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Wet cupping for hypertension: a systematic review and meta-analysis

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ABSTRACT

To assess the efficacy and safety of wet cupping in adults with hypertension, we conducted a systematic review and meta-analysis using 13 databases. Wet cupping alone or in combination with antihypertensive medication or acupuncture was used. Seven randomized trials were included, most not of high methodological quality. A few small studies suggested that wet cupping alone versus antihypertensive medication significantly reduced blood pressure and Traditional Chinese Medicine syndrome (hypertension-related symptoms). However based on current evidence, no firm conclusions can be drawn and no clinical recommendations made. Research projects included need validation. Studies indicate that wet cupping is a safe therapy.

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Wet cupping; hypertension; effect; meta-analysis; systematic review

Introduction

Hypertension is a serious global healthcare problem due to its high prevalence and associated cardiovascular disease risk (1). By the year 2025, it is estimated that 1.5 billion adults (29%) worldwide will have hypertension (1). Major cardiovascular events are caused by high blood pressure (BP) (2), including 62% of strokes and 49% of myocardial infarctions, and result in high mortality (3). The rate of hypertension control with drug treatment remains less than optimal (4), and patients may have antihypertensive medication side effects that reduce treatment adherence (5,6). In contrast, recent attention has focused on benefits of non-pharmacological complementary and alternative medicine (CAM) approaches for hypertension control (7–10). A major component of CAM is Traditional Chinese Medicine (TCM), which includes cupping therapy (11).

The earliest recorded use of cupping was by the famous Chinese Taoist alchemist and herbalist, Ge Hong (281–341 A. D.). The value of cupping as a treatment has been established over thousands of years. Hippocrates in ancient Greece and the famous British doctor, Mr. Arthur Keith, in the early 1900s recommended the use of cups to treat a variety of diseases (12). Cupping became world-famous in 2016 when it was portrayed on the internet as the "newest trend for Rio Olympics athletes", focusing on the swimming performance of a well-known elite athlete, Michael Phelps (13). Currently, many countries including China, Korea, Germany, Norway, Denmark, Saudi Arabia, Egypt, Iran and India use cupping therapy (14,15).

Cupping is a gentle therapy that uses negative pressure, from a vacuum created by slightly heated cups against the skin, to achieve its results. The negative pressure releases tight tissue that helps loosen muscle and tissue adhesions. It brings fresh blood and nutrients to the muscles and skin. It is described as a very powerful and relaxing therapy that is comfortable (16); this therapy with no side effects is increasingly welcomed by hypertensive patients for reducing BP and alleviating hypertension-related symptoms (17–23). This idea of symptoms associated with hypertension is generally accepted in some regions of the world. For example, patients with a diagnosis of hypertension in China, other Asian countries and Arabic nations are troubled by symptoms they associate with hypertension such as dizziness, headache, irritability, physical weakness in the knees and soreness of the waist. This differs from the thinking in the West where hypertension-related symptoms are not emphasized and are believed not to be present; hypertension in the West is described as The Silent Killer.

Cupping is dry or wet. Wet cupping therapy expels fluids and toxins into a cup and has been shown to be better than dry cupping because it removes causative pathological substances and restores normal physiology, whereas dry cupping therapy relies only on the dilution and redistribution of causative pathological substances to new locations (24). Wet cupping has long been used by acupuncturists as a treatment for chronic diseases such as hypertension (25–27). The exact mechanism of wet cupping is not clear, and many theories such as Qi, Yin and Yang have been put forward (28). Wet cupping is thought to act by triggering the suppression of proliferation of harmful inflammatory mediators, biological, chemical or other unwanted substances (24), and removing oxidants from the body, reducing oxidative stress (29). Some researchers report that wet cupping discharges excess liquids,

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increases the flow of blood to the skin and muscle, and stimulates peripheral nerves, neurohormones and the circulatory and immune systems (27,30).

