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Evaluation of Wet Cupping Therapy: Systematic Review of Randomized Clinical Trials

Al Bedah Abdullah M.N., Khalil Mohamed K.M., Posadzki Paul, Sohaibani Imen, Aboushanab Tamer Shaaban, AlQaed Meshari, and Ali Gazzaffi I.M.

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Evaluation of wet cupping therapy: Systematic review of randomized clinical trials.

Abdullah M.N. Al Bedah¹, Mohamed K.M. Khalil¹, Paul Posadzki², Imen Sohaibani¹, Tamer Shabaan Aboushanab¹, Meshari AlQaed¹, Gazzaffi I.M. Ali¹

1 National Center for Complementary and Alternative Medicine (NCCAM), MOH, Saudi Arabia, 2 Lee Kong Chian School of Medicine, Imperial College and Nanyang Technological University

Short running title : Evaluation of wet cupping

Correspondence:

Dr Mohamed Khalil, MD, Head of Research unit, NCCAM,MOH
Riyadh, Saudi Arabia
Tel +966 504955087
Email: statkhl@hotmail.com

Abstract

Background: Wet cupping is a widely used traditional therapy in many countries which justifies a continuous scientific evaluation of its efficacy and safety. **Objectives:** A systematic review to critically evaluate and update the available evidence of wet cupping in traditional and complementary medicine.

Methods: Ten electronic databases were searched from their inceptions to February 2016. Randomised clinical trials (RCTs) that evaluated wet cupping against any type of control interventions in patients with any clinical condition as well as healthy individuals. Cochrane risk of bias tool was used to appraise the included RCTs. **Results:** Fourteen RCTs met the eligibility criteria. The included studies evaluated the following clinical conditions: nonspecific low back pain (NSLBP), hypertension, brachialgia, carpal tunnel syndrome (CTS), chronic neck pain, metabolic syndrome, migraine headaches, oxygen saturation in smokers with chronic obstructive pulmonary disease (COPD), and oral and genital ulcers due to Behçet disease. Two RCTs evaluated physiologic and biochemical parameters of healthy individuals. Overall, 9 RCTs favored wet cupping over various control interventions in NSLBP (n = 2), hypertension (n = 1), brachialgia (n = 1), CTS (n = 1), chronic neck pain (n = 2), oxygen saturation in smokers with COPD (n = 1), and oral and genital ulcers due to Behçet disease (n = 1). Five RCTs showed no statistically significant between-group differences: NSLBP (n = 1), metabolic syndrome (n = 1), migraine headaches (n = 1), and physiologic and biochemical parameters of healthy individuals (n = 2). Included RCTs had a variable risk of bias across all domains and suffered methodologic limitations. **Conclusions:** There is a promising evidence in favour of the use of wet cupping in musculoskeletal pain; specifically NSLBP, neck pain, CTS, and brachialgia. Better quality trials are needed to generate solid evidence and firmly inform policy makers.

Keywords: Wet Cupping; Traditional medicine; Complementary Medicine; Systematic review; Effectiveness.

Introduction

Cupping is a traditional therapy used worldwide and it is divided mainly into dry and wet cupping. Wet cupping is a popular traditional therapy in Asia, Middle East and Central Europe.[1] In the Middle East and in Muslim countries, wet cupping is called “Hijamah” and it is linked to religious beliefs as it was favoured by the Prophet of Islam. [2] Wet cupping has been used for a long time in the treatment of chronic conditions like musculoskeletal pain, headache, radiculopathy and respiratory disorders. [2, 3]

After selecting specific points for each condition to place the cups, wet cupping procedure includes scarification with a blade or puncturing of the skin with a needle before applying bamboo, glass, or plastic cups. [4] Then a vacuum is produced by manual suction, electromechanical, or rarely by heat production so that skin is sucked in, and the stagnant blood is drawn into the cup. [5] There are different techniques used in different regions. In certain regions like the Middle East, cups are placed and suction is performed before and after scarification not only after scarification.

The mechanism of action of wet cupping is not clear, and many theories have been proposed. It may act by triggering a diffuse noxious inhibitory control, [6] or by the removal of oxidants and the decrease of oxidative stress. [7] Some researchers suggest that this therapy drains excess fluids, increases blood flow to skin and muscles, and stimulates the peripheral nervous, neurohormone, circulatory and immune systems. [3, 4]

Several systematic reviews on wet and dry cupping therapy have been published, either on specific conditions like pain[8], stroke rehabilitation[3], hypertension[9], low back pain[10], and herpes zoster[11] or in all medical conditions[2, 12]. But with the growing interest in the subject, increased number of publications in recent years, and relatively improved quality of clinical trials, these reviews should be updated. Also, to separate dry and wet cupping trials in systematic reviews as wet cupping is mainly used in certain regions like the Middle East.

