

Review

Cupping Therapy for Diseases: An Overview of Scientific Evidence from 2009 to 2019

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ABSTRACT Cupping therapy has been accepted worldwide, and many studies have been conducted to reveal its curative effects and mechanisms. To comprehensively evaluate the effect of cupping therapy, database including China Network Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database VIP, Wan Fang Database, Chinese Biomedicine (CBM), PubMed and Web of Science were searched from 2009–2019. We summarized all the meta-analyses, randomized controlled trials, clinical trials and the mechanisms studies of cupping therapy in the previous 10 years, hoping to provide a reference for the clinical applications and studies.

KEYWORDS cupping, overview, clinical trial, efficacy, mechanism, non-drug therapy

Cupping therapy has been used in Chinese medicine (CM) for thousands of years. It is administered by creating negative pressure inside a cup to make the cup suction to the desired acupoints of the patient's skin to create local skin hyperaemia or haemostasis, which can achieve a curative effect on certain diseases.⁽¹⁾ The earliest record of cupping was documented 2,000 years ago in the Bo Shu, an ancient book written on silk and unearthed in a Han Dynasty tomb.⁽²⁾ Other ancient Chinese literatures has described therapeutic cupping methods and case records of treatment. Cupping therapy could dredge the meridians, draw off the extravasate and was primarily used to treat the excess-heat syndrome and yang syndrome of surgical diseases such as sores, ulcerative carbuncles, and haemorrhoids.^(3,4) Approximately 300 years ago, cupping therapy was clinically applied more widely for treatment of diseases of internal medicine because of its effect on regulating qi and blood activities. After millennia of development, cupping therapy has been widely used in surgery, internal medicine, gynaecology, paediatrics, orthopaedics, dermatology, and other fields.^(5,6)

In recent years, China has prioritized the development of traditional medicine. Cupping therapy has undergone constant improvements in methodology, the cupping device used and acupoint selection based on syndrome differentiation. Many types of cupping have been developed, including bamboo cupping, glass cupping, ceramic cupping, metal cupping, air extraction cupping, multifunction

cupping, and vacuum cupping. The methods of exhausting the gas from the cupping device include boiling-water cupping, flaming heat power cupping, suction cupping, and electric cupping. Cupping can also be classified according to syndrome differentiation as retained cupping, bleeding cupping, moving cupping, needle cupping, medicinal cupping, magnetic cupping, electric heating cupping, negative pressure cupping, massage cupping, and scraping cupping.⁽⁷⁾

The number of studies of cupping has increased, and its methodologies of clinical trials have improved after years of growth. Randomized controlled trials (RCTs) and meta-analyses (MAs) have enabled the formation of promising conclusions. To comprehensively evaluate cupping therapy, we summarized all the RCTs, clinical trials and the MAs of cupping therapy in the previous 10 years so as to provide a reference for scientific research and clinical applications.

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METHODS

China Network Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database VIP, Wan Fang Database, Chinese Biomedicine (CBM), PubMed and Web of Science were searched for studies published from 2009 to 2019 on human or animals. The search terms included "cupping therapy", "bleeding cupping", "wet cupping", "dry cupping", "flash cupping", "herbal medicine", "moving cupping" or "retained cupping" without narrowing or limiting search items. Relevant publications with available abstracts and titles were reviewed by 2 reviewers. The Clinical Trials (<https://clinicaltrials.gov/>) and Chinese Clinical Trial Registry (<http://www.chictr.org.cn/>) databases were searched for registered clinical trials of cupping therapy. The search terms were "cupping therapy", "bleeding cupping", "wet cupping", "dry cupping", "flash cupping", "herbal medicine", "moving cupping" or "retained cupping". Trials quality, study selection, data extraction and validation were performed independently by two authors. Cochrane criteria for risk-of-bias were used to assess the methodological quality of the trials.

RESULTS

Clinical Efficacy Study of Cupping Therapy RCTs of Cupping Therapy

Totally 41 RCTs (sample size >50 cases) using cupping as the only therapy published from 2009 to 2019 were included. Studies of cupping combined with other therapy in the clinical treatment were excluded. The details of the included 41 published RCTs⁽⁸⁻⁴⁸⁾ are shown in Appendix 1. Analysis of these RCTs found that 33 studies^(9,10,12,16-21,23-34,36-40,42-44,46-48) were completed by Chinese researchers, and the other 8 studies^(11,13-15,22,35,41,45) were completed by German, Saudi Arabian, Republic of Korean, Indian and Iran researchers. The maximum enrolled participants were only 283 and the sample size was small. The age of the participants ranged from 1 to 79 years. Four studies mentioned complications, including headache, back pain, vertigo, dizzy, loss of appetite, blister and ecchymosis. A total of 35 studies^(8,10-21,23-28,31-43,46-48) showed that cupping therapy had better clinical efficiency than therapy of control group, 6^(9,22,29,30,44,45) showed cupping therapy exerted the same effect as the therapy of control group. In 6 studies,^(10-14,20) the Jadad score was above 4, and the remaining studies scored below 4 scores.

