Systematic Review and Meta-Analysis

Medicine

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The effect of Taohong Siwu decoction combined with antihypertensive medicine in the treatment of hypertension

Meta-analysis

Peng-Cheng Xie, MM[a], Qiu-Er Liang, MD[a], Wan-Qing Tu, MM[a], Ting Xie, MM[a], Lai Kwan Lam, MD[a,*], Li-Guo Chen, MD[a,*]

Abstract

Background: Taohong Siwu Decoction (THSWD) is a classic prescription of traditional Chinese medicine. Recent research has shown that the practical components of THSWD have specific curative effects on various cardiovascular diseases, including hypertension, suggesting THSWD could effectively lower blood pressure (BP) with fewer side effects. However, little information is available regarding the effectiveness of THSWD combined with antihypertensive medicine on hypertension.

Objective: This meta-analysis aimed to study the efficacy and safety of THSWD in treating hypertension.

Methods: According to the search strategy, 8 databases were searched, including China Knowledge Network (CNKI), Wanfang Database, VIP Database, Pubmed, China Biomedical Literature Database (CBM), web of science, EMBASE and Cochrane Library, for the randomized controlled trial of THSWD on hypertension. 9 RCTs were included and 827 patients were involved. This meta-analysis used RevMan 5.4 to evaluate the articles.

Results: This review included 9 RCTs. All studies were THSWD with the antihypertensive drug compared with single antihypertensive western medicine. The total effective rate of THSWD combined with corresponding western medicine was significantly improved (Relative risk = 1.26; 95% CI: 1.16–1.37, $P < .00001$), which could effectively reduce the systolic BP (MD = −15.28 mm Hg; 95% CI: −20.17 to −10.40, $P < .00001$=, diastolic BP (MD = −9.70 mm Hg; 95% CI: −12.66 to −6.73, $P < .00001$), Triglycerides (MD = −1.48, 95%CI: −2.09 to −0.87, $P < .00001$), total cholesterol (MD = −1.43, 95% CI: −1.63 to −1.24, $P < .00001$) and low density lipoprotein cholesterol (MD = −0.93, 95% CI: −1.07 to −0.80, $P < .00001$). Compared with the single routine western medicine group, THSWD combined with the corresponding western medicine increased serum high-density lipoprotein (MD = 0.41, 95% CI: 0.35 to 0.46, $P < .00001$).

Conclusion: THSWD combined with antihypertensive drugs in treating hypertension was curative in lowering BP, improving blood lipid levels and reducing the incidence of adverse reactions compared to antihypertensive medications treatment. However, more high-quality studies are needed due to the biased results and the small number of studies for further verification of the effectiveness of THSWD, and providing a new treatment for clinical reference.

Abbreviations: BP = blood pressure, CHM = Chinese herbal medicine, DBP = diastolic blood pressure, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol, RR = relative risk, SBP = systolic blood pressure, TC = total cholesterol, TCM = traditional Chinese medicine, TG = triglycerides, THSWD = Taohong Siwu Decoction, vWF = VonWillebrand factor.

Keywords: antihypertensive drugs; efficacy, hypertension; meta analysis; systematic review; Taohong Siwu decoction

1. Introduction

Hypertension is 1 of the chronic cardiovascular and cerebrovascular diseases with high mortality and morbidity.[1] Since the fast growth of aging population in China, the proportion of elderly hypertensive patients is gradually increasing. According to the Guidelines for the Management of Senile Hypertension in China 2019, the prevalence rate of

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

[a] School of Traditional Chinese Medicine of Jinan University, Guangzhou, China.

** Correspondence: Lai Kwan Lam and Li-Guo Chen, School of Traditional Chinese Medicine of Jinan University, No. 601 West Huangpu Avenue, Guangzhou 510632, China (e-mail: 1926786051@qq.com and tchenly@jnu.edu.cn).*

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hypertension in elderly over 80 years old is almost 90%.[2] The common antihypertensive drugs are calcium channel blocker, angiotensin receptor antagonist and angiotensin converting enzyme inhibitor, which have side effects such as cough, sore throat, abdominal pain, vomiting and dizziness.[3] Therefore, Chinese medicine becomes more popular in the treatment of hypertension and is known for its positive effect and fewer side effects.