The aim of this systematic review was to critically evaluate and reflect the current research evidence of wet cupping in different conditions to be used as scientific basis for developing a clinical guideline for practitioners and to support the policy of developing integrative health approaches..

Methods

We used PRISMA guidelines and the Cochrane Handbook for Systematic Reviews of interventions. We included Randomized Clinical Trials (RCTs) that used wet cupping alone or in addition to other therapy, in medically compromised or healthy individuals compared with no treatment or other active controls. Participants were without age or gender restrictions. Any primary outcome measures were admissible. Studies were excluded if they were using dry cupping, uncontrolled clinical trials, clinical observation, case reports or not published in English.

Literature Searches

Electronic searches were carried out in February 2016 via OVID in the following databases (from their inception until the dates shown in front of each one.):

ACP Journal Club 1991 to January 2016, Cochrane Central Register of Controlled Trials January 2016, Cochrane Database of Systematic Reviews 2005 to February 12, 2016, Cochrane Methodology Register 3rd Quarter 2012, Database of Abstracts of Reviews of Effects 1st Quarter 2016, Health Technology Assessment 1st Quarter 2016, NHS Economic Evaluation Database 1st Quarter 2016, AMED (Allied and Complementary Medicine) 1985 to February 2016, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present.

We used “cupping” as a broad search term followed by manual screening to ensure that relevant studies were not missed.

All retrieved abstracts were screened to remove irrelevant and duplicates studies. Non-electronic search was conducted through screening of different sources and direct communications with expert authors in the field.

Data Extraction

Data from the included studies were extracted by two reviewers (PP and MK) and subsequently validated by a third reviewer (AA). The Following Information was extracted: first author’s name and publication date, study design, sample size and characteristics of participants (including mean age and demographics), condition, description of wet cupping intervention in terms of duration, frequency, and anatomical cupping sites, comparators, primary outcomes, main results (with p values, confidence intervals where available), study author’s conclusion, and adverse/undesirable or side effects of the intervention. Comments related to validity were added at the end of the descriptive table 1 and disagreements were resolved by discussion and consensus.

Risk of bias Assessment

We used the Cochrane Collaboration's tool for assessing the risk of bias (ROB) of the included RCTs. ROB assessments were performed by two reviewers independently (PP and MK) and validated by a third reviewer. Any disagreements whether a study was judged high, low or unclear in any domain of the tool were settled through discussions[13].

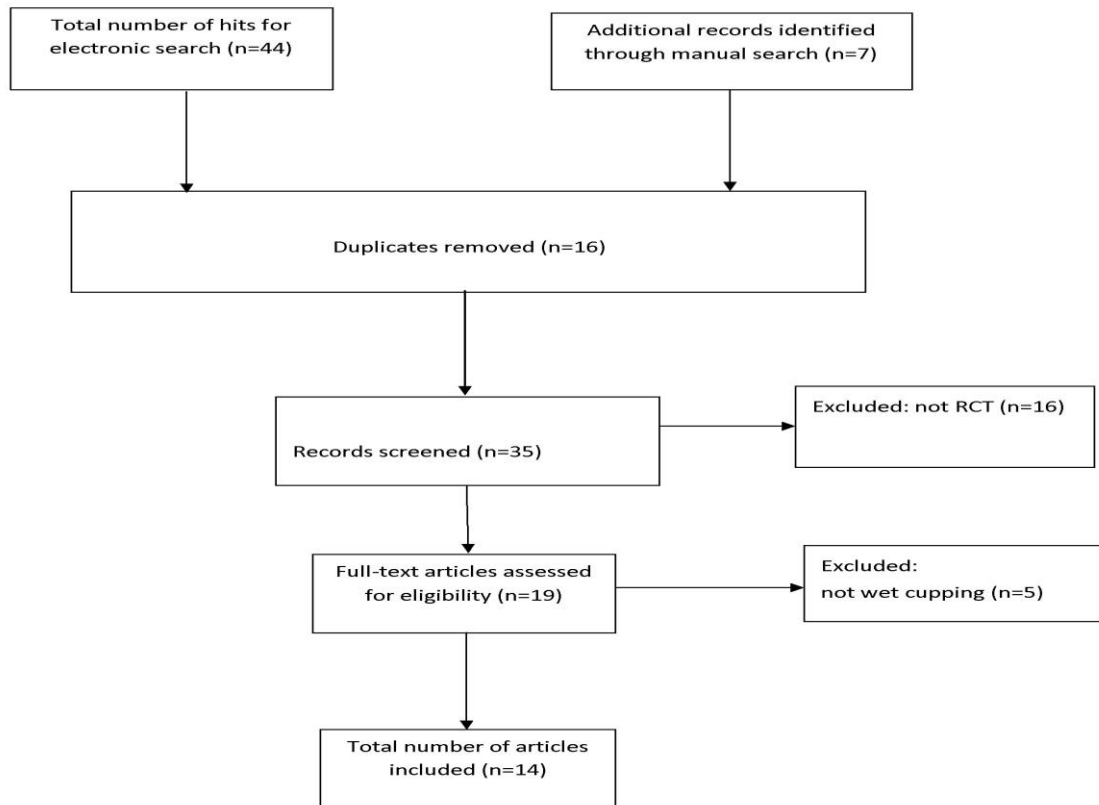
Data Analysis and synthesis

Narrative data synthesis was used as Clinical and methodological heterogeneity in terms of populations, interventions, comparison groups, outcome measures and study designs and the lack of overlap of confidence intervals assessed by visual inspection of scatter of forest plots precluded a formal meta-analysis.

