Complementary Therapies in Medicine (2014) 22, 541—548

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Chinese massage (Tuina) for the treatment of essential hypertension: A systematic review and meta-analysis

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Available online 1 April 2014

KEYWORDS
Hypertension;
Complementary therapy;
Tuina;
Chinese massage

Summary
Background: Chinese massage, named Tuina, is commonly used in China and potentially effective for essential hypertension (EH). However, there is no critically appraised evidence such as systematic reviews or meta-analyses on the effectiveness and safety of Tuina for EH.
Methods: The following electronic databases: Pubmed, the Cochrane library, CNKI, the Wan Fang Database and VIP were searched for published and unpublished randomized controlled trials (RCTs) of Tuina for EH up to 20th August 2013.
Results: Seven randomized trials involving 479 patients were included. The results of meta-analysis showed superior effects of Tuina plus antihypertensive drugs compared to antihypertensive drugs alone, however, Tuina alone was not superior to antihypertensive drugs. The safety of Tuina for EH was still unclear because adverse effects were not assessed in most of the original trials.
Conclusions: The findings from our review suggest that Tuina might be a beneficial adjuvant for patients with EH, although the results are of limited value due to the clinical heterogeneity and low methodological quality of the included studies. Future studies should adhere to high-quality RCTs with long follow-up for demonstrating the effectiveness of Tuina for inpatients with EH.

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http://dx.doi.org/10.1016/j.ctim.2014.03.008
0965-2299/

Contents

Introduction

Hypertension, as an independent predisposing factor for heart failure, coronary artery disease, stroke, renal disease, and peripheral arterial disease, is associated with serious morbidity and mortality.[1] It has been estimated that hypertension accounts for 6% of deaths worldwide.[2] Although antihypertensive drug treatment clearly reduces the risks of cardiovascular and renal disease, large population of the hypertensive patients are either untreated or inadequately treated.[3] It is indicated that both environmental and genetic factors may contribute to high blood pressure and hypertension prevalence, especially for essential hypertension.[4] In addition, the prevalence of essential hypertension increases with age; individuals with relatively high blood pressures at younger ages are at increased risk for the subsequent development of hypertension.[5]

Recently, there is a growing tendency for lowering blood pressure with natural therapy or complementary and alternative therapy.[6–14] Chinese massage, usually named Tuina in China, is an important component of traditional Chinese medicine (TCM), parallel to internal medicine, acupuncture, moxibustion, life cultivation and rehabilitation of Chinese medicine. Massage had been noted in ''Yellow Emperor's Canon of Medicine'', the classic of TCM. It was pointed out that Chinese massage originated and developed in the central region of China. The term Tuina was first seen in the Ming dynasty. It had the function of unblocking or dredging the meridians and collateral, promoting qi to activate blood, and eliminating cold to stop pain. With the hands or needles working on the meridians and acupoints, we can re-establish the proper flow of qi and blood through the channels. When Tuina or acupuncture stimulations are used to the affected parts, these produced energy will regulate the function of body.[15,16]

Several clinical studies, including a substantial number of randomized controlled trials (RCTs), have shown that Tuina is effective and safe for essential hypertension. It can also improve symptoms, such as headache, dizziness, fatigue. And it is common to see patients with essential hypertension are treated with Tuina alone or combined with antihypertensive agents.[17–19] However, the RCTs examining the effectiveness of Tuina for essential hypertension have never been systematically summarized. As a result, we performed this systematic review to critically assess the effectiveness of Tuina for essential hypertension.

Methods

Data sources

We searched the following electronic databases up to 20th August 2013: Pubmed, the Cochrane library, including the Cochrane Central Register of Controlled Trials (CENTRAL, 2013), Chinese bases, including Chinese National Knowledge Infrastructure (CNKI; 1979—2013), the Wan Fang Database (1985—2013), and Chinese Scientific Journal Database (VIP; 1989—2013). The searching terms were 'Chinese massage', 'Tuina', 'Yuan Fa Xing Gao Xue Ya (essential hypertension)', and 'Gao Xue Ya (hypertension)'. No language restriction was applied.