Wet cupping has two major types: puncturing and cupping (PC) and cupping, puncturing and cupping (CPC) also called Al-Hijamah, which has a strong scientific and medical foundation based on Taibah theory suggested by El Sayed (24). The PC method is common in China, Korea and Germany (31,32) and has five steps: skin demarcation, sterilization (disinfection), puncturing the skin, cupping and sterilization. In contrast, the CPC method often used in Arabic countries (24,33) has a different method of application and has six steps: skin demarcation, sterilization, cupping, puncturing of the skin, cupping and sterilization. The difference between the two methods occurs at the third step.

Whether wet cupping is as effective as medication in treating hypertension or whether it works best in conjunction with other CAM therapies has not been established, but it is clear that additional research with more outcomes has been published since the last review on this topic in 2010 (25). Given that wet cupping is already used for hypertension control in some countries, it is essential to determine if a strong evidence base for this practice exists. Therefore, regarding the role of wet cupping in the treatment of hypertension, we conducted a systematic review and meta-analysis to examine the efficacy and safety of this therapy. If we find a strong evidence base, then a short-term goal would be to help practitioners incorporate the scientific evidence into clinical guidelines, and then support policies at medical centers for the possible incorporation of wet cupping into practice for hypertension control.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (34).

Database and search strategy

We searched 9 English databases from inception through 2 May 2018: PubMed, Cochrane Library, CINAHL, EMBASE, MEDLINE, PsycINFO, Scopus, Web of science and Science Direct, using a search strategy with the terms "hypertension" or "blood pressure" or "essential hypertension" AND "wet-cupping" or "wet cupping" or "cupping therapy" or "wet cupping therapy" or "Hijama" or "Al-Hijamah" or "bloodletting therapy." We also searched 4 Chinese databases: Chinese National Knowledge Infrastructure, Wan-fang Data, Chinese Biomedical Literature Database and Chinese Scientific Journal Database. The search terms included "刺络放血"(thorns bloodletting) or "刺络泻血"(thorn spilled blood) or "刺络拔罐"(piercing cupping) AND "拔罐"(cupping) AND "高血压"(hypertension). We manually searched all reference lists in the articles to obtain additional references.

Inclusion criteria and exclusion criteria

We selected RCTs with the following PICO elements and defined the inclusion criteria: 1) population (adult hypertensive patients independent of stage, with SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg) (35), 2) intervention (wet cupping therapy either PC or CPC where the wet cupping was the main focus, but could be in combination with antihypertensive medication or acupuncture), 3) comparison (antihypertensive medicine or acupuncture) and 4) outcomes (the primary outcome measures of SBP and DBP, and secondary outcomes of antihypertensive effect and TCM syndrome effect). All antihypertensive medications refer to Western blood pressure medicine. Studies were excluded if they were nonrandomized or used wet cupping, not well defined as part of a complex intervention.

Data extraction

Two independent reviewers used a predefined protocol to extract data from published literature (36). Data extraction included: author/publication year, sample, age, sex, intervention, control, intervention length and outcome measures.

Risk of bias across studies

First, the risk of bias was assessed using the seven criteria of the Cochrane Handbook for Systematic Review of Interventions, Version 5.1.0 (37): randomization allocation (selection bias), allocation concealment (selection bias), blinding of the participants and personnel (performance bias), blinding of the outcome assessment (detection bias), incomplete outcome data (attrition bias), intention-to-treat analysis (confounding bias) and comparability (other bias). Second, the seven criteria were rated as "Yes" for a low risk of bias, "No" for a high risk of bias and "Unclear" otherwise. As no sham wet cupping condition was available, blinding of the outcome assessors was considered adequate for the purposes of this review. Finally, the overall risk of bias for each trial was categorized as low (all items were at low risk of bias), high (at least 1 item was at high risk for bias) or unclear (at least 1 item was at unclear risk of bias).

