

BMJ Open Acupuncture for neck pain caused by cervical spondylosis: a systematic review and meta-analysis protocol

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ABSTRACT

Introduction Neck pain causes serious social and economic burden. Research on the use of acupuncture for managing cervical spondylosis has increased over time, with the quality of studies showing an improved trend. The present study seeks to use a systematic review approach to understand efficacy and safety of acupuncture for treatment of neck pain caused by cervical spondylosis.

Methods and analysis We will search PubMed, Web of Science, Cochrane Library, Embase, China National Knowledge Infrastructure, Chinese BioMedical Literature, Wanfang database and VIP databases, from their inception to July 2020, to identify and retrieve all randomised controlled trials, describing the use of acupuncture for treatment of cervical spondylosis. Thereafter, two reviewers will independently select the studies, extract data and assess the risk of bias. Any disagreements, between them, will be resolved through a discussion with a third reviewer. Data synthesis and statistical analyses will be performed using the Revman V.5.3 software. Specifically, data will be synthesised by either fixed-effects (heterogeneity less than 50%) or random-effects models, following a heterogeneity test, with outcome measures focusing on pain intensity, functional disability, psychological improvements and adverse events. In cases where no considerable heterogeneity is detected, a meta-analysis will be conducted.

Ethics and dissemination No ethical approval will be required for this study, since it does not infringe on anyone's interests. The findings will be published in a peer-reviewed journal or disseminated through conferences.

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INTRODUCTION

Neck pain (NP) is a prevalent musculoskeletal disorder. The annual prevalence rate of NP exceeds 30%, making it the fourth leading cause of disability.¹ NP is a multifactorial disease being associated with various dysfunctions, among them is cervical spondylosis which causes NP.² The Chinese Association of Rehabilitation Medicine defines cervical spondylosis as a series of clinical syndromes resulting from degenerative changes of cervical intervertebral disc and secondary pathological changes involving surrounding tissue structures (nerve root, spinal cord,

Strengths and limitations of the study

- The protocol was written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol guidelines.
- We will use a broad and comprehensive search strategy to search multiple electronic databases.
- To ensure that the included studies are free of personal bias, study selection, data extraction and bias risk assessment will be performed independently by two reviewers.
- The special nature of acupuncture implies that it will be difficult to perform a double-blind study.
- We anticipate possible heterogeneity among the studies to be included, owing to existence of multiple types of cervical spondylosis.

vertebral artery, sympathetic nerve). On the basis of clinical symptoms, signs and imaging tests (X-ray film, functional magnetic resonance), cervical spondylosis can be divided into nerve root type (ICD-10-CM G54.251), vertebral artery type (ICD-10-CM M47.025+) and other types.³ Previous studies showed that age,⁴ occupational factors,^{5 6} ongoing postures and/or repetitive movements contribute to the development of spondylosis.⁷ In recent years, with the change in people's lifestyles, the age of onset of this condition has decreased.⁸ Cervical spondylosis has become an important healthcare and social problem.

Due to the complexity of its aetiology and high recurrence, the targets of treatment options for NP are poor. Evidence shows that studies on the analgesic efficacy of interventional therapy are mixed, especially surgery and cervical epidural injections.⁹⁻¹² Some medicines (eg, muscle relaxants and non-steroidal anti-inflammatory drugs) have been effective in alleviating acute pain, but its side effects cannot be ignored.¹³ It is therefore imperative to explore and develop complementary and alternative therapies to improve patient outcomes. So far, therapies such as lifestyle interventions,¹⁴ exercise,^{15 16}

psychological therapies¹⁷ and ergonomical interventions have been proven to have a favourable risk ratio (RR) and availability.^{18,19} Among them, acupuncture, a component of traditional Chinese medicine, has been extensively used in the treatment of pain for more than 3000 years.²⁰ In practice, acupuncture involves a series of procedures, including inserting a filament needle into a specific acupuncture point, and then stimulating the acupuncture point by adjusting the needle.

