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Electroacupuncture for treatment-resistant insomnia: study protocol for a randomised, controlled, assessor-blinded, pilot clinical trial

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ABSTRACT

Introduction A considerable number of insomnia patients experience sleep disturbance even with long-term use of hypnotic medication. Previous studies have indicated that electroacupuncture (EA) could be an efficacious treatment for managing insomnia. However, few trials have been conducted to evaluate the effectiveness and safety of EA for treatment-resistant insomnia. This pilot study aims to explore the feasibility and preliminary effectiveness and safety of EA as an adjunct treatment for treatment-resistant insomnia.

Methods and analysis This is a multicentre, randomised, usual care controlled and assessor-blinded pilot study protocol. Fifty patients presenting with sleep problems who have been taking hypnotic medication for more than 3 months will be randomly allocated to either an EA group or a usual care group at a 1:1 ratio. The EA group will undergo 12 EA treatment sessions twice a week for 6 weeks whereas the usual care group will not receive EA treatment. All the participants will receive a brochure containing educational information on sleep hygiene. The primary outcome will be the measured mean change of the total score of the Insomnia Severity Index from the baseline to week 7. The secondary outcome regarding sleep quality will be measured using the Pittsburgh Sleep Quality Index, a sleep diary and actigraphy. Moreover, we will assess the quality of life, the direct and indirect cost of treating insomnia for economic evaluation. After 4 weeks, the subjects will visit the research sites for a follow-up assessment.

Ethics and dissemination Ethical approval of this study protocol was established by the institutional review boards of the each involved study site. All potential subjects will be provided written informed consent. The results of this study will be accessible in peer-reviewed publications and be presented at academic conference.

Trial registration number KCT0003235.

Strengths and limitations of this study

- This is the first randomised, multicentre study in South Korea examining the effectiveness and safety of electroacupuncture (EA) as an adjunct therapy to pharmacotherapy for treatment-resistant insomnia.
- Both subjective and objective tools to assess sleep quality and quantity are used in this study. Also the study population could be representative of patients visiting Korean traditional medical clinics.
- A sham comparator will not be used in these trials, so the participants and practitioner will not be blinded, and complete assessor blinding may be challenging because of the self-reported outcome measurement.
- Participants might be heterogeneous because of the broad age range and possible comorbidities with other conditions.
- The sample size of this pilot study is too small to examine the effectiveness of EA for treatment-resistant insomnia.

INTRODUCTION

Insomnia is a highly prevalent complaints among general population,[1 2] and it can cause a significant socioeconomic burden.[3] Hypnotic medications such as benzodiazepines (BDZ), and non-BDZ hypnotics such as zolpidem and zopiclone (Z-drugs), are most frequently used for treating insomnia. While hypnotics are effective for managing short-term insomnia, there is insufficient evidence concerning their long-term therapeutic effects.[4 5] Despite the potential adverse effects of long-term hypnotics use such as daytime numbness, dizziness, sensitivity to light, decreased motor skills, tolerance and dependence on medication, the use of long-term hypnotics is reported to be common in clinical settings.[4 6 7]

A considerable number of patients with insomnia remain dissatisfied with their sleep, even with the use of long-term hypnotic medication.[8–10] In previous studies,[11 12] treatment-resistant insomnia has been operationally defined as persistent insomnia that has not shown improvement in terms of sleep quality or quantity despite the use of sleeping pills for more than 3 months. In a study by Krakow *et al*,[9] patients with treatment-resistant insomnia

experienced waking impairment and poor quality of life, as well as high rates of maladaptive behaviour, psychiatric complaints and obstructive sleep apnoea.