Data analysis and synthesis

The Revman 5.3 software by the Cochrane Collaboration was used for data synthesis and analysis. For continuous outcomes, the means and standard deviations for each group were extracted. The dichotomous outcomes were antihypertensive effect and TCM syndrome effect. The antihypertensive effect refers to BP improvement according to Guiding Principles of Clinical Research on TCM and includes three levels. Efficacy refers to a reduction in DBP ≥ 10 mmHg and reaching the normal level, or not reduced to normal but reduced > 20 mmHg. Markedly refers to DBP reduced < 10 mmHg and reaching the normal level, or DBP reduced 10–19 mmHg but not reaching the normal level or, in the presence systolic hypertension, SBP reduced ≥ 30 mmHg. Invalid refers to not achieving the markedly standard (17). The TCM syndrome effect refers to clinical improvement for the following hypertension-related symptoms: dizziness, headache, irritability, physical weakness in the knees and soreness of the waist according to Guiding Principle of TCM in Treating Hypertension (18).

Dichotomous data were expressed as relative risk (RR). Continuous data were expressed as the weighted mean difference (WMD). The Z-score and the χ^2 (I^2) were used to measure statistical heterogeneity. If $I^2 < 50\%$ and $p > 0.1$ indicating no heterogeneity, a fixed effect model was applied. Conversely, the random effect model was used if articles were considered clinically similar enough. Otherwise, they were synthesized using descriptive analysis instead of meta-analysis. Meanwhile, subgroup analysis was conducted according to the types of comparisons. Due to the small number of RCTs included in this review, funnel plots were not used (38).

Results

Description of included trials

As shown in Figure 1, the initial search identified 136 records (37 duplicate records), with 99 articles remaining to be analyzed by title/abstract. Out of 16 articles assessed for eligibility, nine were excluded because they were not RCTs, used multimodal interventions or were duplicate publications of data. Information about the RCTs is summarized in Table 1.

Of the 7 RCTs, four came from China, two came from Saudi Arabia and one came from Iran. Sample size varied from 18 to 107 participants. RCTs included a wide range of participants' ages (18–83 years) and both males and females. Wet cupping (PC) was the sole treatment in 3 RCTs (17–19), whereas in 4 RCTs (20–23) wet cupping was used as an adjunct treatment to antihypertensive medication or acupuncture. The control groups were taking antihypertensive medications, except in 1 RCT (23) in which the controls underwent acupuncture.

Participants received wet cupping therapy for a mean of 8.4 weeks (range 5–12 weeks). The most frequently used sites for wet cupping were the seventh cervical vertebra, which is called GV14 in Chinese medicine; the two scapulae opposite T1-T3 on the spine, which are called Al-Kahil in Arabic and both sides of the neck, which are called FengChi Point in Chinese medicine or Al-Akhdaain in Arabic. Four RCTs (19–22) used the BP, four RCTs (17–19,23) used the antihypertensive effect and two RCTs (18,19) used the TCM syndrome effect as an outcome measure. Only 1 RCT (19) included all the outcome measures and used a three-group study design. Three RCTs (19,21,22) described adverse effects.

Methodological quality of included trials

The risk of bias of the trials is summarized in Table 2. According to the predefined quality assessment criteria (37), most of the RCTs did not have high methodological quality. Three (19,22,23) of the seven RCTs had adequate randomization allocation; they used a random number table or computer-generated random number list. Three RCTs (19,21,22) reported allocation concealment. None of the trials mentioned double blinding probably because patients and personnel could not be blinded because wet cupping and antihypertensive medication had to be administered. Only one trial (19)

