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Thread embedding acupuncture for musculoskeletal pain: a systematic review and meta-analysis protocol

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ABSTRACT

Introduction Thread embedding acupuncture (TEA) is a special type of acupuncture that inserts certain medical threads (eg, catgut or polydioxanone) into subcutaneous tissue or muscles at specific points. Although TEA has been widely used for the treatment of musculoskeletal pain in Korea, China and Taiwan, evidence regarding its efficacy is lacking. The aim of this protocol is to evaluate the effectiveness and safety of TEA in the treatment of musculoskeletal pain, by conducting a systematic review and meta-analysis.

Methods and analysis The following 16 databases will be searched from their inception to 14 May 2017: MEDLINE, the Cochrane Central Register of Controlled Trials, EMBASE, the Cumulative Index to Nursing and Allied Health Literature, the Allied and Complementary Medicine Database, three Chinese database (China National Knowledge Infrastructure, the Chongqing VIP Chinese Science and Technology Periodical Database and the Wanfang database) and eight Korean databases (Korean Medical Database, Korean Association of Medical Journal Editors, Korean Studies Information Service System, Korean National Assembly Digital Library, National Digital Science Library, Oriental Medicine Advanced Searching Integrated System, 'Database Periodical Information Academic and Korean Traditional Knowledge Portal'). The WHO International Clinical Trials Registry Platform will also be searched to retrieve the recently completed studies. All randomised controlled studies in which TEA was used on specific points for the treatment of musculoskeletal pain will be included and no restrictions on language will be applied. The risk of bias of each study will be evaluated by the Cochrane risk of bias tool. Mean difference or standardised mean difference for continuous data and risk ratio for dichotomous data will be calculated with 95% CIs using a random effects model or a fixed effects model. Additional subgroup and sensitivity analyses will be conducted according to a predefined protocol.

Ethics and dissemination No ethical issues are predicted. The systematic review will be published in a peer-reviewed journal or conference presentation. These findings will summarise the current evidence of TEA for the treatment of musculoskeletal pain and may provide guidance for clinicians and patients to select TEA for musculoskeletal pain.

PROSPERO registration number CRD42015019046.

Strengths and limitations of this study

- ► To the best of our knowledge, this review will be the first systematic review to evaluate the effectiveness and safety of thread embedding acupuncture for musculoskeletal pain.
- ► Two review authors will select the studies, extract data and assess the risk of bias independently.
- ► This protocol has been conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses Protocols (PRISMA-P) 2015 Statement and registered in PROSPERO (International prospective register of systematic reviews).
- ► There might be few studies with a low risk of bias; hence, they might affect the quality of the evidence.

INTRODUCTION

Musculoskeletal pain is the most frequently reported medical disorder. In the general population, the prevalence of musculoskeletal pain varies from 40.4% to 69.3%.[1] Musculoskeletal pain leads to limitations in daily activities, loss of work productivity and increased medical costs. Moreover, the quality of life (QoL) of patients with musculoskeletal pain, such as chronic whiplash-associated disorders,[2] and chronic non-specific low back pain,[3] is significantly lower than that of healthy controls.

The most commonly prescribed pharmacological agents for musculoskeletal pain are non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen. However, the long-term use of these medications is not recommended because of considerable side effects, such as weight gain or loss, gastrointestinal symptoms and dizziness.[4] A Korean hospital outpatient analysis in 2009 showed that the prevalence of ulcer complications increased from 11.3% to 47.2% as the number of prescribed days of NSAIDs increased.[5] Recently, the US Food and Drug Administration strengthened its warning that NSAIDs can increase the risk of heart attack or stroke.[6] The interest

in non-pharmacological treatments for musculoskeletal pain, including complementary and alternative medicine (CAM), may have increased because of the deleterious side effects associated with pharmacological agents.[7] In particular, CAM modalities, such as manual therapy, yoga, physical therapy, and meditation, are known to have chronic pain-relief effects and are recommended as treatment modalities for pain.[8]

Acupuncture is a common CAM treatment modality, and many studies have demonstrated the effect of acupuncture on musculoskeletal pain, such as shoulder impingement syndrome,[9] acute lumbar sprain[10] and chronic neck pain.[11] A well-designed meta-analysis that compared manual and electroacupuncture with sham and no acupuncture controls revealed that acupuncture had a better effect than sham and no acupuncture controls in chronic pain conditions. However, the effect size was small to moderate, and more specific stimulation methods are warranted to determine the effect above the placebo effect.[12]