Results

Study description

Our searches generated a total of 51 references and 14 RCTs with a total of 863 individuals met the inclusion criteria. Figure 1, shows the PRISMA diagram of the included studies. The key data from the included RCTs are presented in Table 1. The trials originated from Germany (n= 3), Iran (n =5), Jordon (n= 1),..Morocco (n= 1), Saudi Arabia (n =2), and South Korea (n= 2). Sample sizes ranged from 20 to 126 (mean = 61.63; SD = 32.5). All RCTs employed parallel design with two groups,



Risk of bias (ROB) in the included studies

The overall quality of the included RCTs is suboptimal. Regarding high risk of bias; out of the 14 included studies, 2 were assessed as “high risk of bias” on random sequence generation, 3 on allocation concealment, 8 on blinding of participants and outcome assessors, one on addressing of incomplete data, zero on selective outcome reporting and 2 other sources of bias. Table 2, illustrates the ROB in specific domains of the RCTs. Across all

domains, 4 trials had low or unclear ROB, 8 had only one high ROB in one domain mainly in blinding, and the remaining two had high ROB in more than one domain. Table 2

Wet cupping in healthy persons

Two RCTs were included. The first RCT[14] evaluated the effect of wet cupping on selected immune-cytogenetic parameters in 44 healthy males. The study reported that a single session of cupping (approx 20 min) compared with no treatment had no statistically significant effect on the cytogenetic parameters ; and haemoglobin concentration, at one week and one month after intervention. But white cell counts were significantly higher after wet-cupping in the intervention group ($p \leq 0.05$).

The second RCT [4] evaluated the effects of wet cupping on serum lipoprotein concentrations. The authors concluded, that compared with no treatment, a single session of wet cupping (approx 5-10 minutes) had no effect on serum triglycerides, total cholesterol and high-density lipoproteins; and significant effect on serum low-density lipoproteins at 1,2,3 weeks ($p < 0.0001$).

Clinical conditions

Non-specific low back pain

Farhadi (2009)[15] aimed to determine the efficacy of wet-cupping versus usual care (UC) in 98 patients with the condition. They reported that 3 sessions over 7 days / 20 minutes each had a statistically significant reduction in medications consumed, pain and disability scores (all at $p < 0.01$) at 3 months.

Kim (2011) [16] evaluated the effectiveness and safety of wet-cupping in 32 patients with the condition. They reported that 3 times per week for two weeks of wet cupping +UC compared to US, had no significant differences between groups on NRS for pain at 2 weeks

($p=0.52$). But a significant decrease in Present Pain Intensity score in the wet cupping group ($p<0.01$).

Albedah [17] used the same protocol developed by Kim (2011), but UC comprised of only Acetaminophen tablets as rescue treatment. (no stretching or strengthening exercises were given).—In 80 patients with NSLBP, a statistically significant improvement in pain and disability scores ($P =0.0001$ in ODQ) was observed in the wet cupping group compared to the control group. This significant improvement persisted for two weeks after intervention

Neck pain

Kim (2012) [18] evaluated the effectiveness of cupping therapy in 40 patients with neck pain. They reported that 6 sessions of both wet and dry cupping (3 times per week for 2 weeks) in addition to stretching exercises significantly reduced pain intensity at 3 weeks ($p=0.025$) and at 7 weeks ($p=0.005$) compared with heating pads, for 10 minutes, 3 times per week for two weeks in addition to stretching exercises..

Lauche (2012)[19] evaluated the effect of wet cupping therapy in 50 patients with neck pain. They reported that, compared with waiting list, a single session of wet cupping—(approx. 15-0 min) significantly reduced pain intensity($p<0.05$), pressure pain thresholds ($p<0.01$)and improved quality of life ($p<0.05$); but ~~and~~ there were no significant between group differences in disability, mechanical detection threshold and vibration detection threshold.

Carpal Tunnel Syndrome

Michalsen (2009) [5] investigated the effectiveness of wet-cupping in 52 patients with carpal tunnel syndrome. They reported that, compared with heating pad once only for 15 min, a

single session of wet cupping (approx. 5-10 min) significantly reduced symptom severity ($p < 0.001$) at day 7.