Registered Clinical Trials of Cupping Therapy

We also found 16 registered clinical trials (Appendix 2) from <https://clinicaltrials.gov/> and <http://www.chictr.org.cn/>, and the recruiting locations vary from China and Korea to Saudi Arabia, Germany and Turkey, which will provide wider scientific insight into the cupping therapy all over the world.

MAs of Cupping Therapy

Five meta-analysis studies on cupping therapy with strong evidence were included. Yuan, et al⁽⁴⁹⁾ estimated the effect of cupping therapy on neck pain by MA, and results showed that cupping could be more effective than waitlist in improving the visual analog scale (VAS) scores. Wang, et al⁽⁵⁰⁾ conducted a MA based on existing RCTs to study the effect of cupping therapy on lower back pain. The results showed that cupping therapy could significantly decrease the VAS scores and Oswestry disability index (ODI) scores for patients with lower back pain (LBP) compared to the control management. Caroline, et al⁽⁵¹⁾ studied the effect of cupping therapy on chronic back pain by systematic review and MA. The results showed that there was a significant reduction in the pain intensity score in cupping therapy group. Li, et al⁽⁵²⁾ performed a MA to evaluate the effect of cupping therapy on knee osteoarthritis. Their results showed that compared to Western medicine therapy, dry cupping plus Western medicine significantly improved the pain, stiffness, and physical function according to Western Ontario and McMaster Universities (WOMAC) osteoarthritis index. Cao, et al⁽⁵³⁾ performed a MA of herpes zoster treated by cupping therapy to evaluate its efficacy. The results showed that wet cupping had a better effect than medication according to the number of cured patients, the number of patients with improved symptoms, and the reduced incidence of postherpetic neuralgia (PHN). Wet cupping appears to be an effective treatment for herpes zoster virus.

Prognosis of Cupping Therapy

As shown in RCTs, clinical trials and MAs, cupping therapy could effectively treat neck pain, LBP, lumbar pain, knee joint pain, herpes zoster, acne, skin itch, Gibert's disease, senile pruritus, urticaria acuta, exogenous fever, cough, gastrointestinal function, migraine headache and facial disease. Cupping therapy could improve related outcomes of the diseases and the prognosis

of these disease was well.

Mechanism Studies of Cupping Therapy

Effects on Microcirculation

Microcirculation provides nutrients and oxygen to cells and removes metabolic waste. The changes in microcirculatory blood flow and haemoglobin can reflect the curative effects, and these changes have been examined in studies of cupping therapy. Liu, et al⁽⁵⁴⁾ found that cupping could cause changes in dermal blood flow. Removal of the cup immediately, the blood flow at the Dazhui (GV 14), Shenzhu (GV 12) and bilateral Feishu (BL 13) acupoints were obviously increased. Twenty minutes after cupping removal, the blood flow of the above mentioned acupoints was obviously decreased. Li, et al⁽⁵⁵⁾ found that during and post cupping, there was a prominent drop in deoxyhaemoglobin and a significant elevation in oxyhaemoglobin in the infraspinatus, the site of the cupping, which manifested as enhanced oxygen uptake. The results indicated that cupping therapy could improve hemodynamics to facilitate muscular function.

Effects on Skin Temperature

Skin temperature is closely related to the hypothalamic temperature regulation centre, neuroendocrine system, blood vessels, blood flow, energy metabolism, external temperature, and other factors. Studies have found that cupping therapy could influence local skin temperature.^(56,57) Xu, et al⁽⁵⁸⁾ found that immediately upon removal of the cup, the skin temperature of the cupping site dropped compared to that before cupping. Ten minutes after cup removal, the skin temperature increased compared to the temperature immediately upon cup removal. In addition to the impact on skin temperature at the local cupping site, cupping can influence the skin temperature of the neighbouring meridian. Cupping at the GV 14 acupoints of the governor meridian could also increase the skin temperature of acupoints on the bladder meridian.⁽⁵⁹⁾ The above studies have found that cupping therapy could cause changes in skin temperature, but the mechanism of this effect requires further study.