Acupuncture is a widely used complementary and alternative medical treatment for insomnia. In a recent review, Cao *et al*[13] reported that acupuncture showed more benefits than no treatment or estazolam use regarding sleep quality. In a recent clinical trial, acupuncture treatment for perimenopausal insomnia was found to improve sleep quality and sleep architecture compared with placebo acupuncture.[14] Moreover, several studies have reported that electroacupuncture (EA) also can be effective for treating insomnia.[15–17]

In the Korean traditional medical clinical settings, EA has been frequently used for treating insomnia and most insomnia patients visiting the Korean traditional medical clinics had been already taking hypnotics.[18] However, there is lack of research evidence of clinical effectiveness of EA for treatment-resistant insomnia. Only similar study on EA for long-term BDZ uses was conducted in Hong Kong.[11] Therefore, well-designed trials are needed to evaluate the effectiveness and safety of EA for treatment-resistant insomnia. To our knowledge, no study has performed a cost evaluation of EA for insomnia. Our clinical question is whether EA, as an adjunct to pharmacotherapy, would result in sleep improvement for treatment-resistant insomnia when compared with pharmacotherapy alone. The primary aim of this study is to investigate EA as an adjunct to pharmacotherapy in terms of effectiveness, safety and cost-effectiveness for treatment-resistant insomnia. Our secondary objective is to explore the feasibility of a future large-scale clinical trial on EA for treatment-resistant insomnia.

METHOD AND ANALYSIS

Study design

This is a multicentre, randomised, assessor-blind, usual care-controlled, pilot study protocol for examining the effectiveness and safety of EA as an adjunct treatment to usual care in treatment-resistant insomnia patients with sleep disturbance despite taking hypnotic medications for over 3 months. Fifty eligible patients will be randomly assigned to either an EA or a usual care group at a 1:1 ratio and will receive EA treatment or usual care, respectively, for 6 weeks with a 4-week follow-up. The overall schedule of the trial is illustrated in table 1 while the study flow chart is presented in figure 1

Recruitment

This trial will be conducted at two clinical research institutes in South Korea, that is, Pusan National University Korean Medical Hospital and Dong-sin University Korean Medical Hospital in Gwang-Ju. To reach target sample size, we will advertise our clinical trial using the hospitals' home pages, flyers inside and outside the hospitals and through daily local newspapers and subway advertisements.

Participants

In this study, with reference to the previous studies[11 12] 'treatment-resistant insomnia' will be operationally defined as persistent insomnia that has not shown improvement with regards to sleep quality or quantity despite the use of sleeping pills for more than 3 months. We will employ the following criteria in the recruitment of participants:

Inclusion criteria

1. Male and female participants aged 19–80 years.
2. Participants who have taken medications prescribed by physicians, not over-the-counter medications for insomnia for at least the previous 3 months, and who have not changed the regular type and dose of medication within the last 2 weeks.
3. A total Insomnia Severity Index (ISI) score higher than 15.
4. Meeting the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition diagnostic criteria for insomnia disorder.
5. Having agreed to participate in this trial and having provided written informed consent.

Exclusion criteria

1. Having received Korean medical treatment for insomnia, for example, acupuncture, cupping, moxibustion and herbal medicine, within the previous 2 weeks.
2. Having initiated or been scheduled to start dietary supplements or non-pharmacological therapies for treating insomnia, for example, cognitive behavioural therapy (CBT), meditation, etc., within the previous 2 weeks of the beginning of this trial or during the trial.
3. Suffering from unstable (uncontrolled) schizophrenia, mania or bipolar disorder within the previous 6 months or having a subscale score of ≥11 points for either anxiety or depression in the Hospital Anxiety and Depression Scale.
4. A diagnosis of substance abuse or dependence within the last 6 months.
5. Having attempted suicide, murder or self-injury.
6. Shift workers or workers with alternating day/night schedules that could impact their circadian rhythm.
7. Having a severe pain condition or any diseases which can cause sleep disturbance.
8. Taking haemostatic agents, for example, Greenmono, Monoclate-P, Advate, Facnyne and BeneFix, for cardiovascular or haemostatic disorders.
9. Having abnormal findings in the thyroid function test, that is, abnormal levels of free thyroxine (free T4) and thyroid-stimulating hormone (TSH) (<0.1 µIU/mL or >5.1 µIU/mL).
10. Having inappropriate clinical laboratory examination findings for participation in this trial (ie, total bilirubin level exceeding twice the institute's normal limit, aspartate transaminase (AST) or alanine