Thread embedding acupuncture (TEA) is special type of acupuncture that inserts medical threads (eg, catgut or polydioxanone (PDO)) into subcutaneous tissue or muscles at specific points (eg, traditional acupuncture points or tender points).[13] There are two components involved in TEA, a guide needle and the medical threads. TEA involves the insertion of a medical thread, which is attached to a guide needle, into the skin overlying specific acupuncture or tender points. The needle is removed after insertion and the medical threads remain embedded in the subcutaneous tissue or muscle. The embedded thread gradually softens, decomposes and dissolves with time in the subcutaneous tissue or muscle.[14] The complete absorption times differ with the types of threads. The absorption of PDO is known to be slow during first 3 months[15] and proceeds until 180–210 days.[14] When compared with acupuncture, TEA may produce a strong and long-lasting therapeutic effect. One Chinese randomised controlled trial (RCT) confirmed that TEA had a better effect than acupuncture in reducing the pain of patients with lumbar intervertebral disc herniation.[16]

With the availability of safe absorbable medical threads such as PDO, TEA has been widely used for the treatment of musculoskeletal pain in Korea, China and Taiwan. Treatments with TEA include frozen shoulder,[17] chronic low back pain[18] and osteoarthritis of the knee.[19] However, there is a lack of evidence on the contribution of TEA in the treatment of musculoskeletal pain. Therefore, this review will evaluate whether TEA is effective and safe compared with other treatments for the treatment of musculoskeletal pain, based on the pain severity, function, global assessments of participant improvement, QoL, analgesic consumption and adverse events.

OBJECTIVES

This study aims to review the evidence for effectiveness and safety of TEA, compared with other techniques in the treatment of musculoskeletal pain.

Research questions based on the PICOS (population, intervention, comparison, outcome, and study design) approach

- population: patients with musculoskeletal pain;
- intervention: TEA;
- comparison: no treatment/waiting list, sham control or active treatment (eg, physical therapy, oral medication, surgery, injection or other traditional medical treatments), except for herbal medicine;
- outcome: pain severity, function, global assessments of participant improvement, QoL, analgesic consumption and adverse events;
- study design: RCTs.

The details are described below.

METHODS AND ANALYSIS

Study registration

The protocol for this review was registered prospectively (CRD42015019046; http://www.crd.york.ac.uk/PROSPERO). This protocol was designed according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses Protocols (PRISMA-P) 2015 Statement. The PRISMA-P checklist is presented in the online supplementary appendix 1.

Eligibility criteria

Types of studies

Only RCTs of TEA for musculoskeletal pain will be included in this review. Quasi-randomised controlled studies, observational studies and experimental studies will be excluded. There will be no restrictions regarding the language that the studies are published in and only published studies will be included.

Types of participants

Participants with musculoskeletal pain undergoing TEA will be included. Pain induced from headache and systemic illness will not be included.[20] There will not be any restrictions based on disease onset and age of the participants.

Types of interventions and comparisons

Studies about the effect of TEA at specific points (eg, traditional acupuncture points or tender points) will be included. Studies in which the effects of TEA was compared with no treatment/waiting list, sham control or active treatment (eg, physical therapy, oral medication, surgery, injection or other traditional medical treatments) will be included. Studies in which the effects of TEA were compared with herbal medicine will be excluded. In case the participants of the TEA group received another active treatment, only studies in which the participants of all comparison groups

received the same active treatment as a cointervention will be included. Studies that compared general TEA with other types of TEA will be excluded.

Types of outcome measures

Primary outcome measures

1. Symptoms of pain that are identified using any pain scales (eg, numeric rating scale (NRS) or visual analogue scale (VAS)).
2. Functional outcome measures (eg, validated questionnaire or functional scale specific to the musculoskeletal disease, such as the range of motion (ROM)).
3. Severe adverse events related to the treatment.

Secondary outcome measures

1. Global assessment of participant improvement (eg, subjective improvement and proportion of overall improvement).
2. QoL assessed using a validated scale (eg, 36-item Short-Form or Euro-QoL).
3. Analgesic consumption.
4. Adverse events related to TEA or any other treatments.