Brachialgia

Ludtke (2006) [20] investigated the effectiveness of ‘wet cupping’ in 20 patients suffering from brachialgia. They reported that, compared with usual care (UC) alone, a single session of wet cupping (approx 10 min) in addition to UC significantly reduced pain intensity- ($p = 0.002$)-at days 1- 7 post-intervention.

Migraine

Dehghani-Firoozabadi (2014) [21] aimed to examine the efficacy of cupping therapy (monthly for three times) plus serkangabin syrup (a traditional drink used in Iran for headache and other illnesses) in the treatment of migraine headaches in 60 patients. They reported that, compared with conventional treatment alone, wet cupping had no effect on the severity of headache, frequency of attacks in a week, and duration of attacks per hour in 5 visits.

Behcet’s disease:

Erras (2013) [22] aimed to determine the efficacy of wet-cupping as an adjuvant treatment in 24 patients with oral and genital ulcers due to Behcet’s disease. They reported that, compared with UC alone, a single session of wet cupping (approx. 20 min) in addition to UC significantly reduced the number of episodes per month ($p = 0.005$), the number of ulcers per episode ($p = 0.018$) and duration of the episode ($p = 0.018$) at 6 months.

Patients with metabolic syndrome

Farahmand (2012)[23] aimed to determine the effects of wet cupping on lipid profiles and anthropometric characteristics in 126 patients with metabolic syndrome. They reported that compared with dietary advice for 6 weeks, a 2- staged wet-cupping treatments with six-week intervals +dietary advice had no significant effect on anthropometric measures and biochemical parameters

Hypertension

Aleyedi (2015) [24] aimed to evaluate the effect of wet cupping on 80 hypertensive patients. They reported that wet cupping (3 sessions every other day) in addition to conventional hypertension treatment is more effective than conventional treatment alone in reducing the systolic blood pressure ($p=0.046$) for after 4 weeks.

Smokers with Chronic Obstructive Pulmonary Disease

Hekmatpou (2013)[25] evaluated the effect of wet cupping on 110 male smokers with (positive Pulmonary Function Test) and Chronic Obstructive Pulmonary Disease and they reported that wet cupping (approx. 15-20 min) compared to venesection, caused a continued O₂ saturation in the intervention group up to 12 hours ($p < 0.001$). Limitations of all included RCTs are shown in table 1.

Discussion

An increasing number of Systematic Reviews of cupping therapies were published in recent years [2, 3, 8-11, 26]. The majority concluded that there is a favourable effect of wet cupping in pain conditions. A recent SR and meta-analysis (in which 78% of trials concentrated on wet cupping) concluded that cupping therapy combined with other TCM [Traditional Chinese Medicine] treatments was significantly superior to other treatments alone". [12]. All published Systematic Reviews reported that poor methodological quality of included Randomized Clinical Trials is the main factor for not providing a strong recommendation for

practice. Our review included only wet cupping (Hijamah) which is widely used in the Middle East (ME) as evident by the high number and recently published RCTs included in our review . Other reviews usually include dry and wet cupping, and most probably, in addition to other Chinese medicine therapies which may not commonly use elsewhere.

Summary of the main results:

The aim of this Systematic Review was to evaluate the current evidence and to add to the published systematic reviews on the use of wet cupping. Fourteen trials were found; 9 RCTs favoured wet cupping over various control interventions; in Non-Specific Low Back Pain (n=2), hypertension (n=1), brachialgia (n=1), Carpal Tunnel Syndrome (n=1), chronic neck pain (n=2), , Oxygen saturation in smokers with Chronic Obstructive Pulmonary Disease (COPD) (n=1)and oral and genital ulcers due to Behcet's disease (n=1). Five RCTs showed no statistically significant between-group differences compared with various controls; in Non-Specific Low Back Pain (n=1), metabolic syndrome (n=1), migraine headaches (n=1); and physiological and biochemical parameters of healthy individuals (n=2). As reported in other SRs the overall, the methodological quality of the included RCTs was poor.

Out of the fourteen RCTs, eleven reported adverse effects (AEs) of wet cupping.(Table 1); Six of them mentioned that no AEs had occurred. Adverse effects included fainting, discomfort, headache, skin laceration, whole body itching, pain, generalized body pain, ache, circulatory instability, migraine attack, repeating tinnitus and wound healing itches. Various AE related to cupping therapy were reported but these were rare and can be avoided if the practitioners were trained and strictly complying with the safety guidelines.[27]

Quality of evidence and risk of bias:

bias included small sample size with no power of calculations, the unequal distribution between the arms , lack of adequate follow-up, confounding effect of control intervention and

under or poor reporting. But lack of blinding and control for placebo effects were the main causes of Risk of bias. The use of adequate placebo or sham device can minimize performance and detection bias. Unlike dry cupping,[28] creating a sham device for wet cupping is more challenging work especially when we use it in patients who are familiar with the actual skin scarification and blood suction in wet cupping.