Traditional Chinese medicine (TCM) comprehensively treats hypertension and the multiple organ lesion caused by hypertension.[4] Taohong Siwu Decoction (THSWD) is frequently used for blood stasis syndrome in TCM. AS a classic prescription of Traditional Chinese Medicine, it was first seen in the medical books named The Golden Mirror of Medicine. It is mainly used to treat various blood stasis syndromes. There are 6 herbs in THSWD, including peach kernel, safflower, angelica, prepared rhizome of rehmannia, Ligusticum wallichii and white peony root. THSWD can promote blood circulation and remove blood stasis. In TCM theory, peach kernel and safflower are monarch drugs in this prescription and play the dominant role, and ligusticum wallichii has the effect of promoting blood circulation as well. Rehmannia glutinosa, paeonia lactiflora and angelica sinensis can nourish blood. Hypertension with blood stasis syndrome is 1 of the common clinical types of hypertension in China.[4] Modern research have proved that THSWD can improve endothelial cell injury,[5–7] and ameliorate aortic endothelial diastolic function by improving serum nitric oxide, Endothelin-1 and other related factors, so as to play a essential role in reducing blood pressure (BP).[8] The results of network pharmacological analysis showed that anti-cardiovascular compounds, such as kaempferol, quercetin and luteolin, were contained in THSWD which can regulate hypertension-related genes ADRB2 and CALM1, through different pathways like cAMP and Ras pathway to treat hypertension.[9] Moreover, clinical studies demonstrated that THSWD has a prominent clinical antihypertensive effect.[10–12]The clinical symptoms of blood stasis syndrome, such as headache, vertigo, dark tongue with petechiae and pulse astringency, are in line with the indications of THSWD.

This study aimed to assess the efficacy and safety of THSWD combined with western medicine on hypertension in order to enhance the reliability of the THSWD clinical studies and provide reference for clinical application.

2. Methods

2.1. Search strategy

A comprehensive literature search was performed in China Knowledge Network (CNKI), Wanfang Database, VIP Database, Pubmed, China Biomedical Literature Database (CBM), web of science, EMBASE and Cochrane Library. ([BP, High] OR [hypertension] OR [High BP]) AND ([tao hong si wu] OR [THSWD] OR [tao hong si wu decoction]) were listed and used as search terms to search Chinese and English articles from the date of inception to March 1, 2022.

2.2. Inclusion and exclusion criteria

In this study, the inclusion criteria were as follows:

(1) Patients were diagnosed with hypertension according to the relevant criteria of hypertension diagnosis in the Guide.
(2) TCM syndrome type of patients was blood stasis type. According to the diagnostic criteria of blood stasis syndrome drawn up by the Professional Committee of Promoting Blood Circulation and Removing Blood Stasis of Chinese Society of Integrated Traditional Chinese and Western Medicine and related studies, the main symptoms of hypertension blood stasis syndrome include headache, numbness and pain of neck and limbs, mania, dark tongue with ecchymosis, distension of sublingual collaterals and astringent pulse.
(3) THSWD combined with conventional antihypertensive western medicine was the intervention in the experimental groups. Patients could be treated with different doses of THSWD according to the condition.
(4) The study was designed as a randomized controlled clinical study and original study only.
(5) Articles were written in English or Chinese.

The exclusion criteria were as follows:

(1) Patients who were having other non-cardiovascular complications or were taking other hebal medicine.
(2) Acupuncture, massage, cupping and other therapies were included in treatments.
(3) Animal experiments or surgical treatments.
(4) Repeated or retrieved literature.

2.3. Data extraction

Two investigators collected the data independently. The extracted information included as follow: first author, year of publication, number of patients, study design, dosage of medication, duration of therapy, outcomes, and quality assessment of each study.

2.4. Quality evaluation

The quality assessment was independently conducted by 2 examiners. Disagreements were resolved by discussion. The risk bias assessment tool provided by Cochrane Handbook was used to evaluates the methodological quality of literature, including the generation of random sequence, distribution concealment, blind method, incomplete outcome data, selective report and other bias.

