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Protocol

The effectiveness and safety of thread-embedding acupuncture for chronic rotator cuff disease: A study protocol for a randomized, patient-assessor-blinded, controlled, clinical trial

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ABSTRACT

Introduction: This report provides a clinical study protocol designed to verify the effects and safety of thread-embedding acupuncture (TEA) for chronic rotator cuff disease with regard to pain relief, improvement of shoulder function, and quality of life.

Methods/design: This is a study protocol of a randomized patient-assessor-blinded, controlled, clinical trial. This study will be carried out at Kyung Hee University Hospital at Gangdong in Korea. Participants with shoulder pain lasting more than 3 months will be recruited to the study. After eligibility screening, a total of 64 participants will be randomly allocated to one of the 2 groups in this trial, with 32 participants in each group. Over the 8 weeks treatment period, TEA and sham TEA will be performed in the respective groups once a week. In the follow-up phase, participants will undergo a telephone interview after 12 weeks and will visit for a final evaluation after 16 weeks.

Results: The primary outcome measure is the change in pain intensity between baseline and treatment completion (8 weeks). Secondary outcome measures include the values for pain intensity, shoulder disability, safety, satisfaction, and quality of life.

Conclusions: Previous studies have shown that TEA could be an alternative treatment for shoulder pain. However, there is still a lack of scientific evidence regarding the effectiveness of TEA for chronic rotator cuff disease. This study will provide useful evidence regarding the effectiveness and safety of TEA treatment. The findings will serve as important data for conducting additional acupuncture studies on chronic rotator cuff disease.

1. Introduction

Rotator cuff disease is widely known as the most common cause of chronic shoulder pain. In severe cases, this disease can lead to rotator cuff tear. However, the reasons underlying this disease and the process by which the inherent weakening occurs are not clear [1].

In recent years, it has become common to think of rotator cuff disease as a condition caused by multiple factors. The various causes are generally classified into internal factors, which are caused by problems in the rotator cuff itself and external factors, which are caused by the external environment and stimulation. Internal causes include changes in blood supply [2], collagen fibers, and the properties of local tendon tissues [3]. In contrast, external factors include morphological abnormalities of the acromioclavicular arch [4], excessive tension [5], repetitive use, and abnormalities in the motor mechanics [6].

However, it is unclear which of these causes are more important and how these factors differ in their significance. Therefore, definite diagnostic criteria for chronic rotator cuff disease are unclear [7], and clinical diagnosis is made on the basis of characteristic symptoms [8], pain in the rotator cuff area [9], patterns of joint movement [10], pain in specific postures [11], and the results of muscle strength tests [12]. However, it is unclear how clinically linked factors will influence the outcomes of treatment for rotator cuff disease. Conservative treatment is preferred for the treatment of rotator cuff disease, while surgical treatment is performed in cases with severe rotator cuff tears [13]. In general, rest and strengthening of the rotator cuff are the basic

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treatments. In some cases, analgesic agents, non-steroidal anti-inflammatory drugs (NSAIDs) [14], corticosteroid injections [15,16], and physical therapy are used [17–19], In addition, acupuncture [20–22] and moxibustion [23,24] are used as complementary and alternative medicine (CAM) therapies. However, effective therapies for relieving pain and improving shoulder function in chronic rotator cuff disease are lacking [25,26].

Thus, development of effective therapies for rotator cuff disease, which is also the most common cause of chronic shoulder pain and leads to rotator cuff tear, is an important issue in the treatment of shoulder disease. The most important factor for ensuring the eventual therapeutic effect of chronic rotator cuff disease is improvement in pain and shoulder function [27]. In addition, improvement in the patient's quality of life by minimizing rotator cuff weakness due to continuous shoulder use is preferable [28].

Aupuncture has been used worldwide in the treatment of various musculoskeletal disorders that present with pain and dysfunction [29–33]. Recently, various basic and clinical studies have reported that acupuncture is a safe and effective treatment for relieving pain, relieving tense muscles, and improving blood circulation in musculoskeletal diseases [34–38]. In particular, the positive effects of acupuncture for chronic shoulder pain have been reported in case reports [39], retrospective studies [40], and randomized controlled clinical trials [41–44]. However, clinical studies of acupuncture treatment for specific diseases that cause shoulder pain, such as chronic rotator cuff disease, are lacking, and its effect in improving shoulder function is unclear except that it provides temporary pain relief [45].

Continuous needle stimulation is an important acupuncture treatment technique for diseases that cause chronic pain, such as chronic rotator cuff disease [22]. In Korea, there is increasing interest in the use of thread-embedding acupuncture (TEA) which involves sustained stimulation of acupuncture point, for the treatment of chronic pain [46]. In general, acupuncture treatment is perceived to simply involve insertion of a needle into a specific acupoint. However, in clinical practice, various types of needles and acupuncture methods are used depending on the disease or its severity [47]. In particular, the subcutaneous needling therapy used to treat diseases confined to the body surface or shallow muscles has been developed into embedding acupuncture techniques such as intradermal acupuncture for a continuous therapeutic effect [48]. This approach has evolved into modern acupuncture methods such as TEA, which involves embedding absorbable foreign substances, such as catgut and polydioxanone sutures, into acupoints using needles [49]. Recent studies have reported that TEA improves the therapeutic efficacy by inducing a physiological inflammatory response via stimulation of soft tissues, and facilitating the accompanying regenerative response [50–52].