Studies suggest that acupuncture confers analgesic effects through various mechanisms. In terms of the neurophysiological mechanisms, acupuncture activates the activating endogenous antinociceptive systems and decremental suppression systems to relieve pain.²¹ This is achieved via interaction and integration of the two different sensations of the acupuncture signal and the pain signal at different levels of the central nervous system. In terms of the neurochemical mechanisms, a series of studies have shown that interactions between different 'classical' neurotransmitters in the prefrontal cortex mediate the inhibition of pain perception.²² 5-hydroxytryptamine (serotonin) have been implicated in the modulation of central and peripheral pain. Similar to serotonin, norepinephrine (NE) is an important transmitter of the postganglia sympathetic nerve and many other central neurons. The upper and lower NE fibres project to the brain and spinal cord, respectively, and collectively they participate in the analgesic effects of acupuncture.²³ In addition, compelling evidence suggests that acupuncture can increase the release of opioid peptides in the brain, regulate the content of β -endorphin (β -EP), and induce analgesia.^{24,25} This indicates that acupuncture is an effective treatment option for NP.

However, the effect of acupuncture on NP seems controversial based on evidence-based perspective. Several systematic reviews (SRs) have been carried out to assess the clinical benefits of acupuncture therapy for NP, but findings from such studies have been inconclusive. A review conducted by Cagnie *et al* concluded that acupuncture was more effective than placebo intervention, but similar to other interventions.²⁶ Even more, Smith *et al* suggested that it was no more effective than the placebo.²⁷ Furthermore, inconsistent results have been reported across SRs with regard to differences between acupuncture and other interventions.^{28–30} Recently, it has been noticed with great interest that some new randomised controlled trials (RCTs) regarding acupuncture in cervical spondylosis have been published.^{31–34} Thus, we present this SR protocol designed to investigate the efficacy and safety of acupuncture for NP caused by cervical spondylosis.

MATERIAL AND METHODS

Protocol and registration

The protocol was developed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines. The review will be conducted in accordance with the PRISMA guidelines.³⁵

The study is expected to begin searching in July 2020 and end in March 2021.

Criteria for including studies for the review

Types of studies

We will include all RCTs that evaluated acupuncture therapy for NP caused by cervical spondylosis. To avoid risk of bias, crossover trials, cluster-RCTs, quasi-RCTs or trials without control group will be excluded. Only studies written in English and Chinese will be included.

Types of participants

Participants diagnosed with cervical spondylosis will be included. Diagnostic criteria will include the International Statistical Classification of Diseases and Health-Related Problems,³⁶ Treatment and Rehabilitation of Cervical Spondylosis. Participants with cervical spondylosis without NP will be excluded. No restrictions will be applied in terms of age, gender and ethnicity.

Types of interventions

Acupuncture therapies will include body acupuncture, manual acupuncture, warm acupuncture, ear acupuncture, plum blossom needling, fire needling and electroacupuncture. However, studies investigating transcutaneous electrical nerve stimulation, acupressure and laser stimulation as acupuncture interventions will be excluded. In addition, studies comparing between different types of acupuncture therapies will be excluded.

Types of comparator(s)/control

Interventions to be compared will include sham acupuncture (interventions mimicking 'verum' acupuncture, but do not pierce the skin), waiting list control, herbal medicine, moxibustion, wet cupping, western medicine, usual care and psychological intervention. In addition, any control group who underwent skin penetration by needles will be excluded. Furthermore, we will include studies that compared acupuncture combined with any other type of non-acupuncture versus non-acupuncture intervention.

Type of outcome measures

Primary outcomes

Pain intensity will be measured using scales such as the Visual Analogue Scale, Northwick Park Questionnaire and Numeric Rating Scale.