As for other published SRs, there was a high degree of unavoidable heterogeneity in terms of the population, duration, frequency and intensity of wet cupping intervention, control and outcome measures used. The few number of published RCTs in each condition was the main reason to include RCTs in the absence of standardization of wet cupping intervention, or trials with active and inactive controls or wet cupping as monotherapy or in addition to other therapies.

The majority of the included trials used self-reported outcome measures, such as pain scoring scales, as primary outcome measure. Self-reported outcome measures may increase the Risk of Bias in the absence of placebo. The use of multiple dimension pain measurement and overall functioning can improve self-reporting until more objective outcome measures are developed.

Limitations and potential bias of review process:

Our Systematic Review have several limitations. Publication bias is a frequent limitation in the majority of SRs. Specifically, language restriction was an important limitation as it excluded a substantial number of publications, especially from China.

Conclusion and implication for practice: there is a growing evidence for the effectiveness of wet-cupping in pain management in general and specifically in Non-Specific Low Back Pain, and neck pain. Our study and published studies [29] showed that Adverse Effects

related to wet cupping were rare and most of them were related to improper training or low standards of hygiene. Therefore, there is a need for developing a benchmark for training in wet cupping with a consensus agreement on safety standards and techniques used. The small number of RCTs for each condition in addition to the low quality and heterogeneity made it difficult to reach a definite conclusion. High quality, placebo-controlled RCTs are needed with more objective outcome measures to generate solid evidence and firmly inform policy makers and the support the integration of wet cupping in health care practice.

Table 1 RCTs of Wet Cupping for health conditions

| First author (year) [ref] | Design | Sample/condition (mean age) | Therapeutic regimen/ /duration/frequency/intensity | Control intervention | Primary outcome measures | Main results/between-group differences | Author's conclusions | Adverse effects | Comment |
|----------------------------------|----------------------------|-----------------------------|---|------------------------------|---|---|--|--|---|
| Al Bedah (2015)[17] | Parallel RCT with 2 groups | 80/ NSLBP (30.45) | Wet cupping/ 6 sessions over two weeks plus acetaminophen if needed | Acetaminophen if needed | 1.-NRS 2.-PPI 3.-ODQ 4.-Number of acetaminophen | 1-Sig(P=0.0001) 2-Sig(P=0.0001) 3-Sig(P=0.0001) 4-N.S(P=0.1) | "wet cupping is potentially effective in reducing pain and improving disability associated with NSLBP at least for 2 weeks after cupping" | None reported | Lack of blinding No control for placebo effect |
| Aleyeidi (2015)[24] | Parallel RCT with 2 groups | 80/ hypertensive (52.9) | Wet cupping plus conventional treatment/ 3 sessions every other day | Conventional treatment | 1. Mean systolic blood pressure 2. diastolic blood pressure | 1-systolic: sig: (P =0.046) 2-diastolic: n.s: (P=0.68) | "wet cupping therapy is effective in reducing systolic blood pressure in hypertensive patients for up to 4 weeks without serious side effects" | Headache Hijama site pruritus Dizziness Tired and sleepy Nausea Vomiting Pain at site One day insomnia scar | Lack of blinding No control for placebo effect |
| Dehghani-Firoozabadi (2014) [21] | Parallel RCT with 2 groups | 60 migraineurs (32.1) | Cupping therapy (monthly for three times) plus serkangabin | Conventional treatment group | 1. The severity of headache 2. Frequency of attacks in a week 3. Duration of attacks per hour in 5 visits | 1. n.s. (P = 0.80) 2. n.s. (P = 0.63) 3. n.s. (P = 0.48) | "There was no significant difference between cupping plus serkangabin therapy and conventional treatment in the treatment and prophylaxis of migraine" | No info | Insufficient info to judge methodological quality |

| | | | | | | | | | |
|----------------------|----------------------------|---|--|--|--|--|--|----------------|--|
| Erras (2013) [22] | Parallel RCT with 2 groups | 24 patients with oral and genital ulcers due to Behcet disease (37.2) | Single session (approx. 20 min)+UC# | UC only# | 1. nr of episodes/month 2. nr of ulcers/episode 3. duration of episode | 1. sig. (p=0.005) 2. sig. (p=0.018) 3. sig. (p=0.018) all at 6 months | “(…) combining Wet Cupping plus conventional treatment shows great promise as an effective treatment for oral and genital ulceration in patients with Behcet disease” | None reported | Small sample, no confidence intervals, no power calculations |
| Farhadi (2009)[15] | Parallel RCT with 2 groups | 98 patients with NSLBP (43.3) | 3 sessions over 6 days/ 20 min each | UC (education, acetaminophen, bed rest, exercises) | 1. MQS 2. PPI 3. ODI | 1. sig. (P<0.01) 2. sig. (P<0.01) 3. sig. (P<0.01) all at 3 months | “Traditional wet-cupping care delivered in a primary care setting was safe and acceptable to patients with nonspecific low back pain. Wet cupping was significantly more effective in reducing bodily pain than usual care at 3 month follow up” | Fainting (n=3) | Lack of blinding, no control for placebo effects |
| Farahmand (2012)[23] | Parallel RCT with 2 groups | 126 patients with metabolic syndrome | 2- staged wet-cupping treatments with six-week intervals +dietary advice | Dietary advice for 6 weeks | 1. anthropometric 2. biochemical (High sensitivity C reactive | 1. n.s. (P > 0.05) 2. n.s. (P > 0.05) both at 6 and 12 weeks follow-up | “Wet cupping does not have a significant effect on anthropometric or biochemical indices compared to the effect of dietary | None reported | Confounding effects of dietary advice regime |