Search methods for identification of studies

Electronic searches

The following 16 electronic databases will be searched from their inception to 14 May 2017: MEDLINE, the Cochrane Central Register of Controlled Trials, EMBASE, the Cumulative Index to Nursing and Allied Health Literature, the Allied and Complementary Medicine Database, three Chinese databases (China National Knowledge Infrastructure (CNKI), the Chongqing VIP Chinese Science and Technology Periodical Database and the Wanfang database) and eight Korean databases (Korean Medical Database, Korean Association of Medical Journal Editors, Korean Studies Information Service System , Korean National Assembly Digital Library, National Digital Science Library, Oriental Medicine Advanced Searching Integrated System, Database Periodical Information Academic and Korean Traditional Knowledge Portal). The search terms consisted of two parts: pain (eg, pain, analgesic, suffering or discomfort) and embedding therapy (eg, catgut embedding, catgut embedment, needle embedding or thread implantation). The online supplementary appendix 2 shows the detailed search strategies for MEDLINE, CNKI and Korean databases.

Searching other resources

The WHO International Clinical Trials Registry Platform will be searched to retrieve recently completed studies. Relevant publications (eg, textbooks on acupuncture and the references within the included studies) will be manually searched.

Data collection and analysis

Selection of studies

Two independent reviewers (YC and SL) will screen the titles and abstracts to assess their suitability for inclusion. YC and SL will read the full texts of the suitable studies and perform further selection based on the inclusion criteria. Disagreements will be resolved by discussion between the authors.

Data extraction and management

Two independent reviewers (YC and SL) will read the full texts of each article and extract the data using a data extraction form. The data extraction form includes the author, year, disease, duration, type of treatments, numbers of participants analysed/randomised, numbers of treatments, follow-up, outcome measures, results and adverse events. Any disagreements will be resolved by discussion.

Assessment of risk of bias and reporting quality in included studies

Two independent reviewers (YC and SL) will assess the risk of bias based on the Cochrane Collaboration's 'risk of bias' tool. The risk of bias tool covers six domains: sequence generation, allocation concealment, blinding of participants, blinding of outcome assessors, incomplete outcome data and selective outcome reporting.[21] The risk of bias for each domain will be rated as 'low risk', 'high risk' or 'unclear risk'.

Measures of treatment effect

The mean difference or standardised mean difference will be used to assess the treatment effect with 95% CIs for continuous data (eg, VAS, NRS or scores of functional outcome measures). Standardised mean difference will be used when calculating the same outcome variables using different scales and methods. The risk ratio will be used to assess the treatment effect with 95% CIs for dichotomous outcomes (eg, responder or non-responder). Ordinal outcomes (eg, 'almost cured', 'remarkably effective', 'effective' or 'not effective') in two or more categories will be converted to dichotomous outcomes, such as responder and non-responder.

Dealing with missing data

When there are insufficient data or missing data, the corresponding author will be contacted to request additional information or clarification. If the corresponding author cannot be contacted, the available data alone will be analysed.

Assessment of heterogeneity

The heterogeneity between different studies will be measured using a visual inspection of the forest plot and χ^2 test with statistical significance. The I^2 statistic will be calculated to assess inconsistencies in the results of the included studies. The I^2 results will be interpreted as follows: unimportant heterogeneity (0%–40%), moderate heterogeneity (30%–60%), substantial heterogeneity (50%–90%) and considerable heterogeneity (75%–100%)%).[21] When considerable heterogeneity cannot be explained by the diversity in clinical or methodological aspects of the included studies, the data will not be pooled.

Assessment of reporting biases

If the numbers of studies used in the analyses are sufficient, funnel plots will be used to detect reporting biases.[21] When there is a funnel plot asymmetry, possible factors for the asymmetry (eg, small-study effects or poor methodological quality) will be identified.

Data synthesis

The meta-analyses will be performed using the Review Manager (RevMan) software (V.5.3.5 for Windows; the Nordic Cochrane Centre, Copenhagen, Denmark). A random effects model or a fixed effect model with 95% CIs will be used to calculate the pooled estimates of effect size. When there is considerable heterogeneity (I^2>75%) that cannot be explained by the methodological and clinical diversity, the meta-analysis will not be conducted. If the quantitative synthesis is not appropriate, the summary of the studies will be done in a narrative form. When dichotomous data in studies comparing TEA with two or more controls will be assessed for meta-analysis, the data of the TEA group will be divided equally and compared individually with control groups to avoid double counting.[22]

Subgroup analysis and investigation of heterogeneity

When the numbers of available studies are sufficient, subgroup analyses will be utilised to interpret the heterogeneity across studies according to the following:

1. type of thread (eg, absorbability or size);
2. type of control (eg, no treatment/waiting list, sham control, or active treatment);
3. duration of disease (eg, acute (up to 1 month), subacute (1–3 months) or chronic (more than 3 months));
4. duration of follow-up (eg, short term (within four weeks), medium term (up to six months) and long term (more than six months)).