Secondary outcomes

1. Functional disability, measured by the Neck Disability Index and Oswestry Disability Index.
2. Psychological improvements, measured by scales such as the Hamilton Anxiety Rating Scale and Self-rating Anxiety Scale.
3. Adverse events.

Patient and public involvement

The study was a non-clinical trial that did not seek the participation of patients or the public.

Table 1 Search strategy in PubMed

| | |
|-----|--|
| #1 | pain. Mesh |
| #2 | pain. ti, ab |
| #3 | ache. ti, ab |
| #4 | sore. ti, ab |
| #5 | stiff. ti, ab |
| #6 | discomfort. ti, ab |
| #7 | #1 or #2 or #3 or #4 or #5 or #6 |
| #8 | neck pain. Mesh |
| #9 | neck pain. ti, ab |
| #10 | neck disorder. ti, ab |
| #11 | neck muscles. ti, ab |
| #12 | neckache. ti, ab |
| #13 | cervicalgia. ti, ab |
| #14 | cervicodynia. ti, ab |
| #15 | cervical pain. ti, ab |
| #16 | posterior cervical pain. ti, ab |
| #17 | cervical plexus. ti, ab |
| #18 | cervical vertebrae. ti, ab |
| #19 | cervical spine. ti, ab |
| #20 | cervical spondylosis. ti, ab |
| #21 | cervical spondylopathy. ti, ab |
| #22 | cervical spondylitis. ti, ab |
| #23 | cervical radiculopathy. ti, ab |
| #24 | cervical disk. ti, ab |
| #25 | atlanto-axial joint. ti, ab |
| #26 | atlanto-occipital joint. ti, ab |
| #27 | spinal nerve roots. ti, ab |
| #28 | nerveroot. ti, ab |
| #29 | brachial plexus. ti, ab |
| #30 | brachial neuralgia. ti, ab |
| #31 | intervertebral disc degeneration. ti, ab |
| #32 | intervertebral disk degeneration. ti, ab |
| #33 | spondylosis. Mesh |
| #34 | lumbar spine. Mesh |
| #35 | #33 not #34 |
| #36 | #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #35 |
| #37 | Acupuncture. Mesh |
| #38 | acupuncture therapy. Mesh |
| #39 | acupoint. ti, ab |
| #40 | manual acupuncture. ti, ab |
| #41 | scalp acupuncture. ti, ab |
| #42 | ear acupuncture. ti, ab |
| #43 | electroacupuncture. ti, ab |
| #44 | abdominal acupuncture. ti, ab |
| #45 | balance acupuncture. ti, ab |
| #46 | fire needling. ti, ab |
| #47 | warm needling. ti, ab |
| #48 | plum blossom needling. ti, ab |

Continued

Table 1 Continued

| | |
|-----|--|
| #49 | #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 |
| #50 | randomize controlled trial. Pt |
| #51 | controlled clinical trial. Pt |
| #52 | randomize. ti, ab |
| #53 | Placebo. ti, ab |
| #54 | randomly. ti, ab |
| #55 | trial. Ti |
| #56 | #50 or #51 or #52 or #53 or #54 or #55 |
| #57 | humans. Mh |
| #58 | #56 and #57 |
| #59 | #36 and #49 and #58 |

Search methods for identification of studies

The following electronic databases: PubMed, Web of Science, Cochrane Library, Embase, China National Knowledge Infrastructure, Chinese BioMedical Literature, Wanfang database and VIP Database will be searched from inception to July 2020. In addition, we will scrutinise the list of references, relevant conference literature and trial registry database (WHO International Clinical Trials Registry Platform and ClinicalTrials.gov) to identify additional studies.

The search strategy for PubMed is shown in [table 1](#). The following search terms will be used singly or as combinations (MeSH terms and free words): pain, acupuncture, acupuncture therapy and randomised controlled trial. The search terms will be translated into Chinese for study identification in Chinese databases.