Table 1 Schedule of enrolment, intervention assessments

Time point	Screening	Treatment												Follow-up	
Week	–1	1–2				3–4				5–6				7	11
Visit EA group		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Visit usual care group		1				2				3				4	5
Enrolment	●														
Eligibility screen	●														
Informed consent	●														
Allocation		●													
Interventions															
EA		◎	◎	◎	◎	◎	◎	◎	◎	◎	◎	◎	◎		
Assessments															
ISI	●	●		◎		●				●				●	●
PSQI		●		◎		●				●				●	●
HADS	●														
Sleep diary check	●	●		◎		●				●				●	●
Actigraphy check	●	●		◎		●				●				●	●
Pattern identification for insomnia		●													
VAS of physical symptoms accompanying insomnia		●		◎											
Quality of life (EQ-5D, EQ-VAS, SF-36)		●												●	
Cost evaluation		●												●	
Adverse event check		●	◎	◎	◎	●	◎	◎	◎	●	◎	◎	◎	●	●
Laboratory test	●													●	

●, All groups; ◎, EA groups.
EA, electroacupuncture; EQ-5D, the EuroQoL five-dimension questionnaire; EQ-VAS, the EuroQol-visual analogue scale; HADS, Hospital Anxiety and Depression Scale; ISI, Insomnia Severity Index; PSQI, Pittsburgh Sleep Quality Index; SF-36, the 36-Item Short Form Health Survey questionnaire ; VAS, visual analogue scale.

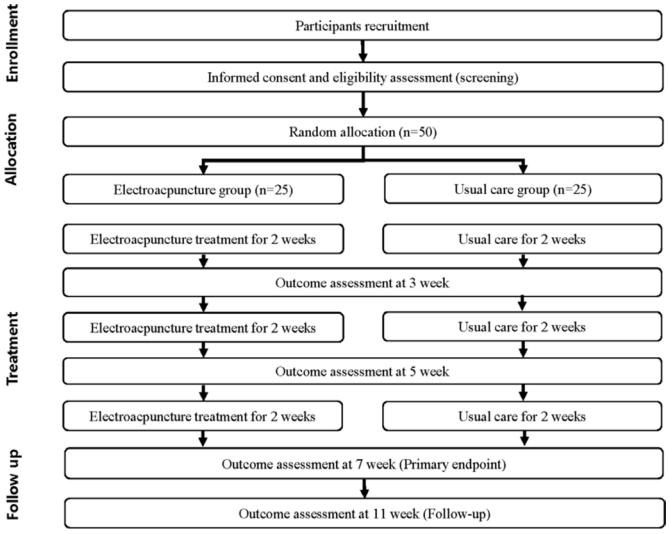

Figure 1 Flow diagram of the study.

transaminase (ALT) exceeding 2.5 times the institute's normal limit, creatinine exceeding 2.5 times the institute's normal limit, white blood cell count $<1.5\times10^9$/L or $\geq10.0\times10^9$/L, absolute neutrophil count <1000, platelets count $<75\times10^9$/L, human chorionic gonadotropin (hCG)-positive urine and other significant findings that may affect this trial based on the clinical researchers' judgement).

11. A diagnosis of severe chronic or terminal disease for example, malignant tumours, tuberculosis, chronic liver disease, chronic renal disease, etc.
12. Previous experience of hypersensitivity reaction to acupuncture or inability to cooperate with acupuncture therapy.
13. Having received any implants that could interfere with EA or having experienced hypersensitivity reaction to electrostimulation.
14. Pregnancy, lactation or having pregnancy plans.

15. Having participated in other clinical trials within the last 4 weeks or currently involved in other clinical studies.
16. Difficulty to comply with the study protocol such as treatment or questionnaires.
17. Any other cases unsuitable for this trial based on the clinical researchers' judgement.