Effects on Pain Threshold

The determination of the pain threshold of the human body is often used to evaluate the analgesic effect of a therapy on a variety of painful diseases. Emerich, et al⁽⁶⁰⁾ found that 160 min after cupping,

the level of lactate and the lactate/pyruvate ratio in the trapezius muscle significantly increased. The increases indicated the occurrence of anaerobic metabolism in the surrounding tissue. Compared to healthy control, the baseline pain thresholds of patients in a neck pain group were not significantly lower, and were slightly increased immediately after cupping. The pain thresholds showed no additional significant changes after 280 min. Short-term increases in the mechanical pain thresholds may be explained by counter-irritation, which is not related to the metabolic changes observed.

Effects on Immune System

Study has confirmed that cupping therapy can exert curative effects by regulating cellular immunity, humoral immunity, and immune-related cytokines.⁽⁶¹⁾ Zhong, et al⁽⁶²⁾ found that cupping on the bladder meridian from the Fengmen (BL 12) to the Shenshu (BL 23) acupoints increased the number of rosette-forming cells. The study indicated that cupping could improve the immunologic function of erythrocytes. Reproductive problems in women have manifested as elevated natural killer lymphocyte cytotoxicity (NKc). Dons'koi, et al⁽⁶³⁾ applied cupping therapy to treat patients with elevated NKc. The results showed that natural killer lymphocyte activity (NKa) was reduced on days 3 and 10 after cupping, and the NK percentage was reduced on day 10 after the last cupping treatment. NKc was most sensitive to cupping treatment, which decreased at 3, 10, and 17 days after cupping therapy.

Effects on Oxidative Stress

When the body is subjected to harmful stimuli, highly active molecular free radicals (FRs) emerge in the body, leading to an imbalance between the oxidation and antioxidant systems, or oxidative stress (OS). FR accumulation causes tissue damage and various diseases. Therefore, the alleviation of OX is the key issue in the treatment of many diseases.⁽⁶⁴⁾ Tagil, et al⁽⁶⁵⁾ applied wet cupping therapy to healthy volunteers and collected venous blood and wet cupping blood samples. The results found that the wet cupping blood samples had higher levels of myeloperoxidase, malondialdehyde, and nitric oxide and lower levels of superoxide dismutase compared to the venous blood.

Effects on Other Substances

Cupping therapy can promote the excretion of

metabolites to generate a curative effect within the body. Sun, et al⁽⁶⁶⁾ observed the effect of cupping therapy on athletes with exercise-induced fatigue. The results showed that after intensive physical training, athletes who received cupping therapy experienced a faster recovery on creatine kinase (CK) levels compared to the control group. Athletes in the cupping group also showed milder fatigue and better interpersonal relationships. The results indicated that cupping therapy could eliminate sports fatigue by improving the levels of certain metabolites.

Niasar, et al⁽⁶⁷⁾ studied the effect of cupping on serum lipoproteins. A total of 47 male (18 to 25 years old) who had no history of chronic disease, hyperlipidaemia, or antihyperlipidemic drug consumption were randomly assigned to control and treatment groups. After treatment, the male who received cupping therapy had significantly decreased low density lipoprotein cholesterol (LDL-C), a 7% decrease in total cholesterol, and a 3% increase in high density lipoprotein cholesterol compared to the control group. The results indicate that cupping therapy can effectively reduce serum LDL-C and prevent atherosclerosis. Tian, et al⁽²⁴⁾ investigated the effect of cupping therapy on PHN. After cupping treatment, the local serum P substance level was significantly reduced compared to pre-treatment. Lin, et al⁽⁶⁸⁾ studied the effects of cupping therapy on lower back pain and reported a significant decrease in plasma cortisol after 5 days of treatment.

Limitation and Perspectives

The effect and the relevant mechanisms behind how cupping therapy work as an effective treatment for various diseases are still controversial. During the past decade, much progress has been made in the research of cupping therapy. RCTs of cupping therapy have been shown to be effective in different diseases and further mechanism studies have begun to reveal how the cupping therapy could emit the curative effect. However, there are some limitations as follows.