Study selection

All randomized controlled trials (RCTs) that compared Tuina with conventional antihypertensive drugs for the treatment of EH were included, regardless of blinding or the published language. RCTs comparing Tuina combined antihypertensive drugs with antihypertensive drugs were also included. Animal studies, clinical trials including case report, case series traditional reviews were not included. Quasi-RCTs were also not considered. The participants were diagnosed as hypertensive, with a systolic BP (SBP) $\geq$ 140 mmHg and/or a diastolic BP (DBP) $\geq$ 90 mmHg or used antihypertensive drugs. We did not intend to make any restrictions

on age, gender, and race. The main outcome measure was blood pressure (BP). The other outcome measures included life quality, heart rate (HR), E-selectin, inducible nitric oxide synthase (iNOS), and endothelial nitric oxide synthase (eNOS).

Data extraction

Two reviewers (X. Yang, and H. Zhao) reviewed the titles and abstracts of potentially relevant reports through the literature search. Discrepancies were resolved by consensus with another investigator (Y. Yang). The following data were extracted: (1) citations (authors of study, year of publication), (2) participants information (sample size, age), (3) detailed information of interventions and controls, (4) the duration of treatments, (5) the follow-up time, (6) outcome measures, and (7) adverse events.

Data analysis

The risk ratio (RR) and weighted mean differences (WMDs) were used in outcome measures between the end of the final intervention and the baseline was used to assess the difference between Tuina group and control group in the meta-analyses. The statistical package (RevMan 5.1.7) provided by Cochrane Collaboration was used for data analyses. And 95% confidence intervals (CIs) were calculated in the meta-analysis. If the intervention, control, and outcome were the same or similar, meta-analysis was performed. Cochrane's I^2-test was used to assess statistical heterogeneity. In the absence of significant heterogeneity, we pooled data using a fixed-effect model ($I^2 < 50\%$), otherwise we using random effects model ($I^2 > 50\%$).[20] Data were further stratified when possible into subgroups based on different types of interventions, in order to maximize the similarities among studies that would be combined.

Trial quality and risk of bias assessment

The methodological quality of RCTs was assessed independently by two authors by Cochrane risk of bias tool. It included the following five domains: selection bias (random sequence generation), selection bias (allocation concealment), performance bias (blinding of participants and personnel), attrition bias (incomplete outcome data), and reporting bias (selective reporting). Trials that met all the criteria were categorized as low risk of bias; those that met none of the criteria were categorized as high risk of bias; and the others were categorized as unclear risk of bias if insufficient information was available to make a judgment. Disagreements were resolved by discussion.

Results

Description of included trials

We identified 297 potentially records from the electronic and manual searches. After the initial titles and abstracts screening, 260 articles excluded because of a large number of duplicate records from three Chinese databases (CNKI, VIP, and Wanfang) and some references did not met the inclusion criteria. 37 full articles were retrieved and reviewed. A total of 7 RCTs were eligible.[21–27] In excluded studies, the trials were excluded due to non RCTs ($n = 4$), duplicated publication ($n = 2$), diagnosis uncertainty ($n = 7$), inappropriate control ($n = 3$), ineligible data extraction ($n = 5$), patients complicated with serious medical conditions ($n = 9$). And all 7 RCTs were included in meta-analyses. The study selection process was summarized in Fig. 1.

Seven included studies included 479 subjects with age varied from 31 to 76 years. All studies were conducted in China between 2002 and 2013. Four different diagnostic criteria of hypertension were used in the included trials, one trial[23] used 1999 WHO-ISH guidelines for the management of hypertension (1999 WHO-ISH GMH), one trial[26] used Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), three trial[21,25,27] used China Guidelines on Prevention and Management of High Blood Pressure-2005 (CGPMHBP-2005), one trial[22] used CGPMHBP-2000, and one trial[24] only demonstrated patients with essential hypertension. Of the 7 trials, two trials[21,26] used Guidelines of Clinical Research of New Drugs of Traditional Chinese Medicine (GCRNDTCM). The disease duration ranged from 1 month to 22 years, and the study duration ranged from 2 weeks to 24 weeks. The time and session of Tuina treatment were ranging from 25 to 50 min and from 3 to 24, respectively. The characteristics of all studies were summarized in Table 1.