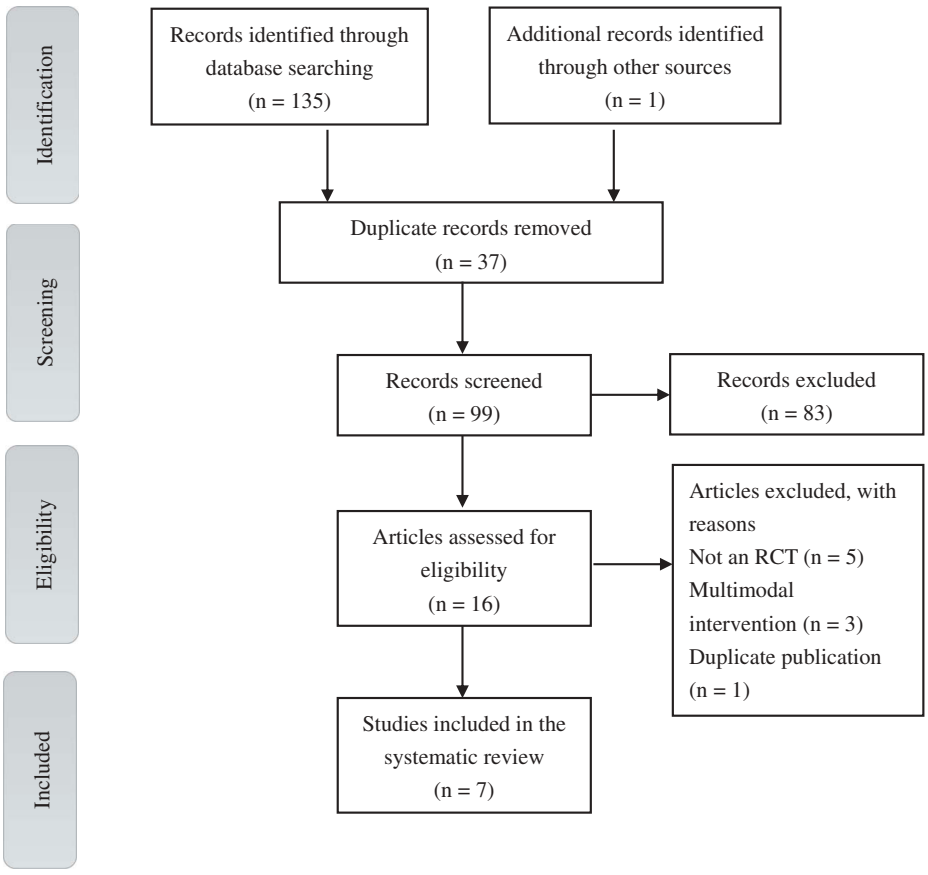

Figure 1. PRISMA flow diagram.

Table 1. Characteristics and methodological quality of included studies.

Author/ publication year	Sample (treatment/ control group)	Mean age (years) or range	Sex (M/F)	Intervention	Control	Intervention length (weeks)	Outcome measures
Wang et al. (1999) [17]	54/53	T: 50.8 C: 51.5	T: 26/28 C: 23/30	PC	Antihypertensive medication	5	Antihypertensive effect
He (2012) [18]	32/34	T: 30–56 C: 30–57	T: 21/11 C: 19/15	PC	Antihypertensive medication	12	Antihypertensive effect TCM syndrome effect
Wang (2013) [19]	33,31/31	T1: 18–75 T2: 18–75 C: 18–75	T1: 14/19 T2: 16/15 C: 18/13	PC	Antihypertensive medication	12	BP Antihypertensive effect TCM syndrome effect
Zarei et al. (2012) [20]	21/21	T: 51.19 ± 6.05 C: 51.29 ± 6.38	T: 11/10 C: 11/10	PC plus antihypertensive medication	Antihypertensive medication	6	BP
Aleyeidi et al. (2014) [21]	10/8	T: 52.0 ± 7.2 C: 49 ± 9.5	T: 4/6 C: 3/5	CPC plus antihypertensive medication	Antihypertensive medication	12	BP
Aleyeidi et al. (2015) [22]	40/40	T: 52.0 ± 9.4 C: 53.8 ± 9.5	T: 13/27 C: 11/29	CPC plus antihypertensive medication	Antihypertensive medication	8	BP
Xu et al. (2015) [23]	30/30	T: 36–83 C: 33–80	T: 11/19 C: 16/14	CPC plus acupuncture	Acupuncture	4	Antihypertensive effect

T, intervention group; T1, higher amount of blood extracted (HABE) group; T2, lower amount of blood extracted (LABE) group; C, control group; PC, puncturing and cupping; CPC, cupping, puncturing and cupping.

Table 2. Quality assessment of included randomized controlled trials.