2.5. Evaluation of outcome

The primary endpoints were BP included systolic blood pressure (SBP) and diastolic blood pressure (DBP), and total effective rate. The secondary endpoints were triglycerides (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and adverse reactions. Clinical symptoms which indicated as" recovery," "improvement" and "marked effect" were all included in the effective range. Also, the diastolic BP decreased less than 10 mm Hg but reached the normal range, or the diastolic BP decreased by 10 to 19 mm Hg were known as effective. In addition, adverse events were selected for safety evaluation.

2.6. Statistical analysis

RevMan5.4 recommended by Cochrane handbook was used for this meta-analysis. The relative risk (RR) was used for statistics, and the confidence interval was 95%. I^2 statistics and Q test served to test heterogeneity. If significant heterogeneity ($I^2 > 50\%$ or $P < .05$) is observed, the random effect model is used for statistical analysis. If the study is homogeneous ($I^2 < 50\%$ or $P > .05$), the fixed effect model is used. Funnel chart was used to evaluate publication bias. This review was conducted following PRISMA guidelines.

All analyses were based on previous published studies, thus no ethical approval and patient consent are required

3. Results

3.1. Basic characteristics of included data

A total of 166 studies were retrieved after a primary search in 8 electronic databases, and 93 duplicate studies were excluded. After reading the title and abstract, 58 articles were excluded because the participants in studies had other non-cardiovascular complications or were taking other herbal medicines at the same time. In addition, animal experiments and the articles that using surgical treatments were excluded. Then, 15 studies were evaluated, and 3 were excluded because they were duplicate publications. 3 studies were excluded because patients were not grouped randomly. Finally, 9 studies were included,[13–21] involving 827 hypertensive patients, as shown in Figure 1.

3.2. Study characteristics

The characteristics of each study were summarized in Table 1. The sample size ranged from 45 to 150. Patients' average ages range from 54.89 to 72.03 years old and the average durations vary from 5.48 to 15.25 years. Western medicine include Amlodipine, Amlodipine besylate, Nifedipine and Valsartan. The components of THSWD-based formula in each study were depicted in Table 2. Treatment durations ranged from 3 to 4 weeks.

Total effective rate were reported in 5 studies.[13,14,16,17,21] BP outcomes were reported in 9 studies, with continuous BP in 7 trials[13–15,17–20] and categorical BP in 2 trials.[16,21] Serum lipid levels were reported in 3 trials.[15,18,19] Adverse events were reported in 2 trials.[14,20]

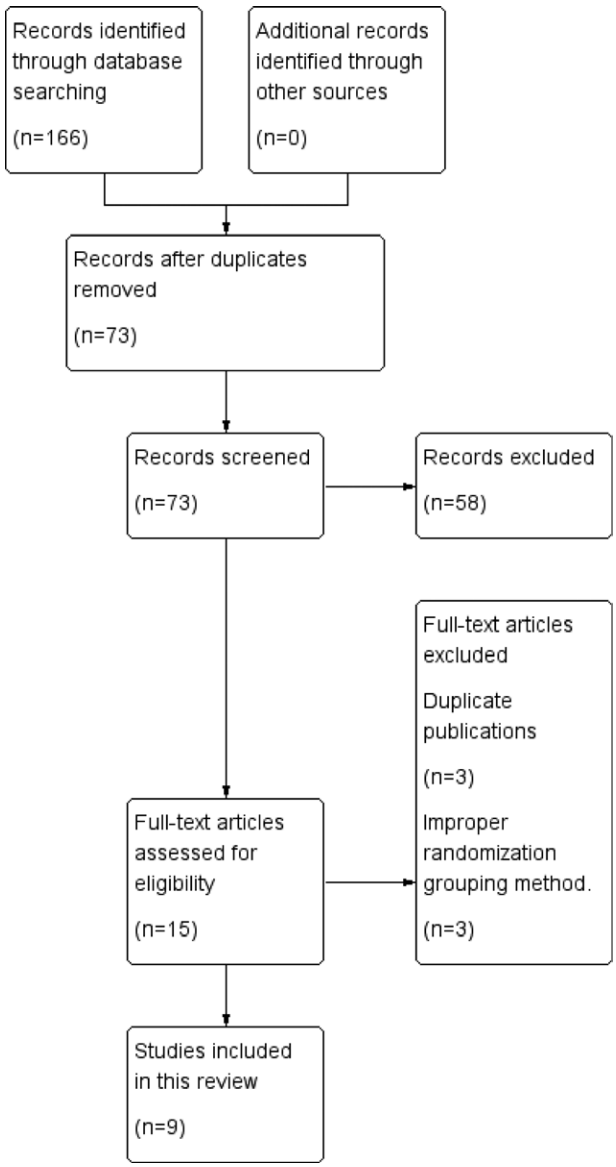

Figure 1. Flow diagram of study selection and identification. Blood pressure; Total effective rate; Triglyceride; Total cholesterol; Low-density Lipoprotein cholesterol; High-density Lipoprotein cholesterol; and Adverse events.