Of seven RCTs, 5 RCTs assessed the effectiveness of Tuina plus antihypertensive drugs versus antihypertensive drugs for patients with EH,[21–23,25] 2 RCTs assessed the effectiveness of Tuina versus antihypertensive drugs.[24,26] The treatments with manual techniques in intervention groups were presented in Table 2. In outcome assessments, the values of blood pressure were used for evaluating the treatment of EH.

Methodological quality of included trials

After assessed the methodological quality of the 7 trials, we found that the methodological quality of included trials was not high. All of the included trials mentioned the randomized allocation of participants. Of seven trials, two trials[21,22] stated the methods of sequence generation of random number table, and two trials[25,26] stated the methods of sequence generation of patients order. Among the 7 trials, allocation concealment and double-blind were not possible for the intervention. Only 1 trial[26] mentioned single-blind of outcome assessment and follow-up. None of the trials reported drop-out or withdraw.

Quantitative data synthesis

Effect of Tuina on the efficacy ratio of blood pressure

The efficacy ratio was used to measure the blood pressure: significant effective (diastolic BP reduced $\geq$ 10 mmHg or to normal level), effective (the diastolic BP reduced to normal level, or, 19 mmHg > diastolic BP reduced $\geq$ 10 mmHg; the systolic BP reduced > 30 mmHg), and ineffective (the diastolic BP do not change, or, diastolic BP reduced < 10 mmHg).

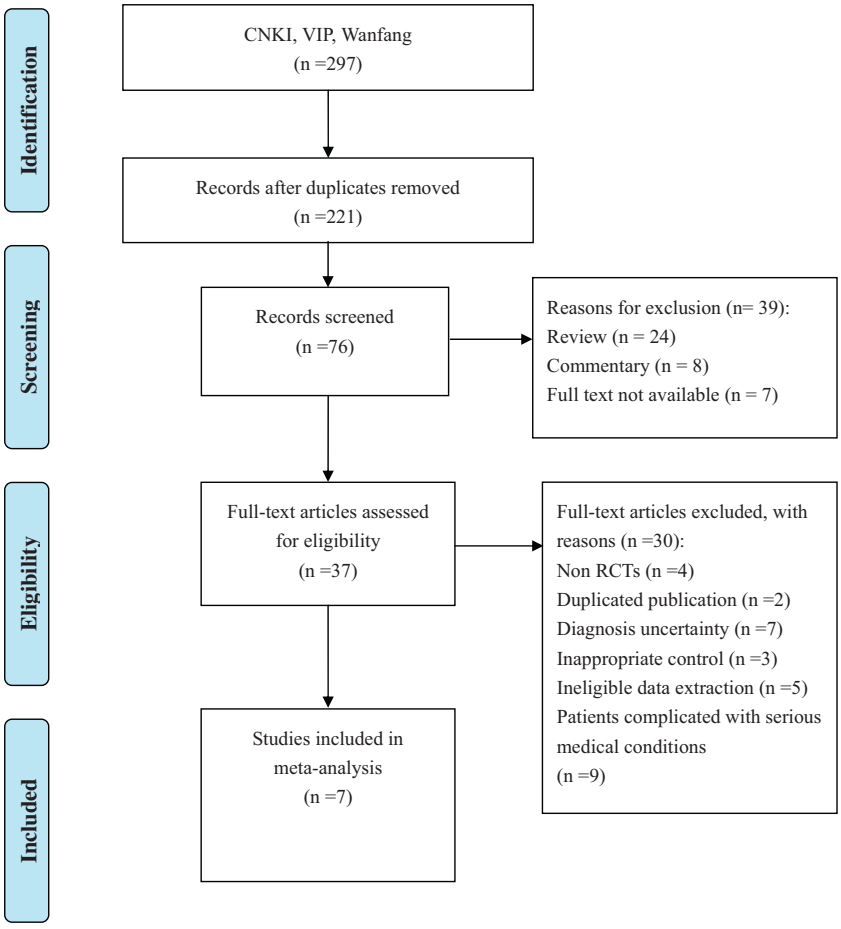

Figure 1 Flow diagram of the literature searching and study selection.