Randomisation and allocation concealment

Fifty subjects who meet the eligibility criteria will be allocated to each group following a randomisation schedule generated by an independent statistician using SAS V.9.4 (SAS Institute). The randomisation list will be sealed in sequentially numbered opaque envelopes and delivered to each institution. The envelopes will be stored in a double-locked cabinet and will only be opened by the practitioner to assign participants to the EA or usual care group after obtaining informed consent and eligibility screening. The opened envelopes will again be separately stored in a double-locked cabinet.

Blinding

In this trial, participant blinding cannot be achieved because the subjects in the usual care group will be aware of the allocated group. Moreover, practitioner blinding is not possible because the practitioner will have to personally administer EA treatment. The outcome assessors will be blinded to the group allocation by not involving in the EA treatment administration.

Interventions

All participants will receive a brochure containing sleep hygiene educational information. The practitioners are licensed doctors of Korean traditional medicine and have at least 2 years of clinical experience. In addition, all investigators will be required to have renewed their certifications of good clinical practice at least within 1 year.

EA group

Patients in the EA group will be treated with 0.25×30 mm disposable sterilised filiform needles (Dong-bang Acupuncture, Seoul, Korea) applied to the Yintang (EX-HN3), Baihui (GV20), bilateral Shenmen (HT7), Neiguan (PC6), Dazhong (KI4) and Jinmen (BL63) acupoints. We selected the acupoints by referring to the studies by Yeung *et al*,[16 19] Kim S-P *et al*[20] and Kim M *et al*.[21]

After *de qi* is attained, an EA device (ES-160, Ito Co., Tokyo, Japan) will be connected to five pairs of acupoints (EX-HN3-GV20; left and right PC6-HT- and left and right KI4-BL63) to apply 4 Hz at a noticeable yet comfortable intensity for 30 min.

Participants will undergo 12 EA treatment sessions twice a week for 6 weeks. Detailed information on the EA treatments is provided in the online supplementary appendix 1.

Usual care group

The usual care group will not receive EA treatment. Instead, they will maintain the type and dose of their regular medications for improving insomnia. After the start of the clinical trial, new or additional use of medications for improving insomnia will be prohibited. They will be allowed to keep their existing self-care but will be prohibited from starting supplementary treatment for improving insomnia during the study period.

Prohibited and permitted concomitant treatment

Any Korean traditional medical treatment (eg, acupuncture, cupping, moxibustion or herbal medicine) aimed at improving insomnia will be restricted during the clinical trial period. Participants change the type or dosage of their regular medication for improving insomnia during the trial period will be dropped from the study.

Non-pharmacological treatment, such as CBT or dietary supplements, taken by the subjects from at least 2 weeks prior to the start of the study will be allowed as long as there are no alterations in the regimens during the trial.

The participants will be instructed to report any newly started treatments to the research investigators or staff members after the start of the trial. Newly started treatments will be documented in the case report form (CRF). Subjects who will be confirmed to have received any prohibited treatments during the study period will be excluded from the trial.

Outcomes

Prior to each of the EA treatments, participants will complete self-reported questionnaires. The assessor, blinded to the group allocation, will ask participants to complete the outcome measurements in a place separate from the EA treatment room.

Primary outcome

The mean change in the ISI score from the beginning to the end of the 6-week intervention will be measured for all participants. The validated Korean translation of ISI will be used in this trial.[22] The ISI is a self-reporting questionnaire that consists of seven items and it is used to diagnose and evaluate the severity of insomnia. The total ISI score ranges from 0 to 28 points with the severity being classified according to the total score: 0–7 points for clinically non-significant insomnia, 8–14 points for subthreshold insomnia, 15–21 points for moderately severe clinical insomnia, and 22–28 points for severe clinical insomnia.

Secondary outcomes

The mean change in the total ISI score from baseline to weeks 3, 5 and 11 (follow-up) will be recorded. In addition, the mean change in the Pittsburgh Sleep Quality Index (PSQI) scores from baseline to the end of the 6-week intervention and from baseline to weeks 3, 5 and 11 (follow-up) will be assessed. The PSQI is the most widely used questionnaire for assessing sleep quality in the previous month. This instrument consists of seven categories, that is, subjective sleep quality, sleep latency, sleep duration, sleep disturbances, habitual sleep efficiency, use of sleeping medication and daytime dysfunction. The total PSQI score ranges from 0 to 21 with a higher score

indicating poorer sleep quality. We will use the validated Korean version of the PSQI.[23]

To obtain details on the participants' sleep state, they will receive a sleep diary[24] and instructions on how to fill in the sleep diary items, which include the bedtime, final waking time, sleep latency, sleep duration, number of awakening episodes and use of sleeping pills.