4. Results

4.1. Primary endpoint

4.1.1. Methodologic quality. 4 trials used the table of random number for random grouping.[14,15,20,21] The other 5 trials mentioned randomization in the text without detailed information.[13,16–19] Details regarding concealment of allocation and blinding of patient, investigator and assessor were unclear in all studies. All trials reported that all the enrolled subjects had completed the trials. Both selective reporting and other potential threat to validity are in low risk of bias in the original trials. Additionally, no study reported the methods of follow-up (Fig. 2).

4.1.2. BP. BP was reported in 7 trials.[13–15,17–20] There were 238 patients in THSWD groups and 239 patients in antihypertensive drugs groups. Both SBP and DBP were with significant heterogeneity (SBP: chi-square = 42.37, $P < .00001$, $I^2 = 86\%$; DBP: chi-square = 40.13, $P < .00001$, $I^2 = 85\%$) and random-effects model was applied. Subgroup analysis was made according to age which was 1 of the important factors of hypertension and the heterogeneity decreased significantly. The results of these 7 trials showed a significant effect of THSWD combined with antihypertensive drugs on SBP (MD = −15.28 mm Hg; 95% CI: −20.17 to −10.40, $P < .00001$) and DBP (MD = −9.70 mm Hg; 95% CI: −12.66 to −6.73, $P < .00001$) compared with antihypertensive drugs (Fig. 3A and B). In the other 2 trials,[16,21] the data was analyzed using a fixed-effects model (chi-square = 1.00, $P = .32$, $I^2 = 0$). A significant decrease on BP was identified in favor of THSWD therapy compared with the antihypertensive drugs (RR = 1.23; 95% CI: 1.11 to 1.36,$P < .0001$) (Fig. 3C).

4.1.3. Total effective rate. 5 studies assessed the total effective rate of THSWD with antihypertensive drugs on both BP and the symptoms.[13,14,16,17,21] There were 211 patients in the THSWD groups and 212 patients in the antihypertensive drugs groups. A fixed-effects model was applied based on the test of heterogeneity (chi-square = 2.60, $P = .63$, $I^2 = 0\%$). THSWD therapy compared with antihypertensive drugs was more efficient in treating hypertension (RR = 1.26; 95% CI: 1.16–1.37, $P < .00001$) (Fig. 4).

4.2. Secondary endpoint

4.2.1. TG, TC. 3 studies reported TG and TC.[15,18,19] There were 113 patients in experiment groups and control groups, respectively. The random effect model was selected for TG data according to the heterogeneity test results (chi-square = 86.73, $P < .00001$, $I^2 = 98\%$) (Fig. 5A). We didn't perform subgroup analysis because there were too few documents. Considering the heterogeneity test results of TC data (chi-square = 1.07, $P = .58$, $I^2 = 0\%$), the fixed-effects model was selected. It showed that THSWD with antihypertensive medicine could effectively reduce TG (MD = −1.48, 95% CI: −2.09 to −0.87, $P < .00001$) and TC (MD = −1.43, 95% CI: −1.63 to −1.24, $P < .00001$) (Fig. 5A and B).

Table 1

Basic characteristics of the included trials.