Two trials[24,26] tested the effectiveness of Tuina for EH compared with antihypertensive drugs. And the meta-analysis showed there was no significant difference between the two groups on blood pressure (RR: 1.01 [0.72, 1.41]; $P = 0.95$; heterogeneity: $I^2 = 76\%$; Table 3).

Five trials[21–23,25,27] assessed the effect of Tuina plus antihypertensive drugs versus antihypertensive drugs on blood pressure for EH. The meta-analysis showed superior effects of Tuina plus antihypertensive drugs on systolic blood pressure (RR: 1.14 [1.05, 1.24]; $P = 0.003$; heterogeneity: $I^2 = 36\%$; Table 3).

Effect of Tuina on systolic blood pressure and diastolic blood pressure

Four trials[22,23,26,27] reported the continuous outcome of blood pressure. So we conducted an analysis of continuous data between groups. One trial[26] tested the effectiveness of Tuina on systolic blood pressure for EH compared with antihypertensive drugs. And the meta-analysis showed superior effects of antihypertensive drugs on systolic blood pressure (WMD: 15.15 [11.49, 18.81]; $P < 0.00001$; Table 4), and on diastolic blood pressure (WMD: 10.5 [8.45, 12.55]; $P < 0.00001$; Table 5).

Three trials[22,23,27] tested the effectiveness of Tuina plus antihypertensive drugs on systolic blood pressure for EH compared with antihypertensive drugs. And the meta-analysis showed superior effects of Tuina plus antihypertensive drugs on systolic blood pressure (WMD: −2.09 [−3.76, −0.42]; $P = 0.01$; heterogeneity: $I^2 = 63\%$; Table 4), and on diastolic blood pressure (WMD: −5.97 [−7.42, −4.52]; $P < 0.00001$; heterogeneity: $I^2 = 77\%$; Table 5).

Other outcomes (life quality, HR, follow-up, E-selectin, iNOS, eNOS). One trial[21] showed that after 6 weeks of treatment, the life quality improved significantly ($P < 0.05$) in Tuina plus metoprolol group compared to metoprolol group. One trial[22] showed that after 4 weeks of treatment, the heart rate (HR) did not increased in Tuina plus nifedipine group compared to the base line ($P > 0.05$), whereas HR increased significantly in nifedipine group compared to the base line ($P < 0.01$). One trial[25] did the follow-up of two months after 4 weeks. The result showed that the blood pressure decreased significantly ($P < 0.05$) in Tuina plus benazepril group compared to the base line, whereas there was no difference in benazepril group compared to the base line ($P > 0.05$). One trial[26] showed that after 4 weeks of treatment, the level of *E-selectin*, *iNOS*, *eNOS* increased significantly ($P < 0.01$) in Tuina plus ramipril group compared to the base line, whereas decreased in ramipril group compared to the base line ($P < 0.05$).

Risk of bias across studies. We did not conduct sensitivity analysis and subgroup analysis because of insufficient

Table 1 Characteristics and methodological quality of included studies.

