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Review article

Effectiveness of pharmacopuncture for cervical spondylosis: A systematic review and meta-analysis

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ABSTRACT

Introduction: The aim of this systematic review was to assess the evidence from randomized controlled trials (RCTs) on the effectiveness and safety of pharmacopuncture in cervical spondylosis patients.

Methods: Seven databases were searched, including Chinese and Korean databases, through to January 2018. Eligible trials were those with intervention groups receiving pharmacopuncture for cervical spondylosis and control groups receiving other conventional treatments including acupuncture. Outcome measures included pain, disability, quality of life, and adverse events (AEs). For statistical pooling, the mean difference (MD) and 95% confidence intervals (CIs) were calculated using a random-effects model.

Results: Twenty RCTs were selected. Eight trials on pharmacopuncture as a single treatment reported significant pain decrease in patients with cervical spondylosis compared to acupuncture (MD −1.79, 95% CI −2.39, −1.19). Add-on pharmacopuncture treatment also showed significant effects in alleviating pain compared to the control (MD −1.79, 95% CI −2.24, −1.34). Add-on pharmacopuncture treatment significantly increased quality of life compared to the control, as shown with SF-36 scores (MD 18.31, 95% CI 13.33, 23.29). However, all analysis results were assessed to be low or very low quality evidence due to considerably high heterogeneity and high risk of bias. In addition, solid conclusions on safety could not be drawn as few studies reported on AEs related with pharmacopuncture.

Conclusions: Pharmacopuncture, both as a sole intervention and as an add-on treatment, was found to decrease pain in patients with cervical spondylosis. These results, however, should be interpreted with caution as the quality of evidence was found to be low.

1. Introduction

Neck pain is a common musculoskeletal condition that affects everyday life, often resulting in disability and increased medical costs. The 2010 Global Burden of Disease reported neck pain to be the fourth major cause of years lived with disability, following back pain, major depressive disorder, and other musculoskeletal disorders [1].

It was reported that approximately two-thirds of the general population experience neck pain at some point in their lives in a study conducted in Saskatchewan, Canada [2]. In contrast, a study conducted

Abbreviations: RCT, randomized controlled trial; AE, adverse event; MD, mean difference; CI, confidence interval; NSAID, non steroidal anti-inflammatory drug; ESI, epidural steroid injection; CAM, complementary and alternative medicine; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; CENTRAL, Cochrane Central Register of Controlled Trials; OASIS, Oriental Medicine Advanced Searching Integrated System; NDSL, National Digital Science Library; CNKI, China National Knowledge Infrastructure; VAS, visual analogue scale; NRS, numerical rating scale; NPQ, Northwick Park pain questionnaire; NDI, Neck disability index

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among the Korean elderly in a rural area reported a lifetime neck pain prevalence of 20.8% [3]. In a 2006 systematic review on neck pain, Fejer et al. concluded that the average global lifetime prevalence of neck pain in adult populations (age 18–84) was close to 50%, although regional disparity does exist [4]. Women tend to experience neck pain more frequently than men [3–5], and neck pain has been shown to be significantly associated with the female sex, obesity, and smoking [3,6].

Acute neck pain is defined as pain within 6 weeks of onset, and usually resolves within 2 months. However, nearly half of all acute cases experience frequent pain recurrence after 1 year or develop chronic pain [7,8]. Of the diverse factors that contribute to development of chronic pain, mechanical loading and stress and degenerative changes are among the most notable. Cervical spondylosis symptoms are mainly defined as neck stiffness, limited range of motion, and cervical pain that tends to be aggravated by movement, and are accompanied by degenerative changes of the intervertebral disc along with osteophyte formation [9].

Injections and medication are regarded to be first-line treatment for neck pain including cervical spondylosis. However, although non-steroidal anti-inflammatory drugs (NSAIDs) are generally effective against pain of spinal origin [10], they often cause adverse events (AEs) such as gastritis, gastric ulcers, internal bleeding, and myocardial infarction [11–13]. While trigger-point and epidural steroid injections (ESIs) are among the most common forms of injection treatment [14], Scott et al. concluded that trigger-point injection use in chronic musculoskeletal disorders lacks firm evidence [15]. ESIs do not yield favorable outcomes when combined with chronic opioid use [16], and ESI use has been associated with such complications as spinal or neuronal injury, infections, epidural hemorrhage, and vascular or arachnoid perforation [17].