Included trials	Randomization allocation	Allocation concealment	Blinding of the participants and personnel	Blinding of the outcome assessment	Incomplete outcome data	Intention-to-treat analysis	Comparability	Risk of bias
Wang et al. (1999) [17]	Unclear	No	Unclear	Unclear	Yes	NA	Yes	Unclear
He (2012) [18]	Unclear	No	Unclear	Unclear	Yes	NA	Yes	Unclear
Zarei et al. (2012) [20]	Unclear	No	Unclear	Unclear	Yes	NA	Yes	Unclear
Wang (2013) [19]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Low*
Aleyeidi et al. (2014) [21]	Unclear	Yes	Unclear	Unclear	Yes	NA	Yes	Unclear
Aleyeidi et al. (2015) [22]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Yes	Unclear
Xu et al. (2015) [23]	Yes	No	Unclear	Unclear	Yes	NA	Yes	Unclear

"Yes" for a low risk of bias, "No" for a high risk of bias, "Unclear" otherwise,
"NA" means not applicable, due to no drop-out or withdrawal
The risk of bias "unclear" designation means at least 1 item was at unclear risk of bias
*The risk of bias "low" designation means all items were at low risk of bias, given an exception for blinding of participants and personnel, which was probably not possible due to the need for active treatment by the researcher.

mentioned blinding of the outcome assessment. All of the trial data were complete; they reported drop-outs or withdrawals. One of the seven trials reported the use of intention-to-treat analysis. All experimental and control groups were matched adequately without baseline imbalance bias (comparability).

Effect of the interventions

Seven RCTs were included. Of all the trials, 1 RCT (19) with a three-group study design included a higher amount of blood extracted (HABE), a lower amount of blood extracted (LABE) and an antihypertensive medication group. So we separated this article into one group labeled h for HABE and one group labeled l for LABE for the meta-analysis. The effect estimates of wet cupping are shown in Figure 2–5.

Effect of wet cupping on BP

Four RCTs (19–22) reported the effect of wet cupping on BP values. The result of meta-analysis showed that, compared with the antihypertensive medication control group, wet cupping had no statistically significant effect in lowering SBP [WMD = −2.24, 95% CI (−9.13, 4.65), p = 0.52] (Figure 2) or DBP [WMD = −2.11, 95% CI (−8.85, 4.64), p = 0.54] (Figure 3) for hypertensive patients.

To explore the separate effect of wet cupping on BP, two subgroups were analyzed according to the interventions. The result of the meta-analysis showed that, compared with the antihypertensive medication control group, wet cupping alone had a significant effect in lowering SBP [WMD = −7.69, 95% CI (−12.18, −3.19), p = 0.0008] (Figure 2) and DBP [WMD = −8.39, 95% CI (−14.08, −2.70), p = 0.004] (Figure 3).

In addition, 3 RCTs (20–22) included wet cupping plus antihypertensive medication. The result of the meta-analysis showed that, compared with the antihypertensive medication control group, wet cupping plus antihypertensive medication had no statistically significant effect on lowering SBP [WMD = 2.83, 95% CI (−9.29, 14.96), p = 0.65] (Figure 2) or DBP [WMD = 2.70, 95% CI (−1.46, 6.86), p = 0.20] (Figure 3).

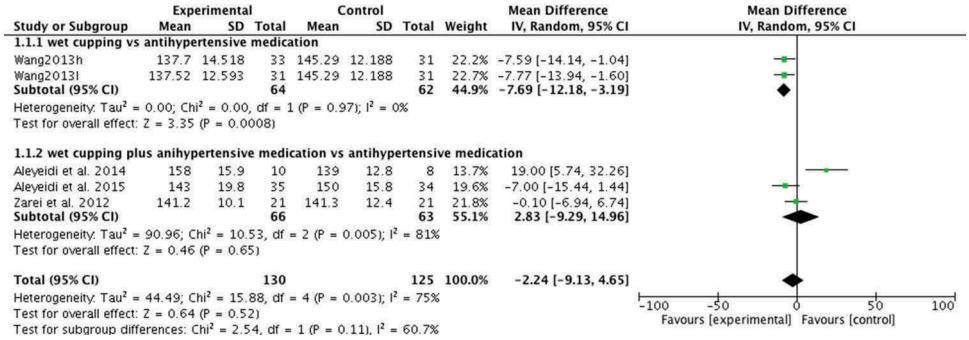

Figure 2. The forest plot of the outcome measure SBP.