Study ID	Sample	Diagnosis standard	Intervention	Control	Study duration (week)	Outcome measure
Yao 2013[21]	60	CGPMHBP-2005	Tuina plus metoprolol 100 mg/d	Metoprolol 100 mg/d	6	BP; life quality
Xue and Liao 2003[22]	64	CGPMHBP-2000; GCRNDTCM	Tuina plus nifedipine controlled release tablet 20 mg/d	Nifedipine controlled release tablet 20 mg/d	4	BP; adverse effect; HR
Luo and Xue 2004[23]	43	1999 WHO-ISH GMH	Tuina plus nifedipine controlled release tablet 20 mg/d	Nifedipine controlled release tablet 20 mg/d	24	BP
Li 2005[24]	72	Hypertension diagnostic criteria (unclear)	Tuina	Captopril 25 mg/d	4	BP
Chen and Li 2010[25]	60	CGPMHBP-2005	Tuina plus ramipril 5 mg/d	Ramipril 5 mg/d	2	BP; E-selectin; iNOS; eNOS
Luo and Xu 2002[26]	100	JNC-7	Tuina	Benazepril 10—21 mg/d	4	BP; follow-up
Wang and Ran 2010[27]	80	CGPMHBP-2005; GCRNDTCM	Tuina plus antihypertensive drugs (unclear)	Antihypertensive drugs (unclear)	8	BP; adverse effect

Abbreviations: WHO-ISH GMH, WHO-ISH guidelines for the management of hypertension; GCRNDTCM, Guidelines of Clinical Research of New Drugs of Traditional Chinese Medicine; CGPMHBP, China Guidelines on Prevention and Management of High Blood Pressure; JNC-7, Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; TCM, Traditional Chinese medicine; BP, blood pressure; HR, heart rate; iNOS, inducible nitric oxide synthase; eNOS, endothelial nitric oxide synthase.

number of trials. In addition, we also failed to perform funnel plot to detect publication bias.

Adverse effect. One trial mentioned the adverse effect in nifedipine group such as palpitation and headache.[22] One trial[27] mentioned there was no adverse effect in two groups. The rest five trials did not assess adverse effect during the treatment.

Discussion

Chinese massage, named Tuina as an adjunctive treatment to antihypertensive drugs has good effect on lowering BP in patients with EH. To the best of our knowledge, this is the first systematic review and meta-analysis of RCTs for Tuina in treating EH. Based on the paper and meta-analyses of the outcomes on BP, Tuina may have good effects for treating hypertension. But the quality of the included studies was poor. Thus, interpretation of these positive findings should be cautions.

Limitations of the review

Several limitations should be considered in our study. First, seven trials included in this paper had risk of bias in terms of design, reporting, and methodology. They provided inadequate reporting of allocation sequence and allocation concealment in the majority of trials. Nearly half of the included trials[23,24,27] just reported randomization without any details, which do not allow a proper judgment of the conduct of the trials. Only one trial[26] described single-blind of outcome assessment in details. It may lead to performance bias due to patients and researchers being aware of the therapeutic interventions. In addition, all the included trials were not multicenter, large scale RCTs and all were conducted and published in China, which may be due largely to the shortage of acceptability and popularization of Tuina in the other countries.

Second, all the included trials used efficacy ratio of blood pressure as outcome measure, which presented the effect as markedly effective, effective, and ineffective. According to our result of efficacy ratio of blood pressure, the meta-analysis showed superior effects of Tuina plus antihypertensive drugs compared to antihypertensive drugs alone, but Tuina alone was not superior to antihypertensive drugs. However, four of the included trials[22,23,26,27] evaluated the effectiveness with continuous outcome of blood pressure. The analysis of continuous data[22,23,27] on systolic blood pressure and diastolic blood pressure also showed superior effects of Tuina plus antihypertensive drugs respectively. But the result was not inconsistent with Tuina used alone for EH compared with antihypertensive drugs. The analysis of continuous data[26] showed superior effects of antihypertensive drugs on systolic blood pressure and on diastolic blood pressure. Our results suggested that when analyzing the outcome of blood

Table 2 Treatments with manual techniques in intervention groups.