Most studies on TEA have focused on beauty or obesity treatments [53,54]. Recently, however, there have been more studies applied to musculoskeletal disorders [46]. In Korea, the efficacy of single or concurrent TEA for shoulder pain [55], ankle ligament injury [56], recurrent dislocation of the patella [57], lumbar disc herniation [58], degenerative knee osteoarthritis [59], and chronic low back pain [60] has been reported through various case reports. In research conducted overseas, subcutaneous needling treatment similar to TEA has been used for cervical spondylosis [61], myofascial pain syndrome [62], and low back pain [63] and has shown a significant effect in reducing pain or improving dysfunction.

The most effective indications for the TEA treatment are localized pain. However, various case reports have shown that TEA could also be an alternative treatment for pain that does not respond to general acupuncture treatment or easily recurs [46]. Nevertheless, there is still a lack of scientific evidence regarding the effectiveness of TEA for functional improvement and systemic pain for specific diseases. Therefore, randomized controlled clinical studies focusing on diseases with high patient demand are needed to confirm the efficacy and safety of TEA therapy and to expand its clinical application. In this study, based on an analysis of previous research, chronic rotator cuff disease was selected as a disease that is suitable for assessment of the expected effect of TEA therapy (local pain relief, tissue recovery through continuous soft tissue stimulation). The inclusion criteria for chronic rotator cuff disease were based on the diagnostic criteria confirmed by large-scale clinical studies and used in clinical practice [64]. In addition, a patient-assessor-blinded, randomized, controlled, clinical trial with sham TEA (STEA) as the control group will be conducted to clearly assess the effectiveness of TEA therapy. Ultimately, we would like to confirm that TEA treatment for chronic rotator cuff disease is effective and safe with regard to pain relief, improvement in shoulder function, and quality of life.

2. Methods and design

2.1. Trial design

This study is a randomized, patient–assessor blinded, sham-controlled trial with a two-group parallel design to be conducted in the Republic of Korea from August 2017 to December 2018. Sixty-two participants with shoulder pain lasting more than 3 months and diagnosed as having chronic rotator cuff disease according to the criteria selected through clinical examination will be randomly allocated to 2 groups in a 1:1 ratio. One group will comprise the treatment group (TEA group), and the other group will comprise the control group (sham TEA group). The primary endpoint will be 8 weeks after baseline. As illustrated in Fig. 1, participants will also be assessed in a follow-up assessment at 12 weeks from baseline. Final assessment will be performed at 16 weeks from baseline.

2.2. Setting and locations (recruitment)

Participants will be recruited from Kyung Hee University Korean Hospital at Gangdong. Clinical trial recruitment notices will be released in the local newspaper, hospital websites and advertisement boards on the subway for adequate subject recruitment.

2.3. Participants

Sixty-four participants with shoulder pain lasting more than 3 months will be recruited in the study. All participants will be interviewed by telephone and scheduled to undergo a screening visit by a clinical research coordinator (CRC). The eligibility of participants who voluntarily sign the consent form will be evaluated by the screening test. The acupuncture specialist will perform a standardized initial screening test. Participants who are diagnosed as having chronic rotator cuff disease on the basis of their medical history, and the results of physical examination, shoulder radiograhy, and blood tests will be referred to the independent investigator, who will perform the final eligibility assessments. After completing the screening test, participants will be provided with detailed information. Eligible participants will be randomly allocated into one of 2 parallel groups at a 1:1 ratio.

2.4. Eligibility criteria

Chronic rotator cuff disease is a term that collectively refers to diseases of the muscles or ligamentous fibrous membranes of the rotator cuff. In comparison with other major disease that cause shoulder pain such as rotator cuff tear, adhesions capsulitis, osteoarthritis calcific tendinitis, it is recognized as clinically distinct disease because of differences in symptoms, causes, prognosis, and treatment response. In this study, the inclusion and exclusion criteria for chronic rotator cuff disease are based on the studies of Hermans [64] and Bennell [65].