Sensitivity analysis

Sensitivity analyses will be performed when possible to determine whether the results are robust according to the following:

1. methodological quality (eg, whether sequence generation and allocation concealment were adequately conducted);
2. sample size (eg, greater or less than 30 participants in each group);
3. analysis-related issues (eg, cut-off point of ordinal scale to dichotomous scale; 'almost cured, remarkably effective and effective' as a responder vs 'almost cured and remarkably effective' as a responder).

Summary of evidence

In case there are sufficient data, the results of the main outcomes will be summarised in the 'Summary of findings' tables using the Grading of Recommendations Assessment, Development and Evaluation approach to evaluate the quality of evidence.[21]

DISCUSSION

The aim of this systematic review is to evaluate the effectiveness and safety of TEA for the treatment of musculoskeletal pain. The first detailed record of the medical application of TEA was in 'Taepyeonghyeminbang (太平惠民方)' published in 982 AD.[23] However, TEA was probably not widely used because of the difficulty of the technique and the absence of proper absorbable materials. With the development of special types of absorbable medical threads, such as chromic catgut and PDO, TEA has become more widely used in Korea, China and Taiwan.

Needle insertion during TEA treatment may induce an analgesic effect through mechanisms similar to that of manual acupuncture. The mechanisms of analgesia with acupuncture include enhanced local circulation,[24 25] segmental effects based on the gate-control theory[24] and extrasegmental effects with descending inhibitory pain control.[26] Moreover, enhanced stimulation induced by an embedded thread might have additional pain relief mechanisms. An animal study demonstrated that TEA produced a regulative effect on nitric oxide,[27] which is an important factor in the processing of persistent neuropathic pain.[28] Another animal study mentioned that the injection of PDO into mice with rheumatoid arthritis had an anti-inflammatory effect by increasing interleukin-10.[29]

This systematic review will provide current evidence on the effectiveness and safety of TEA for musculoskeletal pain. These findings will provide guidance to clinicians and patients on the use of TEA for musculoskeletal pain. Moreover, these results are also available to healthcare professionals in Western countries who are unfamiliar with the use of TEA. Further clinical research will be designed based on this systematic review.

Contributors YC and SL contributed to the development of the search strategy, searched and selected the studies, also read the full texts of studies, extracted data, assessed the risk of bias and reported quality of evidences and contributed to the initial drafting. JDL will act as an arbiter in the selection stage. JK and JWK made revisions. All authors have read and approved the final manuscript for publication.

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Competing interests None declared.

Patient consent Detail has been removed from this case description/these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement All exracted data will be available on request to the extent that it is not reported in the systematic review article.