Recurrent or chronic manifestations of neck pain may develop as a consequence of failed standard first-line treatment or its limitations, and patient interest in complementary and alternative medicine (CAM) care as an alternative to conventional medicine is increasing. In the US, interest in and use of CAM for back pain and neck pain is steadily growing [18]. A recent systematic review reported that acupuncture treatment for neck pain is effective and safe as it has few side-effects and is effective for pain relief [19]. Another study recently reported that herbal medication is effective in cervical spondylosis patients [20]. Pharmacopuncture is a relatively new type of acupuncture treatment used in traditional East Asian medicine [21]. Pharmacopuncture therapy injects purified herbal medicine extracts at specific acupuncture or reflex points based on patient constitution and disease pathology. Pharmacopuncture and acupuncture are both frequently used in Korean medicine clinics and hospitals in Korea to the aim of more effective and intensive care of musculoskeletal disorders [22]. Although a small number of reports suggest use of pharmacopuncture for intractable disorders and to be of heightened clinical effect when used in conjunction with acupuncture [23], there are, as of yet, insufficient research and systematic reviews to support these claims.

The aim of this systematic review and meta-analysis of randomized controlled trials (RCTs) was to comprehensively assess the current evidence on pharmacopuncture for cervical spondylosis out of various CAM methods as assessed through pain, function, and safety outcomes.

2. Methods

The protocol of the current study was registered in the PROSPERO International prospective register of systematic reviews (CRD42016043575). This systematic review was conducted and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [24].

2.1. Data sources and search strategy

In order to identify and collect relevant literature published through to January 8th, 2018, the following databases were searched: Cochrane Central Register of Controlled Trials (CENTRAL), Ovid-Medline (1946 to January 2018), Ovid-EMBASE (1980 to January 2018), Ovid-AMED (1985 to January 2018), Oriental Medicine Advanced Searching Integrated System (OASIS), National Digital Science Library (NDSL), and the China National Knowledge Infrastructure (CNKI). OASIS and NDSL are Korean language-based databases, whereas CNKI is Chinese-based. The search terms used were cervical spondylosis and pharmacopuncture-related terms (e.g., pharmacopuncture, acupoint injection, aquapuncture, and herbal acupuncture). The comprehensive search strategy is presented as a Supplementary file (Supplement 1). Additionally, cited references of relevant publications, publications from relevant journals, clinical guidelines relating to spinal disorders, and reviews were manually searched.

2.2. Study inclusion and exclusion

2.2.1. Types of studies

All RCTs addressing the effect of pharmacopuncture for cervical spondylosis were included. Crossover studies were only included when first phase data were available. Non-randomized, quasi-experimental, observational, qualitative, and animal studies and letters were not included.

2.2.2. Types of participants

Clinical studies conducted in adults with cervical spondylosis with/without radiculopathy were included. Studies on myelopathy, headache or dizziness not accompanied by neck pain were excluded.

2.2.3. Types of interventions

All types of pharmacopuncture and herbal acupoint injection treatments used for cervical spondylosis were covered. Only the interventions where natural herbal extracts were injected into acupoints were regarded to be pharmacopuncture; those that involved chemical compounds such as anesthetics (e.g., lidocaine) or steroids were excluded. Studies involving treatments other than pharmacopuncture were not excluded if the non-pharmacopuncture treatment was uniformly administered to both the pharmacopuncture intervention and control groups. Studies that aimed to assess the combined effect of pharmacopuncture and acupuncture or other modalities (e.g., herbal medicine, moxibustion, and laser acupuncture) were excluded.

2.2.4. Types of controls

All studies where the control was placebo treatment, no treatment (waiting list), or active conventional control (e.g., conventional medicine therapy, and acupuncture) were considered eligible.

2.2.5. Types of outcome measures

The primary outcome was pain intensity (e.g., visual analogue scale (VAS), numerical rating scale (NRS), McGill pain questionnaire (MPQ), and Northwick Park pain questionnaire (NPQ)). Secondary outcomes included disability (e.g., Neck disability index (NDI)), quality of life, daily activities, patient satisfaction, and AEs. However, when the outcome measure was reported (a) as non-standardized general improvement instead of objective outcome measures, or (b) with tools that were neither validated nor reliable, the relating studies were excluded.

2.3. Data extraction

Two reviewers (SK and SYL) independently screened study titles and abstracts to determine whether specific studies should be included based on eligibility criteria. The final decision for inclusion was made after the screened manuscript was reviewed in whole. In cases of disagreement, unanimous agreement was reached through discussion with a third reviewer (YJL).

Data were subsequently independently extracted by two reviewers