We will objectively evaluate the participant's sleep patterns using an actigraphy. The potential participants will place a wearable physical movement monitoring device (ActiGraph wGT3X-BT; MTI Health Services Company, Pensacola, Florida, USA) on their non-dominant wrists for at least 1 week prior to enrolment. The eligible subjects will keep the actigraph device on throughout the 6-week intervention period to measure their sleep and activity. This will allow us to abstract the objective variables on the participants' sleep quality such as the total time in bed, sleep latency, total sleep time, wake after sleep onset and sleep efficiency. We will compare changes in the extracted objective variables between the groups and examine the consistency of the recorded sleep quality between the sleep diaries and actigraph.[25]

To examine the short-term effectiveness of EA on insomnia after 1 week (two EA sessions), the participants will complete the ISI and the PSQI and undergo assessment using the visual analogue scale for physical symptoms accompanying insomnia such as headache, dyspepsia, fatigue, etc.

To investigate the participants' pattern identifications, we will use the Instrument on Pattern Identifications for Insomnia developed by Lee HS *et al*.[26] One of the five pattern identifications will be selected based on the final score of this self-reporting questionnaire composed of 47 questions.

Safety assessment

All adverse events (AEs) will be recorded during the entire study period. The research investigators will determine whether there was any AE occurrence by asking the subjects. The severity of the AEs will be primarily ranked as 'absent', 'mild', 'moderate' or 'severe'. When rating the severity of the AEs is inappropriate, we will instead assess the AEs using Spilker's three-level criteria.[27] The cause of the AE will be rated as definitely related, probably related, possibly related, probably not related, definitely not related or unknown.

Moreover, laboratory tests to examine AEs will be conducted at baseline and week 7. The tests will include the following: complete blood count and differential count, absolute neutrophil count, total bilirubin, albumin, AST, ALT, blood urea nitrogen, creatinine, erythrocyte sedimentation rate, TSH, free thyroxine and hCG urine tests to detect pregnancy (only for women of childbearing age).

Economic evaluation

For economic evaluation, the quality of life, as well as the direct and indirect costs of treating insomnia, will be evaluated at baseline (visit 1) and at the end of the intervention (visits 4 and 13).

The quality of life will be investigated using the EuroQoL five-dimension questionnaire (EQ-5D), the EuroQoL-VAS (EQ-VAS) and the 36-Item Short Form Health Survey questionnaire (SF-36).

The EQ-5D is widely used to assess the health-related quality of life and is designed to allow patients to check the response that most appropriately describes their health status in terms of the degree of the problem ('none', 'some' or 'extreme') on each of the five dimensions, which include mobility, self-care, pain/discomfort, usual activities and anxiety/depression.[28] Therefore, the scores on these five dimensions can be presented as a health profile. The EQ-VAS is a vertical VAS comprised of values between 0 (worst imaginable health) and 100 (best imaginable health) and is used by patients as a tool for global assessment of their health.[29]

The SF-36 is a popular instrument for evaluating health-related quality of life and comprises of eight scales as follows: physical functioning, role physical, bodily pain, vitality, general health, social functioning, role emotional and mental health.[30]

The direct and indirect costs of treating insomnia and loss of productivity will be measured using a self-reporting questionnaire. The quality-adjusted life year is used as the main outcome for cost evaluation in this study.

Feasibility outcomes

The recruitment and completion rate will be measured to investigate the feasibility of a large-scale randomised clinical trial for treatment-resistant insomnia patients. Moreover, the rate of adherence to the scheduled intervention will be calculated. We will also examine the reasons for participants' ineligibility and for dropping out of the study and these will be documented in the CRF.