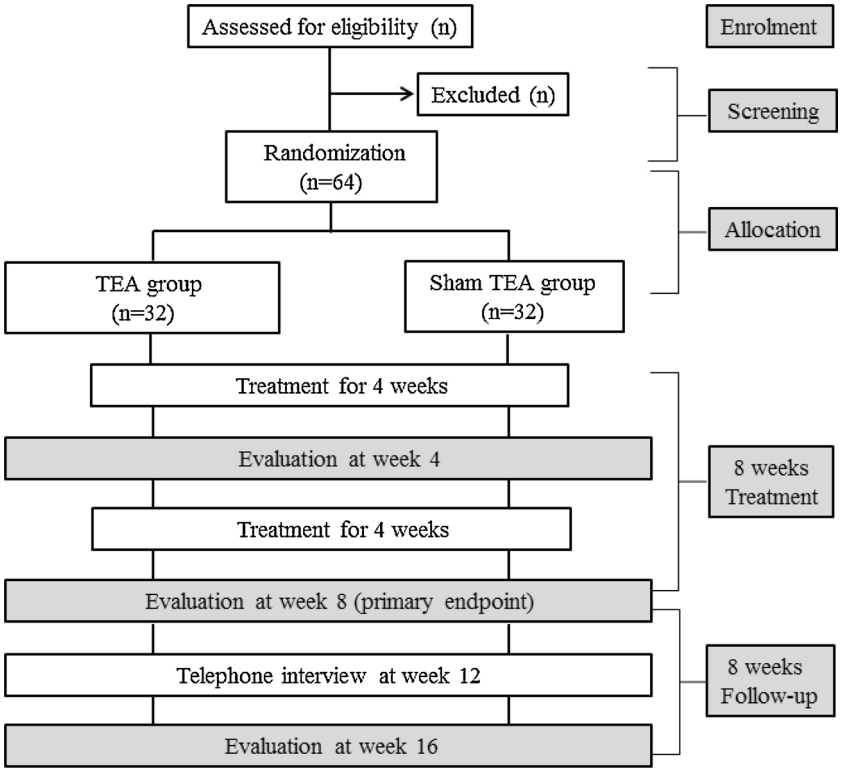

Fig. 1. Study design.

2.5. Inclusion criteria

Participants who meet the following criteria will be considered for enrolment

1 Men or women aged 18 years or over but under 65 years.
2 Shoulder pain lasting more than 3 months.
3 Severity of pain at activity (daily activity or light exercise) greater than 3/10 on a 0–100 mm pain visual analogue scale.
4 A positive painful arch of abduction between 60° and 120°.
5 Positive results in the shoulder abduction (empty can) stress test or external rotation resistance test.
6 Ability to communicate sufficiently with the researcher and complete the questionnaire.
7 Agreement to participate after providing written informed consent.

2.6. Exclusion criteria

Participants who meet any of the following criteria will be excluded.

1 Pain on rest greater than 7/10 on a 0–100 mm pain visual analogue scale.
2 Greater than 50% restriction of range of motion (ROM) of during movement in 2 or more shoulder planes.
3 Suspicion of rotator cuff tear based on the presence of a positive lag test (internal and external rotation).
4 Previous shoulder surgery.
5 Radiological evidence of osteoarthritis, calcific tendinitis or previous fracture.
6 Systemic pathology including inflammatory joint disease or neoplastic disorder.
7 Referred pain from spinal disease related to the cervical spine.
8 Intraarticular steroid injections in the previous 3 months.
9 Anti-inflammatory drugs in the previous 2 weeks.
10 Mental illness that precludes clinical test compliance.
11 Musculoskeletal disorders that may affect efficacy assessment, or any joint disease that is make it impossible for the patient to participate in the clinical trial.

2.7. Dropout or early termination

Dropouts or early termination are defined in the following scenarios

1 If the participant violates the inclusion criteria or meets the exclusion criteria.
2 If a serious adverse event occurs to the participant, or if the participant requests the suspension of the clinical trial due to an adverse event.
3 If participants receive less than 6 out of the 8 thread-embedding treatment sessions.
4 If the participants or their guardians withdraw the consent to participate in the clinical trial.
5 If the participants are taking medicines prohibited during the treatment period or during the observation period.
6 If it is judged by the researcher in charge that the progress of the clinical trial is inappropriate.

2.8. Randomization and allocation concealment

A total of 64 participants will be randomly assigned following the block stratified randomization procedure, with a 1:1 allocation ratio. Random numbers will be generated by an independent statistician using the website 'www.randomization.com' and sealed in sequentially numbered opaque envelopes. The envelopes will be delivered to the research center and kept in a double-blocked cabinet. The interviewer (CRC) will open the envelope after participants who meet the eligibility criteria provide informed consent, and allocate them to the treatment or control group according to the random number in the envelopes.

2.9. Blinding

This clinical trial is designed as a patient-assessor blinded study. Patient-assessor blinding will be conducted as TEA cannot be performed with the practitioner blinded. Practitioners will be prohibited from having any conversations other than those regarding TEA or STEA treatment. The participants will be told that they will receive treatment in one of 2 different ways, namely, “classical thread-embedding therapy” and “non-classical thread-embedding therapy”. All participants will receive the treatment in the same environment as that employed for acupuncture treatment at a Korean medical clinic. Both treatment and control groups will be treated with the same standardized TEA protocol. The STEA protocol is identical in appearance to the TEA protocol, except that the thread is removed and not inserted during the procedure. To assess whether patient-blinding has been successfully achieved in the 2 groups, the participants of both groups will undergo blinding test after final treatment. The outcome measure assessments will be performed by an independent assessor who did not perform the treatment or random assignment. The assessor will simply ask about the content of the assessment and the case record, and detail the content, but will not know abour the type of treatment the participants received. The participants, assessors, statisticians, and all related researchers will not know about the allocation, and the blinding will be maintained until the end of the trial.

2.10. Interventions

In both group, the intervention will be administered once a week for 8 weeks using a 29-gauge, 40 mm TEA or STEA needle (Hyundae Meditech, Wonju, South Korea) on 6 predefined acupoints selected by an expert group according to the Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) checklist. However, the thread will be removed STEA group. All other treatments affecting the outcomes will be prohibited during the trial period. All therapeutic procedures will be performed by acupuncture specialists in Korean medicine.