Study	Sample Size (C/E)	Gender (Male/Female)		Average Age		Average Duration of Disease		Grouping Method	Intervention Measures		Treatment Duration	Outcome Measures
		C	E	C	E	C	E		C	E		
Wang 2020	43/43	23/20	25/18	61.01 ± 1.17	60.19 ± 1.26	7.74 ± 1.49 yrs	7.65 + 1.41 yrs	TRN	Amlodipine (2.5 mg, qd)	TSD (600 mL/d) + C	21 d	①③④⑤⑥
Li 2020	40/40	29/11	30/10	55.65 ± 10.21	54.89 ± 10.16	5.48 ± 1.85 yrs	6.05 ± 1.65 yrs	OMR	Amlodipine (10 mg, qd)	Modified TSD (1 dose/d) + C	1 mo	①③④
Zhong 2015	23/22	9/14	11/11	65.1		-		OMR	ABT (2.5 mg, qd)	TSD + C	21 d	①②
Lou 2018	30/30	17/13	18/12	68.23 ± 1.13	68.24 ± 1.14	15.24 ± 1.26 yrs	15.25 ± 1.23 yrs	OMR	ABT (5 mg, qd)	Modified TSD (1 dose/d) + C	4 wks	①②
Fei 2019	75/75	45/30	46/29	71.67 ± 6.14	71.26 ± 6.26	8.63 ± 3.14 yrs	8.56 ± 3.26 yrs	TRN	ABT (2.5 mg, qd)	Modified TSD (1 dose/d) + C	21 d	②
Liao 2019	30/30	14/16	16/14	60.2 ± 1.8	61.3 ± 1.0	7.6 ± 1.7 yrs	7.7 ± 0.6 yrs	OMR	Nifedipine (20 mg, qd)	TSD (300 mL/d) + Amlodipine (5 mg, qd)	4 wks	①③④⑤⑥
Zhong 2020	29/29	15/14	13/16	71.93 ± 3.88	72.03 ± 3.90	9.01 ± 1.01 mo	8.98 ± 0.98 mo	TRN	ABT (5 mg, qd)	Modified TSD (300 mL/d) + C	30 d	①②⑦
Jin 2021	44/44	27/17	25/19	67.45 ± 2.16	67.48 ± 2.19	9.13 ± 1.45 yrs	9.16 ± 1.47 yrs	TRN	ABT (2.5 mg, qd)	TSD (1 dose/d) + C	21 d	①⑦
Song 2014	55/55	32/23	36/19	58.5 ± 8.0	58.8 ± 8.2	–		OMR	Valsartan (80 mg, qd)	Modified TSD (400 mL/d) + C	4 wks	②

ABT = Amlodipine besylate tablets, C = control group, E = experimental group, N = no, OMR = only mention random, TER = total effective rate, TRN = table of random number, TSD = Taohong Siwu Decoction, Y = yes.

① BP; ② Total effective rate; ③ TG; ④ TC; ⑤ LDL-C; ⑥ HDL-C; ⑦ Adverse events.

Table 2

Components of CHM used in the included trials.

References	Prescription	Medicinal herbs
Jin 2021[20]	THSWD	Angelica sinensis 15 g, Radix Rehmanniae Preparata 15 g, Rhizoma Ligustici Chuanxiong 8 g, Radix Paeoniae Alba 10 g, Semen Persicae 9 g and Carthami Flos 6 g
Song 2014[16]	Modified THSWD	Angelica sinensis 25 g, Radix Paeoniae Alba 20 g, Atractylodes macrocephala 20 g, Rhizoma Ligustici Chuanxiong 20 g, Carthami Flos 15 g, Semen Persicae 15 g, Radix Rehmanniae Preparata 15 g, Radix Codonopsis 10 g, Rhizoma Cyperi 10 g and Radix Glycyrrhizae 8 g
Zhong 2015[13]	THSWD	Angelica sinensis 15 g, Radix Paeoniae Rubra 10 g, Rhizoma Ligustici Chuanxiong 8 g, Carthami Flos 6 g, Semen Persicae 9 g and Radix Rehmanniae Preparata 15 g.
Lou 2018[17]	Modified THSWD	Angelica sinensis 20 g, Radix Paeoniae Alba 20 g, Atractylodes macrocephala 20 g, Rhizoma Ligustici Chuanxiong 20 g, Carthami Flos 15 g, Semen Persicae 15 g, Radix Rehmanniae Preparata 15 g, Radix Codonopsis 10 g, Rhizoma Cyperi 10 g, Glycyrrhrizae Radix 8 g
Fei 2019[21]	Modified THSWD	Angelica sinensis 20 g, Radix Paeoniae Alba 20 g, Atractylodes macrocephala 20 g, Rhizoma Ligustici Chuanxiong 20 g, Carthami Flos 15 g, Semen Persicae 15 g, Radix Rehmanniae Preparata 15 g, Radix Codonopsis 10 g, Rhizoma Cyperi 10 g, Glycyrrhrizae Radix 8 g
Liao 2019[18]	THSWD	Angelica sinensis 15 g, Radix Paeoniae Rubra 15 g, Rhizoma Ligustici Chuanxiong 15 g, Carthami Flos 15 g, Semen Persicae 15 g and Radix Rehmanniae Preparata 15 g.
Li 2020[19]	Modified THSWD	Angelica sinensis 25 g, Radix Paeoniae Alba 15 g, Atractylodes macrocephala 20 g, Rhizoma Ligustici Chuanxiong 15 g, Carthami Flos 15 g, Almond 15 g, Radix Rehmanniae Preparata 15 g, Radix Codonopsis 10 g, Rhizoma Cyperi 10 g, Glycyrrhrizae Radix 8 g, and appropriate amount of liquor
Wang 2020[15]	THSWD	Angelica sinensis 15 g, Radix Paeoniae Rubra 10 g, Rhizoma Ligustici Chuanxiong 8 g, Carthami Flos 6 g, Semen Persicae 9 g and Radix Rehmanniae Preparata 15 g.
Zhong 2020[14]	Modified THSWD	Licorice 8 g, Rhizoma Cyperi 10 g, Radix Codonopsis each 10 g, Radix Rehmanniae Preparata 15 g, Semen Persicae 15 g, Carthami Flos 15 g, Rhizoma Ligustici Chuanxiong 20 g, Atractylodes macrocephala 20 g, Radix Paeoniae Alba 20 g, Radix Angelicae Sinensis 20 g