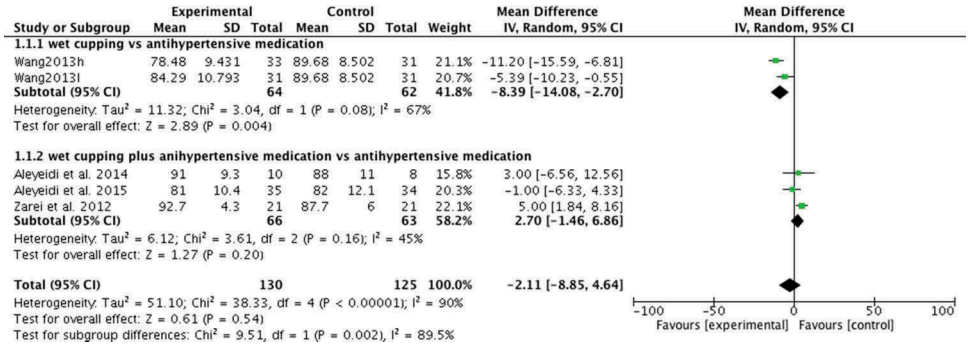

Figure 3. The forest plot of the outcome measure DBP.

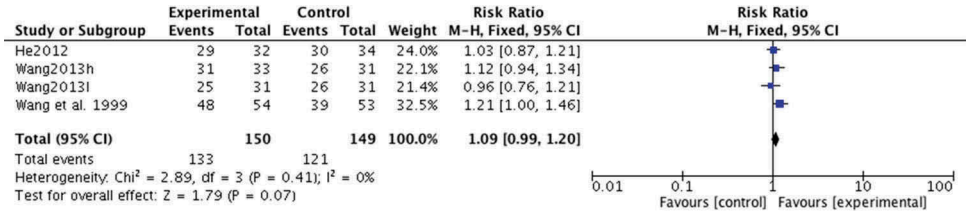

Figure 4. The forest plot of outcome measure antihypertensive effect.

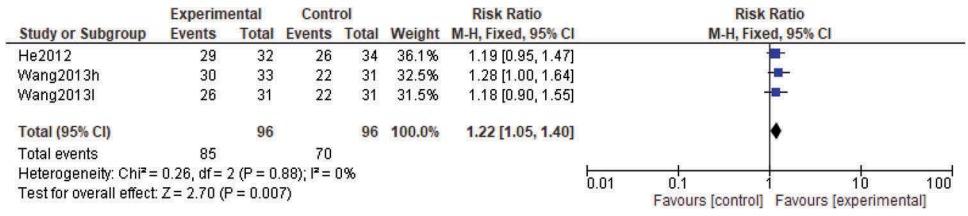

Figure 5. The forest plot of outcome measure TCM syndrome effect.

Effect of wet cupping on the antihypertensive effect

A total of 3 RCTs (17–19) reported the effect of wet cupping compared with antihypertensive medication on antihypertensive effect (Figure 4). One RCT (17) showed the most favorable effect. The result of the meta-analysis showed that, compared with the antihypertensive control group, wet cupping had no statistically significant effect in improving the antihypertensive effect [RR = 1.09, 95% CI (0.99, 1.20), p = 0.07] (Figure 4).

In addition, one trial (23) evaluated the effect of wet cupping plus acupuncture compared with acupuncture on the antihypertensive effect. There was a significant difference between the groups ($p < 0.05$), and the combination of wet cupping plus acupuncture was more effective than acupuncture alone.

Effect of wet cupping on TCM syndrome effect

Two trials (18,19) compared wet cupping to antihypertensive medication. Both RCTs demonstrated that wet cupping alone is better than antihypertensive medication regarding the TCM syndrome effect. The result indicated that, compared with the

antihypertensive medication control group, wet cupping had a significant effect in improving the TCM syndrome effect [RR = 1.22, 95% CI (1.05, 1.40), p = 0.007] (Figure 5).