2.10.1. Thread embedding acupuncture group

The TEA procedure will be applied to acupoints located in the rotator cuff muscles. we have chosen acupoints and insertion methods that can maximize the sustained stimulation effect on the major shoulder muscles in addition to the existing acupuncture effect. For this reason, the transverse embedding will be used for the supraspinatus, infraspinatus, and the deltoid muscle. The perpendicular embedding will be used for teres minor muscle. In the supraspinatus muscle, one transverse embedding will be applied from the LI16 (concave point between the acromial end of the clavicle and the spine of the scapula) to the SI12 (middle point of supraspinatus fossa above spine of scapula) direction, and another transverse embedding from the SI12 to the SI13(concave point of the inner end of the spine of the scapula) direction (Fig. 2a). In the infraspinatus muscle, one transverse embedding will be applied from the SI11 (concave point between the upper one-third and lower two-thirds of the line connecting the midpoint of the spine of the scapula with the inferior angle of the scapula) to the SI10 (concave point below the inner end of the spine of the scapula) direction, and another transverse embedding from the SI11 to the SI12 direction (Fig. 2b). In the deltoid muscle, one transverse embedding will be applied from the middle point of LI15 (concave point between the outer edge of the acromion and the greater tubercle of the humerus) and TE14 (concave point between the acromial angle and the greater tubercle of the humerus) to the center of the deltoid (Fig. 2c). Transverse thread embedding will be performed in the shallow layers of the muscles. In the teres minor muscle, one perpendicular embedding will be applied to SI9 (approximately 3 cm from the back end of the axillary fold to the top) (Fig. 2b). Details of the treatment group intervention are described in STRICTA checklist (Table 1) [66].

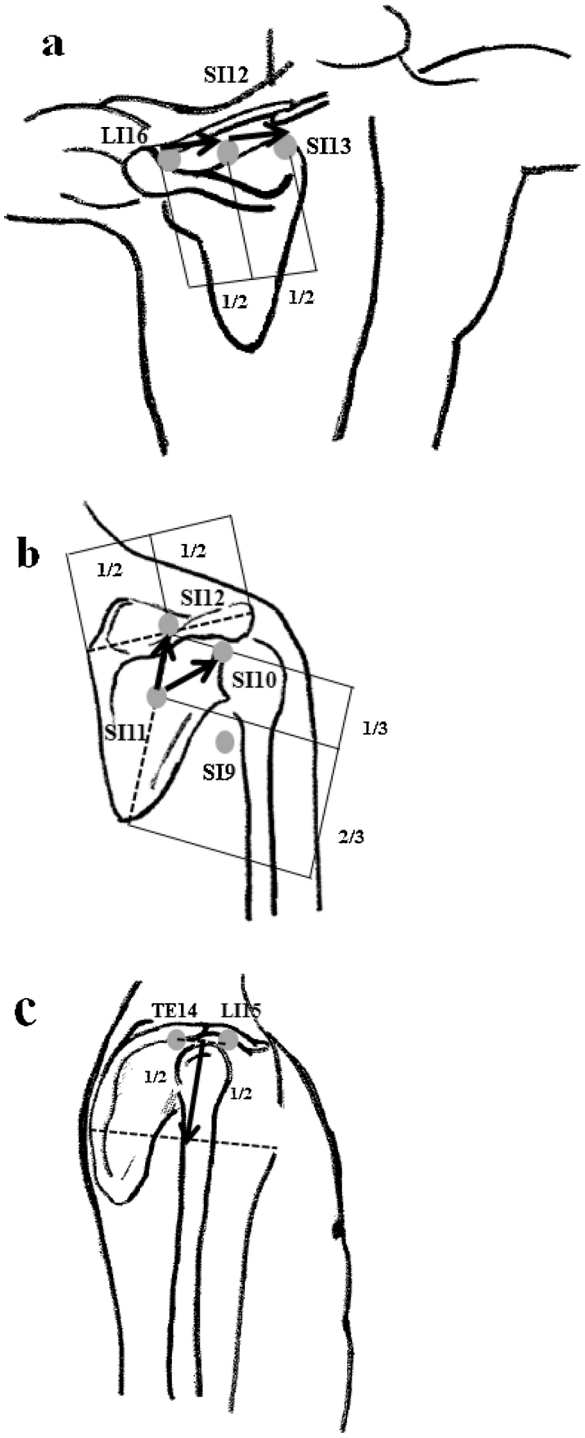

Fig. 2. Acupoint and needle embedding direction.

2.10.2. Sham thread embedding acupuncture group

All procedures in the STEA group, including the treatment period, number of treatments, acupoints, and size of TEA will be the same as that in the TEA group. However, the thread will be removed in the STEA group, and the thread removal procedure will be performed aseptically and secretly for patient-blinding and prevention of infection.

2.11. Prohibited and permitted concomitant treatment

All other interventions for shoulder pain, including surgical procedures, acupuncture, cupping, moxibustion, herbal medicine, physical therapy, or drugs administered for pain control (analgesics, muscle

Table 1
Deatails of acupuncture treatment based on the STRICTA 2010 checklist.