CHM = Chinese Herbal medicine, THSWD = Taohong Siwu decoction.

4.2.2. HDL-C, LDL-C. 2 studies reported HDL-C and LDL-C.[15,18] There were 73 patients in THSWD groups and antihypertensive drugs groups, respectively. Based on the heterogeneity test of HDL data (chi-square = 1.29, $P = .26$, $I^2 = 23\%$), we used random effect model. According to the heterogeneity test results of LDL-C (LDL-C: chi-square = 0.32, $P = .85$, $I^2 = 0$), the fixed effect model was applied. Compared with antihypertensive drugs, THSWD combined with antihypertensive drugs could effectively increase HDL-C (MD = 0.41, 95% CI: 0.35 to 0.46, $P < .00001$) and decrease

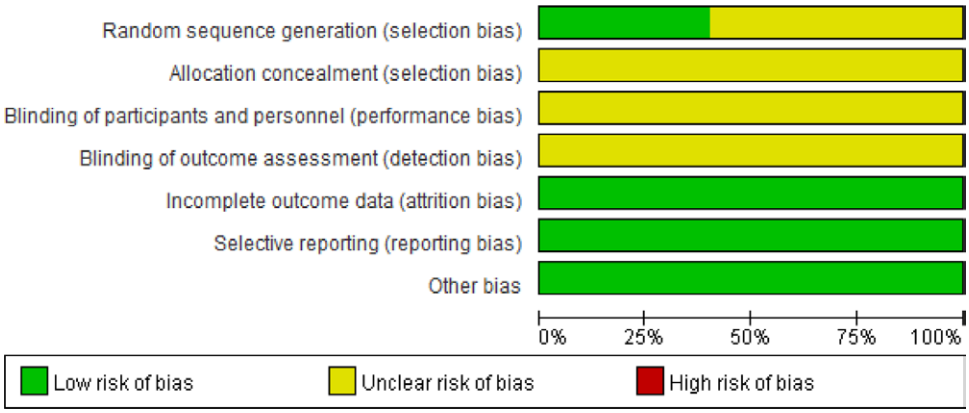

Figure 2. Methodologic quality of the included trials based on the Cochrane handbook.

LDL-C (MD = −0.93, 95% CI: −1.07 to −0.80, $P < .00001$) (Fig. 6A and B).

4.2..3. Adverse events. Two trials (2/9, 22.2%)[14,20] reported adverse events. The fix effect model was used to analyze the data considering the heterogeneity test results (chi-square = 1.01, $P = .32$, $I^2 = 1\%$). There were 10 adverse events in 73 patients in the control group, while only 2 patients in the experimental group, which could be considered that the incidence of adverse events in the experimental groups was fewer than that in the control group (OR = 0.17, 95% CI: 0.04 to 0.81, $P = .03$) (Fig. 7).