Study ID	Time/session	Treatments with manual techniques
Yao 2013[21]	30 min/3 sessions	(1) Digital press and strum the following acupoints of hands one by one: Hegu (LI4), Laogong (PC8), Shixuan (EX-UE11) (2) Press the acupoints at the top of the head: Baihui (DU20), Taiyang (EX-HN5). Press and knead the acupoints at the occipital region: Fengchi (GB20) (3) Dredge the spleen meridians and kidney meridians in the leg: Taixi (KI3), Yinlingquan (SP9), Sanyinjiao (SP6). Knead to relax the local muscles
Xue and Liao 2003[22]	40 min/4 sessions	(1) Wipe with the thumbs from Yintang (EX-HN3) to Shenting (DU24), while the other fingers fixed at the lateral side of the head. The wiping should be slightly and rapidly to make the patients comfortable (2) Knead and grasp the Du meridians, bladder meridians and gall bladder meridians in the neck. And press Jianjing (GB21)
Luo and Xue 2004[23]	50 min/24 sessions	(1) Wipe with the thumbs from Yintang (EX-HN3) to Shenting (DU24), while the other fingers fix at the lateral side of the head. The wiping should be slightly and rapidly to make the patients comfortable (2) Knead and grasp the Du meridians, bladder meridians and gall bladder meridians in the neck. And press Jianjing (GB21) (3) An-press with palm on the abdomen
Li 2005[24]	30 min/4 sessions	(1) Wipe with the thumbs from Yintang (EX-HN3) to Taiyang (EX-HN5) (2) Press and knead the acupoints at the occipital region: Fengchi (GB20) (3) Knead and grasp Jianjing (GB21) (4) An-press with palm from breast to abdomen (5) Dredge the meridians and acupoints in the leg: Zusanli (ST36), Sanyinjiao (SP6), Chengshan (BL57), Yongquan (KI1), Xingjian (LR2). Knead to relax the local muscles. Press the acupoints: Binao (LI14), Quchi (LI11), Neiguan (PC6), Hegu (LI4)
Chen and Li 2010[25]	25 min/2 sessions	(1) Knead and grasp the neck including Fengchi (GB20) (2) Digital press and strum shoulders, arms including Hegu (LI4) (3) Knead and grasp Jianjing (GB21)
Luo and Xu 2002[26]	30 min/4 sessions	(1) Wipe with the thumbs from Yintang (EX-HN3) to Taiyang (EX-HN5) (2) Press and knead the acupoints at the occipital region: Fengchi (GB20) (3) Knead and grasp Jianjing (GB21) (4) An-press with palm from breast to abdomen (5) Dredge the meridians and acupoints in the leg: Zusanli (ST36), Sanyinjiao (SP6), Chengshan (BL57), Yongquan (KI1), Xingjian (LR2). Knead to relax the local muscles. Press the acupoints: Binao (LI14), Quchi (LI11), Neiguan (PC6), Hegu (LI4)
Wang and Ran 2010[27]	20 min/8 sessions	(1) Knead and grasp the local muscles of neck (2) Dredge the back meridians with palm pushing (3) Dredge the muscles in the buttock (4) Knead and grasp the local muscles of leg (5) Dredge the foot with palm pushing

pressure, it would be more dependable to use continuous data.

Third, there is inadequate reporting on adverse events in the included trials. Two trials reported information on the adverse effect, and mentioned there was no adverse effect of Tuina. Definite conclusions on the safety of Tuina should be considered due to the limited information of adverse events. In addition, only one trial[23] has a long duration of 24 weeks, and one trial[26] reported a follow-up of two weeks. Since EH is a chronic cardiovascular disease, the effect of long-term treatment is a great concern of patients. Longer follow-up period with serial measurements of outcomes is suggested to determine the long-term effectiveness of Tuina.

The possible rationale of Tuina for EH

Complementary and alternative medicine therapies have become a common part of health-care for the treatment of EH.[11,13,28–31] The majority of the physicians recommend changing the life-style and non-pharmacological treatments before prescription of the medications in the BP control.[32,33] In traditional Chinese medicine, Tuina at meridians and local acupoints can stimulate qi. The movement of qi can promote metabolism, regulate body functions, accelerate the microcirculation, and improve oxygen supply. Considering that Tuina were beneficial for EH, the mutual adjustment of physical and mental degree may provide a possible rationale. According to the present studies, the manual therapy

Table 3 Analyses of the efficacy ratio of blood pressure.