Item		Detail
1. Acupuncture rationale	**1a) Style of acupuncture**	TEA
	1b) Reasoning for treatment provided, based on historical context, literature sources, and/or consensus methods, with references where appropriate	Based on textbook of acupuncture and moxibustion medicine & consensus of the KMD
	1c) Extent to which treatment was varied	All participants will receive standardized treatment
2.Details of needling	**2a) Number of needle insertions per subject per session**	TEA: 6 ShamTEA: 6
	2b) Names of points used	[TEA] one transversal embedding from the LI16 to SI12 direction (supraspinatus) one transversal embedding from the SI12 to SI13 direction (supraspinatus) one transversal embedding from the SI11 to SI10 direction (infraspinatus) one transversal embedding from the SI11 to SI12 direction (infraspinatus) one transversal embedding from middle point of LI15 and TE14 to center of deltoid (deltoid) one perpendicular embedding on SI9 (teres minor) [Sham TEA] Performed in the same acupoints thread removed Sham Acupuncture used
	2c) Depth of insertion, based on a specified unit of measurement	1) Supraspinatus (2 points): Transverse embedding for 4cm 2) Infraspinatus (2 points): Transverse embedding for 4cm 3) Deltoid (1 points) : Transverse embedding for 4cm 4) Teres minor (1 points) : Perpendicular embedding for 4cm
	2d) Response sought	De-qi
	2e) Needle stimulation	[TEA]
	:	Thread embedded [ShamTEA] There is no needle stimulation since the acupuncture neddle is removed immediately after inserting
	2f) Needle retention time	[TEA] Thread Embedded [ShamTEA] There is no needle retention since the acupuncture neddle is removed immediately after inserting
	2g) Needle type	29 gauge, 40 mm TEA or STEA needle (Hyundae Meditech, Wonju, South Korea).
3. Treatment regimen	**3a) Number of treatment sessions**	8 sessions
	3b) Frequency and duration of treatment sessions	once a week for 8 weeks
4. Other components of treatment	**4a) Details of other interventions administered to the treatment group**	all other interventions for the shoulder pain including surgical procedures, acupuncture, cupping, moxibution, herbal medicine, physical theraphy, drug administered for the purpose of pain control (analgesis, muscle relaxants, antidepressants and anticonvulsant agent) are not allowed during 8 weeks of treatment phase. (It does not apply to follow up phase). However, among all medicines taken 4 weeks prior to participation in the clinical trial, drugs that have no affect shoulder pain related dysfunction are allowed under the investigator's judgment.
	4b) Setting and context of treatment, including instructions to practitioners, and information and explanations to patients	The study will be conducted at Korean Medicine hospitals. Study participants will be outpatients. All information except patient allocated group will be provided to participants.
5. Practitioner background	**5) Description of participating acupuncturists**	Licensed KMDs with at least 15 years of acupuncture clinical experiencetreatment. The practitioners have completed the course of acupuncture specialist graduated from the University of Korean Medicine. Standardized operation procedures were written for practitioners to ensure identical treatments.
6. Control interventions	**6a) Rationale for the control or comparator in the context of the research question, with sources that justify this choice**	Recent research on sham acupuncture has reported that simple insertion alone of the acupoint without any other needle stimulation could be effective. In this study, to confirm the embedding effect of thread, thread removed acupuncture needle was set as the control group so that the stimulation at the insertion of the needle was the same in both the experimental group and the control group. A control group was set up based on the existing sham acupuncture stuies and on textbook of acupuncture and moxibustion medicine, and the final decision was made through consensus of the KMD [42,45]
	6b) Precise description of the control or comparator. If sham acupuncture or any other type of acupuncture-like control is used, provide details as for Items 1 to 3 above.	All procedure of, control group including treatment period, number of treatments, acupoints and size of acupuncture will be same as that of experimental group. However, thread removed thread embedding acupuncture will be used for control group instead of normal thread embedding acupuncture

STRICTA, Standards for reporting interventions in clinical trials of acupuncture; Thread Embedding Acupuncture, TEA ; KMD, Korean Medicine Doctor.

relaxants, antidepressants and anticonvulsant agents) will not be allowed over the 8 week treatment period. (this does not apply to the follow-up phase). However, among the medicines taken 4 weeks prior to participation in the clinical trial, drugs that have no effect on shoulder pain-related dysfunction will be allowed under the investigator's judgment. Information on concomitant medications (name of the product, purpose of administration, dose, and duration of administration) will be recorded in the case record form at every visit.

Table 2
Schedule of enrolment, intervention, and assessments.

	STUDY PERIOD						
	Enrolment	Allocation	Post-allocation			Fallow-up	Close-out
TIMEPOINT**	$-Wk_2$	Wk_0	Wk_1[†]	Wk_4[†]	Wk_8[†]	Wk_{12}[*,†]	Wk_{16}[†]
ENROLMENT:							
Eligibility screen	X						
Informed consent	X						
Allocation		X					
INTERVENTIONS:							
TEA			◆———	———◆			
Sham TEA			◆———	———◆			
ASSESSMENTS:							
100 mm Pain VAS	X	X	X	X	X		X
SPADI		X	X	X	X		X
ROM of Shoulder		X	X	X	X		X
RC-QoL		X	X	X	X		X
EQ-5D-5L		X	X	X	X		X
Safety evaluation		X	X	X	X	X	X
Satisfaction evaluation					X		X
Blinding test							X
Confirmation of dropout		X	X	X	X	X	X

TEA, Thread Embedding Acupuncture; VAS, Visual Analogue Scale; SPADI, Shoulder Pain and Disability Index; ROM, range of motion; RC-QoL; Rotator Cuff of Quality of Life; EQ-5D-5L, EuroQol 5-Dimension 5 Levels.

