



Cupping therapy for treating ankylosing spondylitis: The evidence from systematic review and meta-analysis

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ABSTRACT

Objective: Cupping therapy has been widely used in Eastern Asia, the Middle East, or Central and North Europe to manage the symptom of ankylosing spondylitis (AS). The aim of this systematic review was to review data from randomized controlled trials (RCTs) of cupping therapy for treating patients with AS.

Methods: Databases that were searched from their inception until December 2017 included: MEDLINE, CINAHL, EMBASE, AMED, Cochrane Central Register of Controlled Trials, four Chinese databases [Chinese BioMedical Database, China National Knowledge Infrastructure, Wan-Fang Data, and the Chinese WeiPu Database], KoreaMed, The Korean National Assembly Library, Japana Centra Revuo Medicina (<http://www.jamas.gr.jp/>) and CiNii. In this systematic review, only RCTs that were related to the effects of cupping therapy on managing AS were included. A quantitative synthesis of RCTs will be conducted using RevMan 5.3 software. Study selection, data extraction, and validation were performed independently by two reviewers. Quantitative analysis of RCTs were performed using RevMan 5.3 software, and cochrane criteria for risk-of-bias were used to assess the methodological quality of the trials.

Results: A total of 5 RCTs met the inclusion criteria, and most were of low methodological quality. Participants in cupping therapy plus Western medicine group showed significantly greater improvements in the response rate [RR = 1.13, 95%CI (1.06, 1.22), $p < 0.01$] with low heterogeneity ($\text{Chi}^2 = 2.88$, $p = 0.41$, $I^2 = 0\%$). Moreover, when compared with western medicine alone, meta-analysis indicated favorable statistically significant effects of cupping therapy plus western medicine on the Bath Ankylosing Spondylitis Functional Index (BASFI) [MD = -16.63, 95%CI (-17.75, -15.51), $p < 0.01$] and Bath Ankylosing Disease Activity Index (BASDAI) [MD = -9.93, 95%CI (-10.34, -9.52), $p < 0.01$], with low heterogeneity ($\text{Chi}^2 = 0.32$, $p = 0.85$, $I^2 = 0\%$ in BASFI; ($\text{Chi}^2 = 2.46$, $p = 0.29$, $I^2 = 19\%$ in BASDAI). Furthermore, when compared with western medicine alone, meta-analysis demonstrated statistically significant effects of cupping therapy plus western medicine on the serum level of ESR [MD = -1.28, 95% CI (-1.44, -1.13), $p < 0.01$] and the serum level of CRP [MD = -3.97, 95%CI (-4.71, -3.22), $p < 0.01$], with low heterogeneity ($\text{Chi}^2 = 0.50$, $p = 0.78$, $I^2 = 0\%$ in the serum level of ESR; $\text{Chi}^2 = 0.19$, $p = 0.91$, $I^2 = 0\%$ in the serum level of CRP).

Conclusion: Taken together, only weak evidence supported the hypothesis that cupping therapy had potential benefits for patients with AS.

1. Introduction

Ankylosing spondylitis (AS) is a common chronic inflammatory disorder of unknown etiology affecting approximately 0.9–1.4% of the United States populations [1,2]. It can be the consequence of a pathological process characterized by enthesitis, sacroiliitis, bone hyperostrophy, and new bone formation [2]. AS most frequently presents with

clinical symptoms which include inflammatory back pain (IBP), stiffness, spinal fusion and ankylosis [3]. In addition, with the disease progression, AS has a significant negative effect on patients' quality of life (QoL) [4]. Moreover, It can cause reactive anxiety and frustration, and it influences patients' social interactions and increased their heavy economic burden [4,5].

So far, Assessment of Spondyloarthritis International Society (ASAS)

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and the European League Against Rheumatism (EULAR) have both recommended that non-steroidal anti-inflammatory drugs (NSAIDs), disease modifying anti-rheumatic drugs (DMARDs), are clinically common agents for treating AS [6]. The regular intake of NSAIDs medications may be first-line medicine choices for relieving AS symptoms [7]. However, these agents are frequently associated with some undesired complications, and increase the risk of serious adverse events (AEs) in the long-term therapy period [8,9]. Recent studies have recommended that DMARDs are mainly used in AS patients with peripheral arthritis. However, these agents are generally not effective in the management of axial manifestations of AS patients [10–12]. TNF- α receptor antagonist (infliximab, etanercept, adalimumab, etc), as novel pharmacological agents, are not only shown to be effective in controlling the disease activity of AS, but also reduced the development of bone bridge progression in many AS patients [13]. Nevertheless, this biological agent may be too expensive for purchase by clients in the developing country [14]. Given these limitations, consequently, it is therefore not surprising that AS patients might tend to seek complementary and alternative treatment (CAM) therapies for help in alleviating their pain, stiffness and improving their physical function ability [15].