Lack of Further Research on Mechanism of Cupping Treatment

There have been some improvements in the mechanism research of cupping therapy. As mentioned above, cupping therapy can affect the local skin blood flow, improve hemodynamics, influence local skin temperature, increase the local mechanical

pain threshold, alter the biomechanical properties of the skin, regulate immunity and immune-related cytokines, and improve the excretion of metabolites such as creatine kinase, LDL-C, local serum P substance, and plasma cortisol. However, additional studies are needed to determine the mechanism of cupping therapy.

Non-standard Randomization

We evaluated the quality of these 41 RCTs according to CONSORT checklist (Appendix 3). Only 36.6% of the studies included in this review described the method used to generate the random allocation sequence; 7.32% recorded the type of randomization; 19.51% used an allocation concealment mechanism; and 14.63% described the generation of the randomization sequence, registration of participants, and assignment of the patients into groups. The results of the methodology studies have shown that papers without proper randomization could possibly exaggerate the clinical effects of trials by 50% and result in false positive results.⁽⁶⁹⁻⁷¹⁾

Inadequate Blinding Method

Among the 41 papers included in this review, none used a blinding method (Appendix 3). In clinical trials, it is impossible and impractical to blind the treating physician, but it is possible to blind the researchers and patients. This could result in the bias caused by the evaluators and fail to achieve more reliable results. Lee, et al⁽⁷²⁾ developed a sham cupping device by establishing a small hole on the cup to reduce the negative pressure after suction so that negative pressure cannot be maintained. They then conducted a pilot study to evaluate the validity of the sham cupping device. A total of 34 healthy participants were enrolled and allocated into two groups. One group received real cupping and the other received sham cupping. The results showed that the two groups felt similar sensations. There was a tendency for subjects to feel that real cupping created a stronger sensation than sham cupping. The sham cupping device seemed to provide a credible control for real cupping therapy by producing little or no negative pressure.

Absence of Sample Size Estimation

Most of the trials included in this study (78.05%, Appendix 3) did not calculate the sample size, which may lead to the use of a sample size that is too small, and result in random error and false negative results.

Lack of Standards for Reporting Interventions

In 2010, international standards for reporting interventions in clinical trials of acupuncture (STRICTA) were published.⁽⁷³⁾ The standards can be used to report the results of acupuncture RCTs studies. However, STRICTA is not suitable to describe the procedures of cupping in clinical trials. Today, there are some protocols and national standards for cupping therapy, but a uniform, globally recognized standard is necessary to reduce the occurrence of adverse events and promote cupping therapy.⁽⁷⁴⁻⁷⁶⁾ The standards should include items such as the syndrome differentiation principle of cupping, an acupoint selection method, the intensity of the negative pressure generated, and the frequency and duration of treatment.

Adverse Events

Anaemia, factitial panniculitis, and herpes viral infection are the most frequently reported adverse events (AEs) in observational studies.⁽⁷⁷⁾ Unexpected lumbar abscess was reported due to scarification after wet cupping. Epidural abscess is possible when applying cupping and acupuncture, as reported in a clinical case.⁽⁷⁸⁾ Haemorrhagic stroke may develop after cupping of the cervical area due to an acute increase in blood pressure.⁽⁷⁹⁾ Cupping therapy is also related to post-inflammatory hyperpigmentation⁽⁸⁰⁾ and keloids.⁽⁸¹⁾ These AEs are likely caused by the misapplication of cupping therapy, inadequate disinfection procedures and risky application sites. Researchers should carefully consider the recording of AEs, and should provide treatment in compliance with safety guidelines.

Other Problems

Most of RCTs reports lacked a long-term follow-up endpoint-specific indicator such as mortality or disability. There have been few large-scale multi-centre or randomized double-blind placebo-controlled trials of cupping therapy. In addition, not all negative results (referring to the lack of a significant difference between main outcome measures) are published, which may lead to publication bias. Moreover, clinical trial institutions and evaluation agencies that conform to international standards have not yet been established, which limits the realization of comprehensive studies of existing clinical research.

In conclusion, as mentioned above, the evidence-based clinical researches confirmed that

cupping therapy could effectively treat different kinds of diseases, because it could regulate body function through multiple mechanisms. Cupping therapy is a promising treatment worthy of promotion and attention. In the future, we should focus on conducting further research on the mechanism of cupping, avoiding AEs, and optimizing the design and implementation of clinical study.

Conflict of Interest

The authors declare no conflicts of interest.

Author Contributions

Liu LT designed the manuscript, Wang SZ wrote the manuscript, Chen KJ revised the manuscript, Wu M and Liu Y searched the literature, Lu YH aided in the design of the tables. All authors approved the manuscript for publication.

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