* Telephone interview.

† Allowed ± 3 days on the specified date.

2.12. Study schedule of enrolment, allocation, and assessments

The schedule of assessments are shown in Table 2. This study is composed of screening, treatment and follow-up phases. In the screening visit, participants will sign informed consent forms. The investigator will conduct physical examinations, medical history-taking, shoulder radiography, blood tests, concomitant treatment assessment, and initial visual analogue scale (VAS) assessments to determine whether the participant is suitable for the clinical trial according to the eligibility criteria. After eligibility screening, the participant will be randomly allocated to one of 2 groups. In the treatment phase, baseline measurements will be obtained before the initial intervention begins. For the 8 week treatment period, participants will receive TEA or STEA once a week from visit 1 to visit 8. In the follow up phase, CRC will contact participants after 12 weeks (visit 9) by telephone interview, and participants will visit for a final evaluation after 16 weeks (visit 10). Outcomes for shoulder pain, dysfunction, and quality of life will be assessed after 4 weeks (visit 4), 8 weeks (visit 8), and 16 weeks (visit 10). Investigation of adverse events and concomitant treatment will be performed at every visit, and treatment satisfaction will be evaluated at 8 weeks (visit 8) and 16 weeks (visit 10).

2.13. Outcomes

The following outcome measures will be evaluated by assessors blinded to the group allocations. The primary outcome measurement will be intensity of shoulder pain and the secondary outcome measures will include values for pain intensity, shoulder disability and quality of life.

2.13.1. Primary outcome measure

Scores on the 100-mm pain VAS between baseline and treatment completion (8 weeks; primary endpoint) will be used as a primary outcome measure of this study and marked in 3 conditions, namely “VAS at rest”, “VAS at night”, and “VAS during motion”. “A painless state” will be recorded as 0, and “the most excruciating pain imaginable” will be recorded as 100. Participants will be asked about the pain intensity they felt during the past 24 h and they will record the state themselves.

2.13.2. Secondary outcomes measure

1 VAS for pain intensity

The intensity of shoulder pain will be assessed by determining changes in the average 100-mm pain VAS scores from baseline to 4 and 16 weeks using the same measurement method as primary outcome measure.

2 Shoulder pain and disability index

Shoulder pain-related dysfunction will be assessed using the Shoulder pain and disability index (SPADI) at visit 1 (baseline), visit 4 (after 4 weeks), visit 8 (after 8 weeks), and visit 10 (after 16 weeks). The SPADI consists of items divided into 2 subscales, with 5 items for pain and 8 items for disability [67]. Items are checked on a 10-point Likert scale (0 indicates “no pain” or “no difficulty”, 10 indicates “worst imaginable pain” or “so difficult it required help”). A SPADI score is calculated out of 100 (a higher score means more pain/disability).

3 Shoulder range of motion

The shoulder ROM of participants will be examined in 5 motions, namely, forward flexion (range, 0°-180°), external rotation at the side (range, 0°-90°), external rotation at 90° shoulder abduction (range, 0°-90°), internal rotation at 90° shoulder abduction (range, 0°-90°), and internal rotation behind the back [68]. Shoulder ROM will be measured using the goniometer at visit 1 (baseline), visit 4 (after 4 weeks), visit 8 (after 8 weeks), and visit 10 (after 16 weeks).

4 Rotator cuff of quality of life assessment

The rotator cuff quality of life index (RC-QOL) is a disease-specific health-related patient-reported outcome measure that was developed for use in patients with the “full spectrum of rotator cuff disease” [69]. The RC-QOL consists of 34 questions and 5 subscales: (1) symptoms and physical complaints, 16 items; (2) work-related concerns, 4 items; (3) recreational activities, sports participation, or competition concerns, 4 items; (4) lifestyle concerns, 5 items; and (5) social and emotional concerns, 5 items. Items are checked on a 100-mm VAS from 0 to 100;

the “the most excruciating pain or discomfort” will be recorded as 0, and “no pain or discomfort” will be recorded as 100. The RC-QoL score will be calculated by obtaining an average of the items answered by participants. It is calculated out of 100. The lowest score is 0%, indicating the worst quality of life, and the best quality of life or asymptomatic score was 100%.

5 EuroQoL 5-dimension 5 levels

The general health state of participants will be assessed using the Korean version of EuroQoL 5 dimensions 5 levels (EQ-5D-5 L) [70,71] at visit 1 (baseline), visit 4 (after 4 weeks), visit 8 (after 8 weeks), and visit 10 (after 16 weeks). The EQ-5D-5 L consists of 5 questions: morbidity, personal care, daily activities, pain/discomport, and anxiety/depression. Each question is rated from 1 to 5 (1, no problems; 2, slight problems; 3, moderate problems; 4, severe problems; 5, extreme problems). The EQ VAS scale can be used to assess a patient’s current health status. It is a 20-cm scale numbered from 0 to 100 (0, worst health condition imaginable; 100, best health condition imaginable) [72].