Cupping therapy is an important integral part of CAM. It is described as an ancient, holistic method mainly using glass, plastic or bamboo cups on patients' skin (including acupuncture points, painful area, or a reflex zone on the skin) by creating localized pressure inside the cups [16]. Though the exact origin of cupping therapy is a matter of controversy, this specific technique has widely been utilized and practiced in diverse human civilizations like Eastern Asia, the Middle East, or Central and North Europe [17]. In general, cupping therapy can be divided mainly into dry cupping therapy and wet cupping therapy [18]. Wet cupping, also called *Hijama* in the Muslim countries, was favored by the Prophet of Islam [19]. This technique was popular among the CAM practitioners in the Middle East. After selection of specific areas on which to place the cup, wet cupping practitioners make the incision of the skin with a needle before the suction is created by a cup. A localized pressure is then produced by the suction so that skin is sucked in and excess blood, fluids or toxins is drawn into the cup [20]. In dry cupping, CAM practitioners can stimulate the skin by applying cups with a vacuum pressure. The difference between the two main cupping therapy lies in whether the skin is punctured to allow blood and other body fluids to flow [21]. In addition to two main types of cupping therapy, other subtypes of cupping therapy include retained cupping, quick-cupping, moving cupping, shaking-cupping and balance-cupping.

A bibliometrics analysis of papers published from 1950 to 2010 in China showed that cupping therapy has been widely used in the treatment of a wide spectrum of chronic musculoskeletal diseases [22]. Nowadays, various systematic reviews have investigated the effects of cupping therapy on stroke rehabilitation [23], hypertension [24], herpes zoster [25] and pain conditions [26]. However, no systematic review has targeted the trial evidence specifically for AS populations. Therefore, we carried out this systematic review with an aim to summarize and critically evaluate the evidence from clinical trials testing the benefits and harms of cupping therapy for the treatment of AS.

2. Materials and methods

This study has been registered with the international Prospective Register of Systematic Reviews (PROSPERO): CRD 42017078972.

2.1. Data sources

The following databases: MEDLINE, CINAHL, EMBASE, AMED, Cochrane Central Register of Controlled Trials, Chinese BioMedical Database, China National Knowledge Infrastructure, Wan-Fang Data, the Chinese WeiPu Database, KoreaMed, The Korean National Assembly

Library, Japana Centra Revuo Medicina (<http://www.jamas.gr.jp/>) and CiNii were searched from their inception until December 2017. Search strategies which based on the guidance of the Cochrane handbook were presented in *online supplementary A*, and these search terms were slightly modified for other databases. To identify 'grey' literature/unpublished studies, we identified relevant studies through review of the Chinese Clinical Trial Registry (<http://www.chictr.org.cn/>), Registry ClinicalTrials.gov (<http://clinicaltrials.gov/>), WHO International Clinical Trials Registry Platform (ICTRP) (<http://apps.who.int/trialsearch/>) and the Australian New Zealand Clinical Trials Registry (ANZCTR). Moreover, we also searched the reference lists of review articles and/or conference articles to identified RCTs for any potential interesting titles matching the inclusion criteria of the study. Furthermore, some important relevant journals in the Middle East (Iranian red crescent medical journal Archives of Iran medicine saudi medical journal) were also hand-searched from 1980 to December 2017.

2.2. Selection of studies

In this systematic review, only RCTs related to the effects of cupping therapy in AS were included. Trials that were published in the form of dissertations were also selected as eligible studies. All studies included met the following inclusion criteria with the PICOS principle (population, intervention, comparison, and outcome). No language restrictions were imposed.

P (population): Patients diagnosed with AS using definitive modified New York criteria for AS diagnostic criteria were included [27]. Studies were excluded if they include patients with rheumatoid arthritis, osteoarthritis, inflammatory bowel disease, psoriasis and non-specific low back pain.

I (intervention): Studies were included if cupping therapy was used as the sole intervention or as an adjunct therapy in conjunction with western medicine therapy for AS. In addition, studies in which other CAM therapies (e.g. moxibustion, Chinese Tuina, acupuncture, Chinese herbals) were utilized as an adjunct treatment in conjunction with the western medicine therapy were excluded.

C (comparison): A sham cupping device/placebo or western medicine was included as controls. Moreover, studies were excluded if treatments of the control group were not relevant to western medicine or when other CAM therapies (e.g. acupuncture, moxibustion, Chinese herbals, Chinese patent medicine) were used as an adjunct treatment in conjunction with western medicine.

O (outcomes): (1) Primary outcomes: ① Functional condition: measured by recognized scales including Bath Ankylosing Spondylitis Functional Index (BASFI) [28]. BASFI consists of 10 scales: 8 visual analogue scales (VAS) dealing with physical function and two scales reflecting the patient's physical mobility (including cervical rotation, tragus-to-wall distance, modified Schober index, lateral lumbar flexion, and intermalleolar distance). Lower scores can indicate worse physical function of AS. ② Disease activity: associated indicators measured on the Bath Ankylosing Disease Activity Index (BASDAI) [29]. BASDAI score was used to assess patients with AS in the clinical settings. This questionnaire includes 6 items (spinal pain, joint pain and swelling, dealing with fatigue, areas of localized tenderness and the severity and duration of morning stiffness.). Higher scores can indicate the high disease activity of AS. (2) Secondary outcomes: ① Treatment efficacy: the proportion of patients who achieved GPCRND-response rate [30]. Similar to the international standardized evaluation of clinical efficacy, GPCRND response rate is a reliable and valid Chinese Culture-specific assessment of AS, which includes pain intensity associated with the affected joint, activities of daily living (ADL), tragus-to-wall distance, modified Schober index, and serum level of erythrocyte sedimentation rate (ESR) and C reactive protein (CRP). To date, several complementary and alternative therapy (CAM) evidence based medicine

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