, et al. The efficacy of acupuncture in post-operative pain management: a systematic review and meta-analysis. *PLoS One* 2016;11:e0150367.

33 Zhang R, Lao L, Ren K, et al. Mechanisms of acupuncture-electroacupuncture on persistent pain. *Anesthesiology* 2014;120:482-503.

34 Chi H, Zhou WX, Wu YY, et al. Electroacupuncture intervention combined with general anesthesia for 80 cases of heart valve replacement surgery under cardiopulmonary bypass. *Zhen Ci Yan Jiu* 2014;39:1–6. Article in Chinese.

35 Wu J, Zhao Y, Yang CM, et al. Effects of electroacupuncture preemptive intervention on postoperative pain of mixed hemorrhoids. *Zhongguo Zhen Jiu* 2014;34:279–83. Article in Chinese.

36 Zhang H, Wang L, Zhang M, et al. Effects of electroacupuncture on postoperative functional recovery in patients with gynaecological laparoscopic surgery. *Zhongguo Zhen Jiu* 2014;34:273–8. Article in Chinese.

37 Zhang Z, Wang C, Li Q, et al. Electroacupuncture at ST36 accelerates the recovery of gastrointestinal motility after colorectal surgery: a randomised controlled trial. *Acupunct Med* 2014;32:223–6.

38 Park KB, Shin JS, Lee J, et al. Minimum Clinically Important Difference and Substantial Clinical Benefit in Pain, Functional, and Quality of Life Scales in Failed Back Surgery Syndrome Patients. *Spine* 2017;42:E474-81

39 Kim SI, Lee KB, Lee HS, et al. Acupuncture experience in patients with chronic low back pain(2): a qualitative study - focused on participants in randomized controlled trial. *Korean J Acupunct* 2012;29:581–97.

40 Lee H, Bang H, Kim Y, et al. Non-penetrating sham needle, is it an adequate sham control in acupuncture research? *Complement Ther Med* 2011;19Suppl1:S41–8.

Figure 1. CONSORT trial flow diagram. EA, electroacupuncture; UC, usual care.

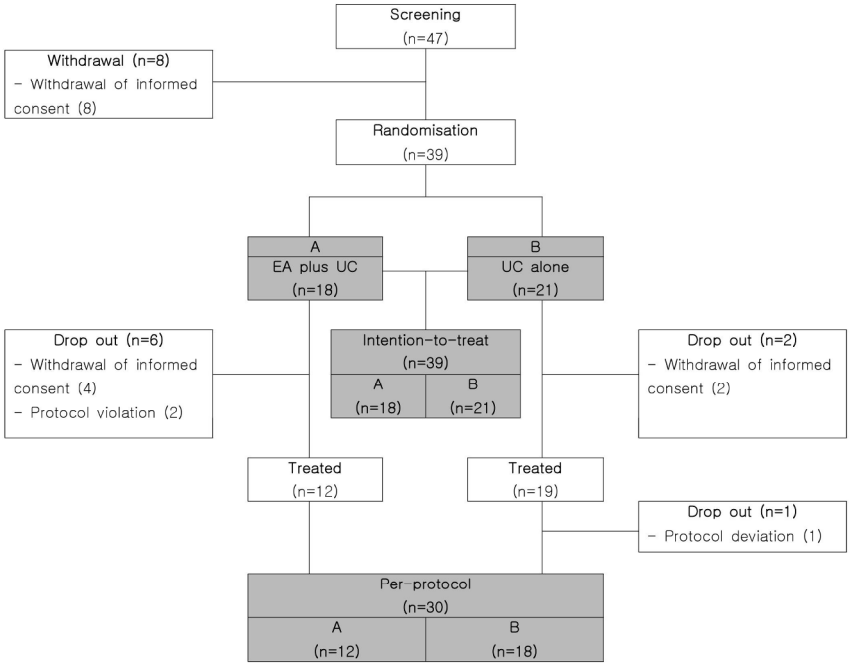

Figure 1. CONSORT trial flow diagram. EA, electroacupuncture; UC, usual care.

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CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	3~4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	6
	2b	Specific objectives or research questions for pilot trial	6~7
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	7
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	-
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	7
	4c	How participants were identified and consented	8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8~10
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	10~11
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	-
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	-
Sample size	7a	Rationale for numbers in the pilot trial	13
	7b	When applicable, explanation of any interim analyses and stopping guidelines	-
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	11
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	11
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	11

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	11
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	12
	11b	If relevant, description of the similarity of interventions	-
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	12~13
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	13~14
	13b	For each group, losses and exclusions after randomisation, together with reasons	13~14
Recruitment	14a	Dates defining the periods of recruitment and follow-up	7
	14b	Why the pilot trial ended or was stopped	-
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	14~15
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	13~14
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	14~16
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	-
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	16
	19a	If relevant, other important unintended consequences	-
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	18~19
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	17
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	16~17
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	17~19
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	7
Protocol	24	Where the pilot trial protocol can be accessed, if available	7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	9
	26	Ethical approval or approval by research review committee, confirmed with reference number	7

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.
*We strongly recommend reading this statement in conjunction with the CONSORT 2010, extension to randomised pilot and feasibility trials, Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.