2.13.3. Safety outcomes

The investigator will check any adverse events (AEs) reported by the participant at each visit. An AE is an undesirable and unintended sign, symptom, or disease that occurs in a participant receiving an intervention used in a clinical trial. Changes in laboratory test valus at baseline and after 8 weeks will also be checked. Laboratory test will include assessments of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, blood urea nitrogen (BUN) level, creatinine (Cr) level, alanine transferase (AST) level, and alanine aminotransferase (ALT) level. The investigator will assess the severity of each AE and the major AEs reported during the trial based on WHO guidelines, with the severity rated as mild (no restriction on temporary or routine activity), moderate (some restricted activities), or severe (severely restricted activities or when medical treatment is absolutely required). A causal relationship between AEs and the intervention used in a clinical trial will be categorized to one of the following 6 criteria: definitely related, probably related, possibly related, probably not related, definitely not related, unknown. The investigator will record all information related to AEs in the case report form, including the name of the AE, date of occurrence, end date, severity, relevance to the drug, and treatment.

2.14. Blinding test

A blinding test will be conducted for the participants of the TEA and STEA groups at visit 10 (after the end of the study). The assessor will ask the participants what group they think they belong to. Participants will respond with one of the following answers; TEA, STEA, no idea.

2.15. Data monitoring

Data collection will be performed in accordance with the standard operation protocol of the KHUHGD Institutional Review Board (IRB), and the quality of the study will be managed by the clinical research associate (CRA) of independent contract research organization (CRO). Monitoring will include assessment of compliance of the recruitment and intervention procedures with the protocol and evaluation of the consistency between the records in the case report form and the original document. The monitoring process will also manage and report AEs that may occur during clinical trials.

2.16. Ethical approval

All patients will voluntarily participate and will be able to withdraw from the study at any time, if desired. All data obtained during the clinical trial will be recorded in the CRF and will confidentiality of this data will be maintained. Clinical trials will be conducted in compliance with Korea Good Clinical Practice (KGCP) and the Declaration of Helsinki. The trial has been approved by IRB of KHUHGD (IRB No: KHNMCOH 2017-06-006), and has been registered with the Clinical Research Information Service (CRIS) of South Korea, which has been registered as a Registry on the WHO International Clinical Trials Registry Platform (identifier : KCT0002563).

2.17. Sample size calculation

The sample size was calculated based on a previous study using the same primary outcome measure (100-mm pain VAS) among randomized controlled clinical trials of acupuncture for rotator cuff disease [73]. According to the study, the standard deviation (SD) was 26.246. The mean difference before and after treatment was set at 20 mm based on a study of minimal clinically important differences (MCID) of pain VAS for rotator cuff disease [74]. With a 5% significance level and 80% power, 1:1 ratio, the sample size was calculated to be 28, using the formula below (assuming $\sigma = 26.246$ and $d = 20$):

$$n = (1 + \lambda)\sigma^2(Z_{\alpha/2} + Z_{\beta})^2/\lambda d^2$$

Considering a 10% dropout rate, a total of 64 participants were needed (32 participants per group).

2.18. Statistical analysis

An independent statistician blinded to group allocation will perform statistical analysis using the Statistical Package for the Social Sciences (SPSS) for Windows version 18.0, and significance will be set at $P < 0.05$.

In efficacy analysis, both intention-to-treat (ITT) analysis set and per-protocol (PP) set will be used in this study, as follows. ITT analysis will be the main analysis method, while the PP analysis group will be analyzed as the assisted analysis method. The primary outcome measure of this study will be the mean change in the average 100-mm pain VAS scores acquired at baseline and 8 weeks. To validate significant changes between groups, changes in the VAS scores will be expressed as the mean ± SD, and independent t-tests will be performed for comparisons between groups. Trends over time and time-by-treatment interactions will be analyzed using repeated-measures analysis of variance (ANOVA). In the secondary outcome analysis, continuous variables will be analyzed in the same manner as the primary outcome analysis. Binomial variables will be presented as descriptive statistics (frequency, percentage) and Chi-squared test or Fisher's exact test will be performed for comparisons between groups.

3. Discussion

The analgesic effects of acupuncture have been demonstrated through various experimental studies [75]. Clinical studies of acupuncture treatment for musculoskeletal disorders with pain as a main symptom have also increased rapidly in recent years. In particular, there have been various clinical studies on the effectiveness of acupuncture treatment for shoulder pain [39,41–45].

The latest systematic review focusing on acupuncture treatment for shoulder pain suggests that acupuncture has short-term benefits for pain and function and may be superior to conventional drug therapy. However, there is little evidence supporting or refuting the use of acupuncture for shoulder pain due to the small sample sizes, inadequate blinding of patients and/or investigators, incomplete intervention descriptions, and lack of methodologically diverse attempts. Moreover, it has been reported that a better designed clinical trial is needed for translate the results into clinical practice [20,22]. Thereafter, various randomized controlled clinical studies were conducted to confirm the effectiveness of acupuncture treatment for shoulder pain. Recently,

several studies have reported that acupuncture for chronic shoulder pain is effective in improving pain and shoulder function [43–45].