Data collection and analysis

Selection of studies

Two reviewers will be required to screen the retrieved studies independently. Briefly, they will exclude duplicate studies and those not matching the inclusion criteria by reading title and abstracts. They will read the full text of each study to select those meeting the inclusion criteria. Any disagreements will be resolved through discussion with a third reviewer. The entire study selection process is shown in the flow diagram ([figure 1](#)).

Data extraction

Data extraction from the included studies will be done independently by two reviewers following a data acquisition list. The list will include the basic information (author, title, journal, year of publication and country of publication), study design (study size, randomisation, allocation concealment, blinding methods, type of interventions and treatment duration), outcome measures and conflicts of interest. If necessary, a third reviewer will double-check the data to ensure consistency.

If data are missing or incomplete in any study, we will contact with the authors to obtain such data. In case it is impossible to obtain the data, to ensure the statistical power and avoid bias, the last observation carried forward

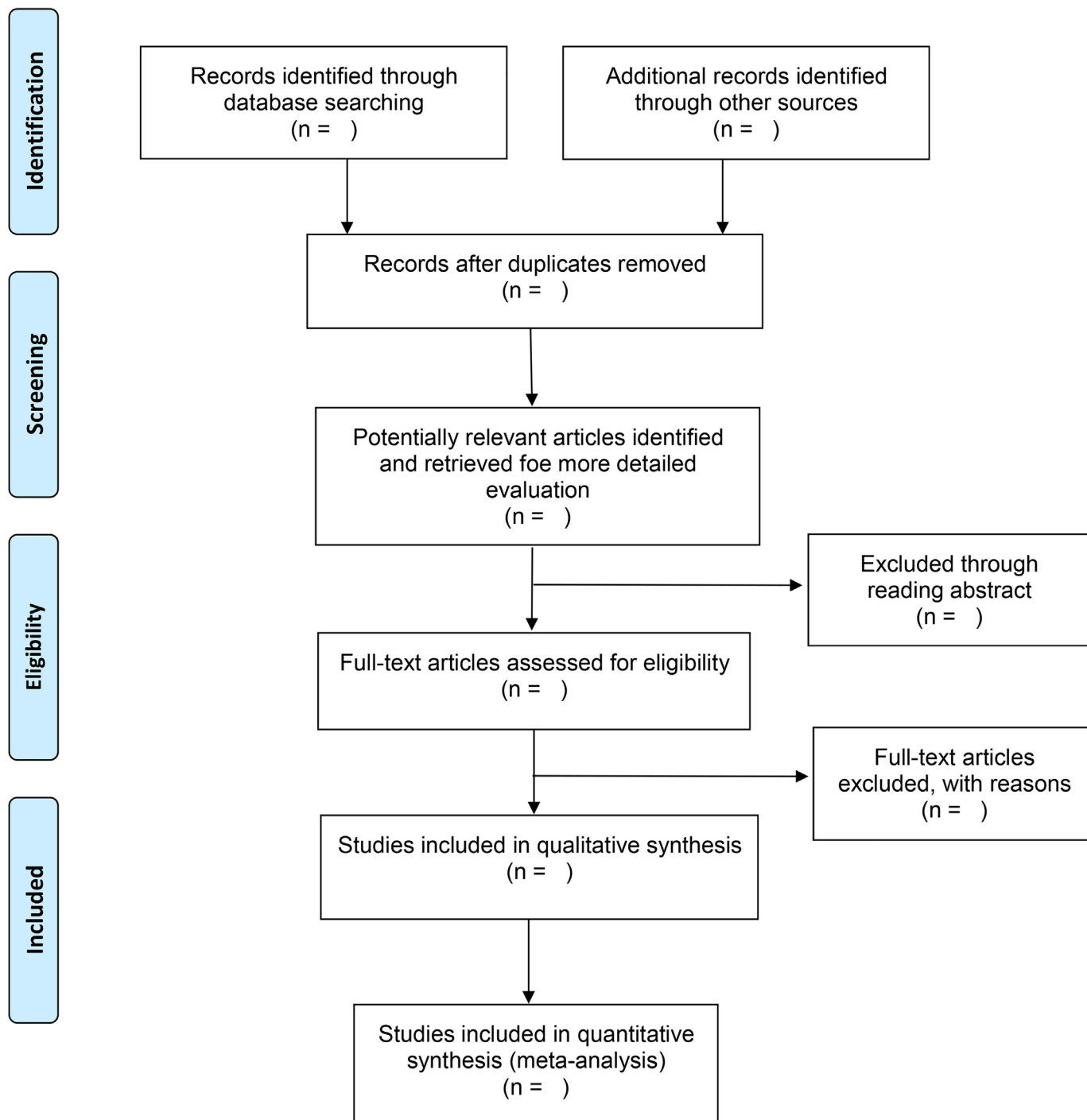


Figure 1 Flow diagram of the study design.

imputation method will be used to assume a missing value and then an intent-to-treat analysis and sensitivity analysis will be performed to assess whether that the results are consistent.

Assessment of risk of bias

The risk of bias in the included studies will be determined by two reviewers independently using the Cochrane Collaboration tool.³⁷ The Cochrane Collaboration's tool covers six aspects, sequence generation, allocation concealment, blinding, incomplete outcome data,

selective reporting and other bias. The risk will be divided into three levels (low risk, high risk and unclear) in accordance with the item in the checklist. If any disagreements, the risk assignment will be settled through arbitration of a third reviewer.

Measures of treatment effect

For continuous outcome data, the standardised mean difference or weighted mean difference with 95% CIs will be used. For dichotomous data, the RR with 95% CIs will be used for analysis.

Assessment of heterogeneity

We will evaluate heterogeneity using the standard χ^2 test ($\alpha=0.1$) and I^2 test, if the $p \geq 0.1$, and if $I^2 \leq 50\%$, the fixed-effects model will be used. Random-effects models will be used if the $p < 0.1$ or the $I^2 > 50\%$. A subgroup analysis will be performed to explore the possible causes. If the heterogeneity is greater than 75%, a meta-analysis will not be performed. We will provide a narrative, qualitative summary.