Data collection and management

After obtaining informed consent from the participants, the collected data will be documented in the CRF by trained clinical research coordinators. The assessors blinded to the group allocation will implement the outcome assessment.

To improve participant adherence, the researchers will telephone the participants in advance of every visit and follow-up session. If participants fail to attend treatment sessions, we will enquire as to the reasons for non-attendance and aim to encourage adherence to treatment and attendance at sessions via telephone contact. Once a week, we will also telephone the participants in the usual care group to determine the occurrence of any AEs.

Monitoring

Data monitoring and auditing will be conducted to ensure the quality of the study. An initial meeting will be held prior to the beginning of the study. Monitoring staff will visit the institutions at every important time point in the trial, for example, participant enrolment, the study

midway point and study completion. Monitoring staff will ensure consistency concerning data documented in the CRF and data documented in the source document and ensure that the entire study process is in accordance with the approved protocol. A standard operating procedure will be prepared and provided to investigators at each research site prior to the start of the trial to ensure that the research procedure remains consistent across the research sites.

Sample size

The effectiveness and safety of EA for treatment-resistant insomnia has not been previously studied. To calculate the sample size for this trial, we reviewed similar studies on EA for insomnia and referred to the study by Yeung *et al*[15] who used the ISI score as the primary outcome. The mean ISI scores before and after treatment in the experimental control group were estimated as 5.8 (SD=3.2) and 2.1 (SD=4.7), respectively. With an assumed effective size of 0.92, the sample size per group was calculated to be 20 using a two-sided 0.05 significance level and 80% statistical power. The subjects in this study will be allocated to the two groups at a 1:1 ratio. The total sample size will be 50 (25 per each group) after allowing a dropout rate of 20% during the 10-week study period.

Statistical analysis

An independent statistical expert blinded to the group allocation will implement statistical analysis.

A full-analysis set (FAS) will be the main set for the primary analysis. The FAS will include all the participants initially allocated to either group in this study. However, we will not use data from illegible participants, subjects who have not received any interventions and subjects who have not undergone any outcome measurement. A per-protocol set will be used for sensitivity analysis to compare with the results from the FAS. The per-protocol set will consist of participants who completed the trial without major violation of the protocol, who received at least 75% of the planned intervention and who provided all outcome values. A two-sided significance level will be set at 0.05, and the imputation method will be adopted for missing data if needed. SAS V.9.4 will be used for statistical analysis.

Demographic characteristics and baseline measurements of the variables of each group will be summarised. The two-sample T-test or Mann–Whitney U-test will be used for baseline comparisons of continuous variables while the χ^2 test or Fisher's exact test will be used for categorical variables. A 95% CI will be presented as needed.

The primary outcome will be the mean change in the ISI score from baseline to week 7. Depending on the normality of distribution, we will either use the independent two-sample T-test or Mann–Whitney U-test. In case there are significant between-group differences in the demographic characteristics or baseline variable measurements, adjustments will be made according to the covariates.

To identify superiority of EA group compared with usual care group in the primary and secondary outcome measure, blow two hypothesis are assumed.

H0 (null hypothesis): There is no difference in the mean change of ISI score before and after intervention between EA group and usual care group.

H1 (alternative hypothesis): There is a difference in the mean change of ISI score before and after intervention between EA group and usual care group.

The secondary outcome measures will be analysed using the same methods used for the primary outcome measure analysis. Within-group changes in the outcome measures before and after the intervention will be analysed using a paired T-test or Wilcoxon signed-rank test. Repeated measures analysis of variance with post hoc test will be used to validate trend differences per visit.

After two EA treatment sessions, we will compare changes in the score of each PSQI component, the VAS score of physical symptoms accompanying insomnia and the quality and quantity of sleep reported in the sleep diary and actigraph. We will also examine the number of participants in all groups at each assessment whose ISI and PSQI scores decreased by a clinically minimal important difference.

Subgroup analysis will be conducted to determine whether the severity of insomnia and the pattern identification of insomnia at baseline affect the clinical response to EA. We will also determine the correlation between objectively obtained sleep-related variables (actigraphy) and subjectively obtained ones (patient-reported questionnaires).