However, there are a variety of diseases that can cause chronic shoulder pain, including frozen shoulder, impingement syndrome, rotator cuff disease, and biceps tendinopathy. In addition, because chronic rotator cuff disease, the most common cause of chronic shoulder pain, occurs due to the combined involvement of various causes, including internal factors (blood circulation abnormalities, collagen fiber abnormalities, abnormalities in tendon tissue structure) and external factors (abnormal acromial type, excessive tensile force, repeating use), practical application of conservative treatment including acupuncture is limited [25,26].

Clinically, there is a more effective method of acupuncture treatment for shoulder pain, depending on the purpose of the treatment. Generally, manual acupuncture is preferred to alleviate muscle tension, and bee venom acupuncture is more effective for analgesic and anti - inflammatory treatment [76]. Recently, there has been growing interest in the use of TEA in the treatment of musculoskeletal disorders to control pain and strengthen soft tissue [46]. Moreover, previous studies have been reported that TEA has the potential to be a candidate for single or collaborative treatment for chronic pain [55,58–60,63]. However, in order to apply new therapeutics techniques with some efficacy in clinical practice, the techniques must be evaluated through strictly designed clinical studies.

In this study, we will establish detailed diagnostic criteria for chronic rotator cuff disease on the basis of previous studies, and conduct a randomized controlled clinical study using the intervention procedure available in clinical practice to verify the efficacy and safety of TEA. This trial has several strengths: first, the inclusion criteria for participants with chronic rotator cuff disease were established through a detailed literature review and expert discussion. The diagnostic criteria of previous acupuncture studies for chronic shoulder pain were too broad to clarify the efficacy of acupuncture, and clinical studies for specific diseases such as chronic rotator cuff disease have rarely been performed. Second, to blind the participants and prevent needle-specific physiological effects, a sham TEA treatment was set as a control group. Because of the needle-specific physiological effects that occur when inserting a needle, it is impossible to blind the participants through sham acupuncture. However, in this study, we will perform patient blinding by achieving the same needle-specific physiological effect at needle insertion using a sham needle of the same size and shape. Finally, we will perform a blinding test to confirm whether patient blinding had been successfully achieved in these 2 groups. Third, experienced practitioners in acupuncture interventions will perform the procedures to increase the validity of the findings. To recognize the extent to which acupuncture provided in the context of a clinical trial reflects acupuncture in real-world clinical practice, an acupuncture specialist with abundant clinical experience will perform every treatment. Fourth, the effectiveness of TEA will be assessed synthetically using a variety of outcome measures. Although pain relief is the main treatment goal in shoulder-related diseases, improvement in shoulder function and recovery of daily life are more important. In this study, we will evaluate the effectiveness of acupuncture on pain, shoulder function, quality of life, and patient satisfaction. For quality of life, we will assess both the overall quality of life and the quality of life associated with rotator cuff disease. Thus, we will comprehensively evaluate the effect of TEA in various aspects of everyday life. Fifth, we will assess whether the clinical impact of TEA treatment persists. To investigate the clinical application range of TEA, we will evaluate the clinical effects after 2 months' follow-up as well as after treatment.

In addition to these strengths, in performing randomized controlled trials for TEA, the protocol and the selected acupoints have been rigorously designed and chosen by a process of consensus among experts according to STRICTA checklist [66]. All trial procedures will be performed by researchers trained to adhere to the study protocol and good clinical practice guidelines. In order to achieve a patient-assessor-blinded design, a sham TEA group was set as a control group, and the evaluation of outcomes will be conducted by an independent assessor. Data will be collected and verified through predefined database quality control procedures by the independent researchers and will be analyzed by independent statistical experts. All stages of clinical research conduct will be strictly conducted, monitored, and supervised by the independent CRO

There are some limitations to this study. When calculating the sample size, there is a limit to setting the sample size because there is no previous study consistent with this study. Moreover, the practitioner cannot not be blinded. In order to minimize the bias by the practitioner, during the procedure, we will restrict communication with the participants that is not related to the procedure.

4. Conclusion

Sample size and practitioner blindness might be limitations of our study protocol. Despite these limitations, our trial would provide useful evidence about the effectiveness and safety of TEA treatment for chronic rotator cuff disease. The findings will serve as important basic data for designing and conducting additional acupuncture clinical studies on chronic rotator cuff disease

Trial status

This trial is currently recruiting participants. It began on October 10, 2017 after IRB approval. The first participant was enrolled on November 2, 2017. We expect recruitment to be completed by the end of 2018.

Ethics approval and consent to participate

This study has been approved by the Institutional Review Board of Kyung Hee University Korean Medicine Hospital at Gangdong (IRB No: KHNMCOH 2017-06-006). The study will be performed in accordance with the approved protocol, and written consent will be obtained from every participant. This trial has been registered with Clinical Research Information Service (CRIS) of South Korea, which is registered as a Registry on the WHO International Clinical Trials Registry Platform (identifier : KCT0002563).

Conflict of interest

The authors declare that they have no conflict of interests.

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