| | | | | | | | | | |
|------------------------|----------------------------|---|---|--|------------------|---|---|------------------------|---|
| | | | | | protein) | | advice alone” | | |
| Hekmatpou D (2013)[25] | Parallel RCT with 2 groups | 110 male smokers with (positive Pulmonary Function Test) and (COPD) | Wet cupping (from 15 to 20 minutes)/ (50-75 ml blood drawn out) | Venesection/ (100-200 ml blood drawn out) | O2 saturation | 1-Immediately after: n.s(P=0.88) 2-after 6 H: Sig(P<0.001) 3-after 12 H: Sig(P<0.001) | "wet cupping caused a continued O2 saturation in the intervention group up to 12 hours afterword" | Not Reported | Lack of blinding No control for placebo effect |
| Khalil (2013) [14] | Parallel RCT with 2 groups | 44 healthy males (30.5) | Single session (approx. 20 min) | No treatment | 1. physiological | 1. n.s. (P>0.05) at 1 week and 1 month | “No correlation between cupping and cytogenetic parameters (CRI and SCE) was observed. However , cupping seems to play a role in activation of complement system as well as cellular part of immune system” | Discomfort, headedness | Lack of active controls; no power and sample size calculations |
| Kim (2011) [16] | Parallel RCT with 2 groups | 32 patients with NSLBP (46.1) | Wet-cupping 3 x per week for 2 Weeks +UC (including stretching and strengthening exercises) | Waiting-list (including acataminop hen, stretching and strengthenin g exercises) | 1. NRS | 1. N.s. (p = 0.52) at 2 weeks | "This pilot study may provide preliminary data on the effectiveness and safety of wet-cupping treatments for persistent NSLBP" | None reported | Small sample, unequal distribution between the arms, no control for placebo effects |

| | | | | | | | | | |
|----------------------|----------------------------|--|--|---|--|--|--|--|--|
| Kim (2012) [18] | Parallel RCT with 2 groups | 40 patients with neck pain | 6 sessions of both wet and dry cupping (3 x per week for 2 weeks)+stretching exercises | Heating pads for 10 min, 3 x per week for 2 weeks+ stretching exercises | 1. Pain (1-100 NRS) | 1. sig. at 3 weeks ($p=0.025$) and 7 weeks ($p=0.005$) | "Two weeks of cupping therapy and an exercise program may be effective in reducing pain and improving neck function (...)" | N=4 skin laceration, whole body itching, pain at the cupping sites and generalized body ache. | Small sample; confounding effect of exercises |
| Lauche (2012)[19] | Parallel RCT with 2 groups | 50 patients with chronic nonspecific neck pain | Single session (approx. 15-20 min) | Waiting list | 1. VAS 100mm for PM and PR 2. SF-36 3. NDI 4. MDT 5. VDT 6. PPT 7. NRS (1-10) 8. Medication diary | 1. sig. ($P < 0.05$) 2. sig. ($P < 0.05$) ^{^^} 3. n.s. ($p=0.168$) 4. n.s. ($p=0.686$) 5. n.s. ($p=0.447$) 6. sig. ($P < 0.01$) 7. sig. at days 2,3,4 ($P < 0.05$) 8. n.r. | "A single application of traditional cupping might be an effective treatment for improving pain, quality of life, and hyperalgesia in CNP [chronic neck pain]" | Pain, circulatory instability, tension headaches, a migraine attack, a reappearing tinnitus, wound healing itches. | Lack of blinding; power calculations; underreporting |
| Ludtke (2006) [20] | Parallel RCT with 2 groups | 20 patients with brachialgia (50.4) | Single session (approx. 10 min)+UC* | UC* only | 1. 11-point NAS** | 1. Sig. at days 1-7 post-intervention ($p = 0.002$) | "This study suggests short-term effects of a single wet cupping therapy, which remain at least for 1 week." | None reported | Small sample; lack of follow-up |
| Michalsen (2009) [5] | Parallel RCT with 2 groups | 52 patients with CTS (58.5) | Single session (5-10 min) | Heating pad once only for 15 min | 1. Symptom severity measured with 100-mm VAS | 1. Sig. at day 7 ($P < .001$) | "(...)a single course of wet cupping of the shoulder triangle [...] appears to be effective in relieving | None reported | Lack of blinding |