Safety of wet cupping

Three trials (19,21,22) described adverse events; none reported serious side effects in the wet cupping group. In 1 RCT, a participant who did not drink water and rest before cupping experienced some dizziness and nausea. Eleven of 98 participants had a mild headache and cupping-site pruritus. One participant had bullae formation due to the prolonged application of the cup for more than the recommended time; the area was completely healed after 1 week with treatment.

Discussion

There is strong evidence from randomized trials that even a small reduction in BP can help to prevent cardiovascular events (especially strokes) (39), yet BP control in the population is still unsatisfactory, and no more than 25% of hypertensive patients worldwide have BP values < 140/90 mmHg.[2] Largely due to antihypertensive medication side effects, self-paid medical costs and insufficient doses of prescribed medication, patients have poor treatment outcomes (40,41) and run the risk of having uncontrolled BP. Therefore, exploring novel CAM methods is important today to try to improve these poor hypertensive treatment outcomes.

CAM has been recognized and accepted in Europe and America and has been included to a great extent in modern medicine as an important supplement to mainstream medical care in the West (42,43). Previous reports estimate that 29% to 69.5% of hypertensive patients are treated with CAM (44–46). Wet cupping, an ancient form of alternative medicine (28), has physiological effects conducive to BP control without severe side effects. It has been reported that pressure exerted on the skin for more than a few seconds can benefit patients through reactive hyperemia. After a few minutes of wet cupping, blood vessel compression leads to an increase in the skin's blood supply, resulting in a buildup of vasodilator chemicals. Once the blood vessel pressure is removed, the blood flow to the skin increases dramatically. This cycle could bring more blood to the skin for filtration and removal of causative pathological substances (24).

Overall, the current meta-analysis examining the efficacy and safety of wet cupping in hypertensive patients provides a timely update to a 2010 review (25), which contained only one research study on wet cupping for hypertension control. Although wet cupping therapy is common in at least 9 countries, we found RCTs only from three (China, Saudi Arabia and Iran). Even with the small number of studies on this topic found in the literature today, some effects were noted but should be viewed with caution. The analysis indicates that wet cupping alone versus antihypertensive medication significantly reduced systolic and diastolic BP in one study (19) and reduced TCM syndrome in two studies (18,19). This evidence is not strong enough to suggest that wet cupping alone, a TCM approach, may produce the same benefits as antihypertensive medication.

Next in 3 RCTs (20–22), a clinically useful comparison of wet cupping plus antihypertensive medication versus a group on antihypertensive medication alone yielded no additional benefit on SBP and DBP from the wet cupping. In these 3 trials, antihypertensive effect and TCM syndrome effect were not studied. Finally, when wet cupping was added to acupuncture in one study (23), the antihypertensive effect was significantly improved. It is important to note that, overall, the research projects used in this meta-analysis need validation. Therefore, based on the current state of the science regarding wet cupping and hypertension in adults, it would be inappropriate to put forth specific clinical recommendations at this time.

This meta-analysis has several limitations. The intervention length across the studies varied from 4 weeks to 12 weeks, and we did not have enough studies to examine its influence. Although youth have diagnosed hypertension, the meta-analysis focused on adults only. Also, the review of literature did not explore specific mechanisms underlying wet cupping therapy.

Conclusion

Wet cupping shows promise in adults with hypertension, yet firm conclusions cannot be drawn due to the small number of studies and quality of their methodology. The evidence base is not yet strong enough to encourage the clinical use of wet cupping in adults with hypertension. Future studies examining all the outcomes (BP, antihypertensive effect and TCM syndrome effect) with larger, more diverse samples are needed overall. The conduct of research examining differences between PC and CPC types of wet cupping has been suggested recently by Mahmoud (24). In addition, using wet cupping as an adjunct to acupuncture is an interesting idea, but more research is warranted. Finally, based on current evidence, wet cupping is a safe therapy with no serious side effects.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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