Assessment of reporting biases

We will use funnel plots to demonstrate potential reporting biases in cases involving more than 10 studies.

Subgroup analysis

If data are available, subgroup analysis will be performed to assess the heterogeneity according to the types of interventions, types of cervical spondylosis, acupuncture frequency and different outcomes.

Sensitivity analysis

If possible, sensitivity analysis will be used to evaluate how uncertain assumptions of data and usage affect the robustness of the combined results. We will exclude low-quality studies, reanalyse the included studies, and assess whether there are significant differences between the combined effects.

Grading the quality of evidence

The quality of the evidence will be used the Grading of Recommendations Assessment, Development and Evaluation (GRADE)³⁷ to assess the quality of evidence for each outcome. The following criteria will be applied: design of the study, soundness of implementation, imprecision and indirectness of evidence, consistency or homogeneity of the results and other biases. The level of evidence will be classified into four: 'high', 'moderate', 'low' or 'very low' according to the GRADE rating standards.

Ethics and dissemination

This review will not require ethical approval as it does not infringe on anyone's interests. The results will be published in a peer-reviewed journal or disseminated through conferences.

DISCUSSION

Cervical spondylosis has a high prevalence, and greatly affects quality of life in patients with such condition. Acupuncture might be effective for the treatment of cervical spondylosis, and findings of this update to former SRs are intended to provide state-of-the-art overview.

Contributors ZG is responsible for the conception and design of research, the formulation of retrieval strategies, data extraction and analysis and article writing; G-FL participates in the formulation of retrieval strategies, data acquisition and article revision; JZ participates in data extraction, analysis and interpretation, article revision; L-XJ participated in the formulation of search strategies and critical revision of articles. All authors contributed to the research and agreed to be responsible for all aspects of the work.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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