| | | | | | | | | | |
|--------------------|----------------------------|----------------|---------------------------|--------------|---|---|--|---------|---|
| | | | | | | | symptoms and pain for at least 1 week in patients with manifest CTS” | | |
| Niasari (2007) [4] | Parallel RCT with 2 groups | 47 healthy men | Single session (5-10 min) | No treatment | 1. Serum triglycerides 2. Serum total cholesterol 3. Serum low-density lipoproteins 4. Serum high-density lipoproteins | 1. n.s. (P>0.05) 2. n.s. (P>0.05) 3. sig. at 1,2,3 weeks ($p < 0.0001$) 4. n.s. (P>0.05) | ‘Wet cupping may be an effective method of reducing LDL cholesterol in men and consequently may have a preventive effect against atherosclerosis.’ | No info | Lack of active controls; poor reporting |

Table 1 legend: CTS- carpal tunnel syndrome; MDT- mechanical detection threshold; MQS- Medication Quantification Scale Version III; NDI- neck disability index; NRS- numeric rating scale; NAS- numeric analog scale; n.r.-not reported; n.s.-not significant; NSLBP-non-specific low back pain; ODI- Oswestry Pain Disability Index; PM- pain related to movement PPI- Present Pain Intensity Scale of the McGill Pain Questionnaire; PR- Pain at rest; PPT- pressure pain thresholds; sig.-significant; SF-36- Short-form quality of life; UC-usual care; CRI -The Cell Replication Index ; SCE- Sister Chromatid Exchanges; VAS- Visual Analog Scale; VDT- vibration detection threshold

*- usual care also included analgesic drugs (peripheral or central acting), physiotherapies (manual therapy, hydrotherapy, electrotherapy, physical exercise), psychological care (single or group therapy) and musicotherapy.

**-average of three subscales: pain, tingling and numbness

#-colchicine, corticosteroids and imurel

Table 2 Risk of bias of the included RCTs

| First author (year) [ref] | Sequence generation | Allocation concealment | Blinding of participants, personnel and outcome assessors | Addressing of incomplete data | Selective outcome reporting | Other sources of bias |
|----------------------------------|---------------------|------------------------|---|-------------------------------|-----------------------------|-----------------------|
| Al Bedah (2015)[17] | L | L | U | L | L | U |
| Aleyeidi (2015)[24] | U | L | U | L | L | U |
| Dehghani-Firoozabadi (2014) [21] | L | H | U | U | U | U |
| Erras (2013) [22] | H | H | H | H | U | H |
| Farhadi (2009)[15] | U | L | H | L | L | U |
| Farahmand (2012)[23] | L | U | H | L | L | U |
| Hekmatpou D (2013)[25] | U | U | U | U | U | H |
| Khalil (2013) [14] | U | U | H | U | U | U |
| Kim (2011) [16] | L | L | U | L | L | U |
| Kim (2012) [18] | L | L | L | L | L | U |
| Lauche (2012)[19] | U | L | H | L | U | L |
| Ludtke (2006) [20] | L | L | H | L | L | U |
| Michalsen (2009) [5] | L | L | H | L | L | U |
| Niasari (2007) [4] | H | H | H | U | U | U |

Table 2 Legend: H-denotes high risk of bias; L- denotes low risk of bias; and U- denotes unclear risk of bias

Author Disclosure Statement

One of the included trials was conducted by the authors involved in this review (A.M.N.A. and M.K.M.K.). An external evaluator (P.P.) was involved to independently evaluate the quality of all RCTs. No competing financial interests exist.