Ethics and dissemination

Any protocol amendments will be reapproved by the institutional review boards of the participating research centres, revised in the Clinical Research Information Service and reflected in the participants' informed consent form. A signed consent form reflecting the modification will be acquired from all participants. Licensed doctors of Korean medicine at each research centre will obtain informed consent.

The results of this trial will be reported in the relevant academic journals and conferences.

Patient and public involvement

The patients and public were not involved in planning and design of this study.

DISCUSSION

This study will be a randomised controlled, assessor-blinded, multicentre pilot clinical trial aiming to explore the effectiveness, safety and economics of EA for treatment-resistant insomnia. It will determine the feasibility of future large-scale clinical trials on treatment-resistant insomnia patients who have been on long-term sleeping pill use but are not satisfied with their sleep.

This study has some strengths. First, this is the first randomised trial in South Korea investigating EA as an adjunct therapy to hypnotic medication for treatment-resistant insomnia patients with moderately severe sleep disturbance despite taking sleeping pills for more than 3 months. Second, our study for treatment-resistant insomnia can provide the evidence reflecting the Korean traditional medical clinical practice settings, because most patients visiting Korean traditional medical clinics are already taking hypnotic medications. Finally, we will collect both subjective and objective data regarding sleep quality and quantity using self-reported questionnaires and actigraphy.

There are some limitations to this trial. First, participants and treatment providers are not blinded since a sham acupuncture procedure will not be applied in this trial. Therefore, when interpreting the study results, consideration should be given to the effects that other factors such as participants' expectations or the doctor–patient relationship may have had concerning treatment. Our objective is to evaluate the overall effectiveness and safety of EA for treatment-resistant insomnia, to explore the feasibility of a future large-scale clinical trial and not to examine the efficacy of EA compared with sham acupuncture. Second, while the assessor will be separated from the group allocation and will only distribute and ask participants to complete the outcome measurement in a separate room from where the EA treatment is conducted, complete blinding of the assessor may be difficult. Third, polysomnography is recommended when there is clinical suspicion of treatment-resistant insomnia; however, no objective diagnostic tools are used for the diagnosis of treatment-resistant insomnia in this study. In the absence of an international consensus, previous studies have defined treatment-resistant insomnia based on the duration of hypnotic use, which we will use in this study. Fourth, due to the broad age range of the inclusion criteria and the possibility of comorbidities with other medical conditions, the participants might be heterogeneous; therefore, heterogeneity should be considered when interpreting the results. Fifth, it might not be possible to completely control for new or additional sleeping pills used by participants after the start of the clinical trials. We will identify and analyse changes or additions to the participants' medication through monitoring their sleep diaries and undertaking interviews at every visit. Participants who take any prohibited treatment will be excluded from the study. Finally, the sample size of this trial is small (25 people per group) to examine the effectiveness of EA for treatment-resistant insomnia. This study is a pilot study to explore the effectiveness of EA for treatment-resistant insomnia and the feasibility of a large-scale clinical trial. The result of this study may have preliminary data for further full-scale randomised controlled trial to obtain strong evidence on the effectiveness and safety of EA for treatment-resistant insomnia.

Trial status

This study is in the process of recruiting participants, and it is expected to complete in September 2020.

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Contributors B-KK is responsible for supervising the clinical study and for communicating important protocol modifications to relevant parties. J-HL, S-HK and K-OK conceived the idea and designed this trial. J-HL and K-OK are responsible for the recruitment and treatment of participants. C-WK is responsible for the statistical analysis. This manuscript was drafted by J-HL and revised by S-HK. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study protocol has been ethically approved by the Institutional Review Boards of Pusan National University Korean Medical Hospital IRB (PNUKH2018006) and Dong-sin University Korean Medical Hospital in Gwang-Ju IRB (DSGOH-049_6). The approved trial protocol was registered at the Clinical Research Information Service (CRIS) of South Korea (CRIS-KCT0003235).

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