REFERENCES

1. Abdulmonem A, Hanan A, Elaf A, *et al*. The prevalence of musculoskeletal pain and its associated factors among female Saudi school teachers. *Pak J Med Sci* 2014;30:1191–6.
2. Coppieters I, Ickmans K, Cagnie B, *et al*. Cognitive performance is related to central sensitization and health-related quality of life in patients with chronic whiplash-associated disorders and fibromyalgia. *Pain Physician* 2015;18:E389–401.
3. Murthy V, Sibbritt DW, Adams J. An integrative review of complementary and alternative medicine use for back pain: a focus on prevalence, reasons for use, influential factors, self-perceived effectiveness, and communication. *Spine J* 2015;15:1870–83.
4. Ussai S, Miceli L, Pisa FE, *et al*. Impact of potential inappropriate NSAIDs use in chronic pain. *Drug Des Devel Ther* 2015;9:2073–7.
5. Cho J, Lee E, Shin WG. Evaluation of NSAID usage and appropriateness for prevention of NSAID-related ulcer complications. *Kor J Clin Pharm* 2012;22:211–9.
6. Food US, Administration D. FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can cause heart attacks or strokes. http://www.fda.gov/Drugs/DrugSafety/ucm451800.htm2015 (accessed 11 Nov 2016).
7. Ventola CL. Current issues regarding complementary and alternative medicine (CAM) in the United States: part 1: the widespread use of CAM and the need for better-informed health care professionals to provide patient counseling. *P T* 2010;35:461–8.
8. Bauer BA, Tilburt JC, Sood A, *et al*. Complementary and alternative medicine therapies for chronic pain. *Chin J Integr Med* 2016;22:403–11.
9. Rueda Garrido JC, Vas J, Lopez DR. Acupuncture treatment of shoulder impingement syndrome: a randomized controlled trial. *Complement Ther Med* 2016;25:92–7.
10. Lin R, Zhu N, Liu J, *et al*. Acupuncture-movement therapy for acute lumbar sprain: a randomized controlled clinical trial. *J Tradit Chin Med* 2016;36:19–25.
11. MacPherson H, Tilbrook H, Richmond S, *et al*. Alexander technique lessons or acupuncture sessions for persons with chronic neck pain: a randomized trial. *Ann Intern Med* 2015;163:653–62.
12. Vickers AJ, Cronin AM, Maschino AC, *et al*. Acupuncture for chronic pain: individual patient data meta-analysis. *Arch Intern Med* 2012;172:1444–53.
13. Shin HJ, Lee DJ, Kwon K, *et al*. The success of thread-embedding therapy in generating hair re-growth in mice points to its possibly having a similar effect in humans. *J Pharmacopuncture* 2015;18:20–5.
14. Bhargava D, Anantanarayanan P, Prakash G, *et al*. Initial inflammatory response of skeletal muscle to commonly used suture materials: an animal model study to evaluate muscle healing after surgical repair – histopathological perspective. *Med Oral Patol Oral Cir Bucal* 2013;18:e491–6.
15. Molea G, Schonauer F, Bifulco G, *et al*. Comparative study on biocompatibility and absorption times of three absorbable monofilament suture materials (polydioxanone, poliglecaprone 25, glycomer 631). *Br J Plast Surg* 2000;53:137–41.
16. Jaing Y, Cheng J, Ding M, *et al*. Clinical observation of lumbar disc herniation treated with material modified embedding. *J Tradit Chin Med* 2015;42:846–7.
17. Ny J, Roh JD. Effects of embedding therapy on frozen shoulder: a prospective study. *J Korean Med* 2015;36:1–7.
18. Kim SW, Shin JC. The effects of Korean medical treatment combined with embedding acupuncture on patients with chronic lower back pain: a retrospective study. *The Acupuncture* 2016;33:165–71.
19. Lee JH, Yang TJ, Lee DG, *et al*. The effect of needle-embedding therapy on osteoarthritis of the knee combined with Korean medical treatment: report of five cases. *The Acupuncture* 2014;31:195–204.
20. Law D, McDonough S, Bleakley C, *et al*. Laser acupuncture for treating musculoskeletal pain: a systematic review with meta-analysis. *J Acupunct Meridian Stud* 2015;8:2–16.
21. Hj GS. The Cochrane Collaboration. Cochrane handbook for systematic reviews of interventions version 5.1.0, 2011. www.cochrane-handbook.org.
22. Lee S, Park J, Kim J, *et al*. Acupuncture for postoperative pain in laparoscopic surgery: a systematic review protocol. *BMJ Open* 2014;4:e006750–5.
23. Park YE. Medicine wire injection therapy. *Seoul: Haenglimseowon* 2003:23.
24. White A, Cummings M, Filshie J. *An introduction to western medical acupuncture*. Churchill Livingstone Elsevier Edinburgh, New York 2008:19–40.
25. Carlsson C. Acupuncture mechanisms for clinically relevant long-term effects – reconsideration and a hypothesis. *Acupunct Med* 2002;20:82–99.
26. Silva JR, Silva ML, Prado WA. Analgesia induced by 2- or 100-Hz electroacupuncture in the rat tail-flick test depends on the activation of different descending pain inhibitory mechanisms. *J Pain* 2011;12:51–60.
27. Xie XX, Kou ST, Pu ZH, Zh P, *et al*. [Effects of scalp catgut embedding on SOD, NO, MDA in the rat with Parkinson's disease]. *Zhongguo Zhen Jiu* 2007;27:753–6.
28. Schmidtko A. Nitric oxide-mediated pain processing in the spinal cord. *Handb Exp Pharmacol* 2015;227:103–17.
29. Gollapudi S, *et al*. Safety and efficacy of polydioxanone nano-fibers as anti-inflammatory agents. *J Nanomedine Biotherapeutic Discov* 2014;04:1–6.