References

1. Chirali, I.Z., *Traditional Chinese Medicine-Cupping Therapy* 2000, London: Churchill Livingstone.
2. AlBedah, A.K., M; Elolemy, A; Elsubai, I; Khalil, A., *Hijama (cupping): a review of the evidence. . Volume 16(1) March 2011 12–16*. Focus on Alternative and Complementary Therapies, 2011. 16(1): p. 6.
3. Lee, M.S., et al., *Cupping for stroke rehabilitation: a systematic review*. J Neurol Sci, 2010. 294(1-2): p. 70-3.
4. Niasari, M., F. Kosari, and A. Ahmadi, *The effect of wet cupping on serum lipid concentrations of clinically healthy young men: A randomized controlled trial*. Journal of Alternative and Complementary Medicine, 2007. 13(1): p. 79-82.
5. Michalsen, A., et al., *Effects of Traditional Cupping Therapy in Patients With Carpal Tunnel Syndrome: A Randomized Controlled Trial*. Journal of Pain, 2009. 10(6): p. 601-608.
6. Calvino, B. and R.M. Grilo, *Central pain control*. Joint Bone Spine, 2006. 73(1): p. 10-6.
7. Tagil, S.M., et al., *Wet-cupping removes oxidants and decreases oxidative stress*. Complement Ther Med, 2014. 22(6): p. 1032-6.
8. Kim, J.I., et al., *Cupping for treating pain: a systematic review*. Evid Based Complement Alternat Med, 2011. 2011: p. 467014.
9. Lee, M.S., et al., *Cupping for hypertension: A systematic review*. Clinical and Experimental Hypertension, 2010. 32(7): p. 423-425.
10. Huang, C.Y., M.Y. Choong, and T.S. Li, *Effectiveness of cupping therapy for low back pain: a systematic review*. Acupunct Med, 2013. 31(3): p. 336-7.
11. Cao, H., C. Zhu, and J. Liu, *Wet cupping therapy for treatment of herpes zoster: A systematic review of randomized controlled trials*. ALTERN THER HEALTH MED, 2010. 16(6): p. 48.
12. Cao, H., X. Li, and J. Liu, *An updated review of the efficacy of cupping therapy*. PLoS ONE, 2012. 7(2).
13. Higgins, J.P.T., et al., *The Cochrane Collaboration's tool for assessing risk of bias in randomised trials*. The BMJ, 2011. 343: p. d5928.
14. Khalil, A.M., Al-Qaoud, K.M., Shaqqour, H.M., *Investigation of Selected Immunocytogenetic Effects of Wet Cupping in Healthy Men* Spatula DD., 2013. 3(2): p. 51-57.
15. Farhadi, K., et al., *The effectiveness of wet-cupping for nonspecific low back pain in Iran: A randomized controlled trial*. Complementary Therapies in Medicine, 2009. 17(1): p. 9-15.
16. Kim, J.I., et al., *Evaluation of wet-cupping therapy for persistent non-specific low back pain: A randomised, waiting-list controlled, open-label, parallel-group pilot trial*. Trials, 2011. 12(146).

17. AlBedah, A., et al., *The Use of Wet Cupping for Persistent Nonspecific Low Back Pain: Randomized Controlled Clinical Trial*. J Altern Complement Med, 2015. 21(8): p. 504-8.
18. Kim, T.H., et al., *Cupping for treating neck pain in video display terminal (VDT) users: a randomized controlled pilot trial*. J Occup Health, 2012. 54(6): p. 416-26.
19. Lauche, R., et al., *The effect of traditional cupping on pain and mechanical thresholds in patients with chronic nonspecific neck pain: a randomised controlled pilot study*. Evid Based Complement Alternat Med, 2012. 2012: p. 429718.
20. Ludtke, R., et al., *Brachialgia paraesthetica nocturna can be relieved by "wet cupping"--results of a randomised pilot study*. Complement Ther Med, 2006. 14(4): p. 247-53.
21. Dehghani-Firoozabadi, M., Navabzadeh, M., Khodashenas-Roudsari, M., Zahmatkash, M. , *Comparative efficacy trial of cupping and serkangabin versus conventional therapy of migraine headaches: A randomized, open-label, comparative efficacy trial*. . J Res Med Sci, 2014. 19(12).
22. Erras, S., Benjilali, L., Essaadouni, L. , *Wet-cupping in the treatment of recalcitrant oral and genital ulceration of Behçet disease: A randomized controlled trial*. Indian Journal of Traditional Knowledge, 2013. 12(4): p. 615-618.
23. Farahmand, S.K., et al., *The effects of wet cupping on coronary risk factors in patients with metabolic syndrome: A randomized controlled trial*. American Journal of Chinese Medicine, 2012. 40(2): p. 269-277.
24. Aleyeidi, N.A., et al., *Effects of wet-cupping on blood pressure in hypertensive patients: a randomized controlled trial*. J Integr Med, 2015. 13(6): p. 391-9.
25. D, H., M. L, and H.N. S, *The effectiveness of wet cupping vs. venesection on arterial O2 saturation level of cigarette smokers: A randomized controlled clinical trial*. Pak J Med Sci, 2013. 29(6): p. 1349-53.
26. Cao, H. and J. Liu, *Cupping therapy for facial paralysis: A systematic review of randomized controlled trials*. BMC Complementary and Alternative Medicine, 2012. 12.
27. Zhou, X., J.W. Ruan, and B.F. Xing, *[Analysis on the adverse events of cupping therapy in the application]*. Zhongguo Zhen Jiu, 2014. 34(10): p. 1023-5.
28. Lee, M.S., et al., *Developing and validating a sham cupping device*. Acupunct Med, 2010. 28(4): p. 200-4.
29. Kim, T.H., Kim, K.H., Choi J.Y, Lee M.S. , *Adverse events related to cupping therapy in studies conducted in Korea: A systematic review* European Journal of Integrative Medicine, 2014. 6(4): p. 434-440.