Trials		Intervention (n/N)	Control (n/N)	RR [95% CI]	*P* value
Tuina versus antihypertensive drugs					
Tuina versus captopril	1	44/46	21/26	−1.18 [0.97, 1.44]	0.09
Tuina versus benazepril	1	22/30	26/30	0.85 [0.65, 1.09]	0.20
Meta-analysis	2	66/76	47/56	1.01 [0.72, 1.41]	0.95
Tuina plus antihypertensive drugs versus antihypertensive drugs					
Tuina plus ramipril versus ramipril	1	26/30	22/30	1.18 [0.91, 1.53]	0.20
Tuina plus nifedipine versus nifedipine	1	33/36	35/39	1.02 [0.88, 1.18]	0.77
Tuina plus antihypertensive drugs (unclear) versus antihypertensive drugs (unclear)	1	38/40	31/40	1.23 [1.02, 1.47]	0.03
Tuina plus nifedipine versus nifedipine	1	27/28	28/30	1.03 [0.92, 1.16]	0.59
Tuina plus metoprolol versus metoprolol	1	27/30	21/30	1.29 [0.99, 1.67]	0.06
Meta-analysis	5	151/164	137/169	1.14 [1.05, 1.24]	0.003

Table 4 Analyses of systolic blood pressure.

Trials		MD [95% CI]	*P* value
Tuina versus antihypertensive drugs			
Tuina versus benazepril	1	15.15 [11.49, 18.81]	<0.00001
Meta-analysis	1	15.15 [11.49, 18.81]	<0.00001
Tuina plus antihypertensive drugs versus antihypertensive drugs			
Tuina plus nifedipine versus nifedipine	1	−5.50 [−9.97, −1.03]	0.02
Tuina plus antihypertensive drugs (unclear) versus antihypertensive drugs (unclear)	1	−1.00 [−2.90, 1.90]	0.30
Tuina plus nifedipine versus nifedipine	1	−6.00 [−11.50, −0.50]	0.03
Meta-analysis	3	−2.09 [−3.76, 0.42]	0.01

Table 5 Analyses of diastolic blood pressure.

Trials		MD [95% CI]	*P* value
Tuina versus antihypertensive drugs			
Tuina versus benazepril	1	10.50 [8.45, 12.25]	<0.00001
Meta-analysis	1	10.50 [8.45, 12.25]	<0.00001
Tuina plus antihypertensive drugs versus antihypertensive drugs			
Tuina plus nifedipine versus nifedipine	1	−3.80 [−7.00, 0.60]	0.02
Tuina plus antihypertensive drugs (unclear) versus antihypertensive drugs (unclear)	1	−7.97 [−9.93, −6.01]	<0.00001
Tuina plus nifedipine versus nifedipine	1	−3.40 [−6.29, −0.51]	0.02
Meta-analysis	3	−5.97 [−7.42, −4.52]	<0.00001

delivered to the local body may lead to a series of physical changes that increase the elasticity of blood vessels, modulate local blood circulation, reduce blood viscosity, relieve stress, and prevent arterial spasm and atherosclerosis.[34] The effect of Tuina on head and neck may subsequently promote intracranial blood circulation according to rheoencephalogram. And on chest and back (especially at Du and bladder meridians), it influences neural activity at the spinal cord segmental level (especially T1—T10 spinal cord), thereby modulating the activities of cerebral cortex that improve dysfunction due to EH.[35]

Conclusions

Seven RCTs were analyzed in our systematic review, evaluating Tuina for the treatment of EH. The findings from the present reports suggest that Tuina might be an effective complementary treatment for patients with EH, although

the results are of limited value due to the clinical heterogeneity and low methodological quality of the included studies. Future studies should adhere to high-quality RCTs with long follow-up for demonstrating the effectiveness of Tuina for inpatients with EH.

Conflict of interest statement

All authors declare that they have no conflicts of interest.

Acknowledgments

The current work was partially supported by the National Basic Research Program of China (973 Program, No. 2003CB517103) and the National Natural Science Foundation of China (No. 90209011). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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