5. Discussion

5.1. Findings of this study

The main goal of hypertension management is lowering BP, which is a vital strategy to decrease the morbidity and mortality of cardiovascular diseases (CVD) and other diseases.[22] Chinese herbal medicine (CHM) is widely used in China as a pharmacological intervention, and many studies have been conducted on CHM for hypertension. An evidence map review in 2020 showed that CHM was chiefly used in the treatment of elderly hypertension and as a prevention of its complications; it also reported the benefits of CHM in lowering BP, increasing total effective rate and reducing adverse events.[23] Also, Blood stasis is 1 of the main syndrome elements of hypertension.[24] THSWD is a classic Chinese medicine decoction for blood stasis syndromes such as pains in the body, and dark purple lips, THSWD commonly uses in the treatment of hypertension. This meta-analysis reveals the overall efficacy of THSWD as the treatment for hypertension.

Our results suggested that THSWD with antihypertensive drugs markedly improved the BP, TC, TG, LDL-C and HDL-C, and showed a increase in total effective rate and a decrease in adverse events compared to the control groups. The pooled analysis presented in Figure 3 suggested that THSWD with antihypertensive drugs is likely more effective in patients aged 60 to 65 years old. The control groups in the studies were using THSWD with amlodipine,[13–15,17,19–21] nifedipine,[18] valsartan[16] respectively. THSWD can decrease the whole blood viscosity, plasm viscosity[25,26] and hemoglobin[27] of the blood stasis model. It can also reduce BP, improve endothelium-dependent relaxation and the level of nitric oxide, Endothelin-1, endothelial cell protein C receptor, vonwillebrand factor, showing the protection to vascular endothelial cells.[8]The study conducted by Qi Wu et al[28] demonstrated that THSWD relaxes blood vessels through an endothelium-dependent way. Amlodipine and nifedipine are dihydropyridine calcium channel blockers, amlodipine acts on the vascular smooth muscle to reduce BP and decrease peripheral resistance[29]; nfedipine acts on small and large arteries to increase arterial compliance for reducing BP.[30] Valsartan is an angiotensin receptor blockers, it blocks the action of angiotensin II to relax the blood vessels.[31]These 3 drugs are commonly used for hypertension.[32] The promoting blood circulation function of THSWD can remove blood stasis and act on vascular endothelial cells for relaxation, it may cause THSWD combined with different antihypertensive drugs showing more prominent in our study.

The increase in blood lipid levels leads to a decrease in vascular compliance in elderly, causing an increased risk of mortality for hypertensive patients.[33] The results showed a significant decrease in TC, TG and LDL-C compared with the control group, THSWD combined with anti-hypertensive drugs could more effectively improve combined with different antihypertensive drugs. It is noticed that the average decrease is 1.48 mmol/L in TG and 1.43 mmol/L in TC. The heterogeneity of TG was high ($I^2 = 98\%$). After deepening the analysis, the reason of the great heterogeneity may be related to age. Some studies have shown the cholesterol clearance rate of the elderly over 60 years old is lower than that of the young.[34,35] Moreover, there was a statistically significant difference between the experiment group and the control group in the incidence of adverse events (Fig. 7). It suggested that THSWD with anti-hypertensive drugs is safer than using anti-hypertensive drugs alone. We also observed a significant increase in HDL-C which were still in the normal range.

5.2. Limitations of this study

There are several limitations in this study. Firstly, only 9 RCTs studies were analyzed even with a comprehensive literature review. Secondly, the frequency of treatment, length of the duration, time interval, and efficacy standard were all different in studies. Thirdly, no follow-up was performed in all studies. Besides, the random allocation method and blinding were not completely described in some studies. Only 3 studies reported the diagnostic criteria of TCM syndrome. All limitations above could have affected the results but the conclusion is still reliable.

6. Conclusion

THSWD combined with conventional therapy demonstrated the efficacy in the treatment of hypertension in improving the BP, TC, TG, LDL-C and HDL-C. It is probably safer than using antihypertensive drugs alone. The effects of THSWD should be considered in the treatment for further verification and a long-term study should be conducted.

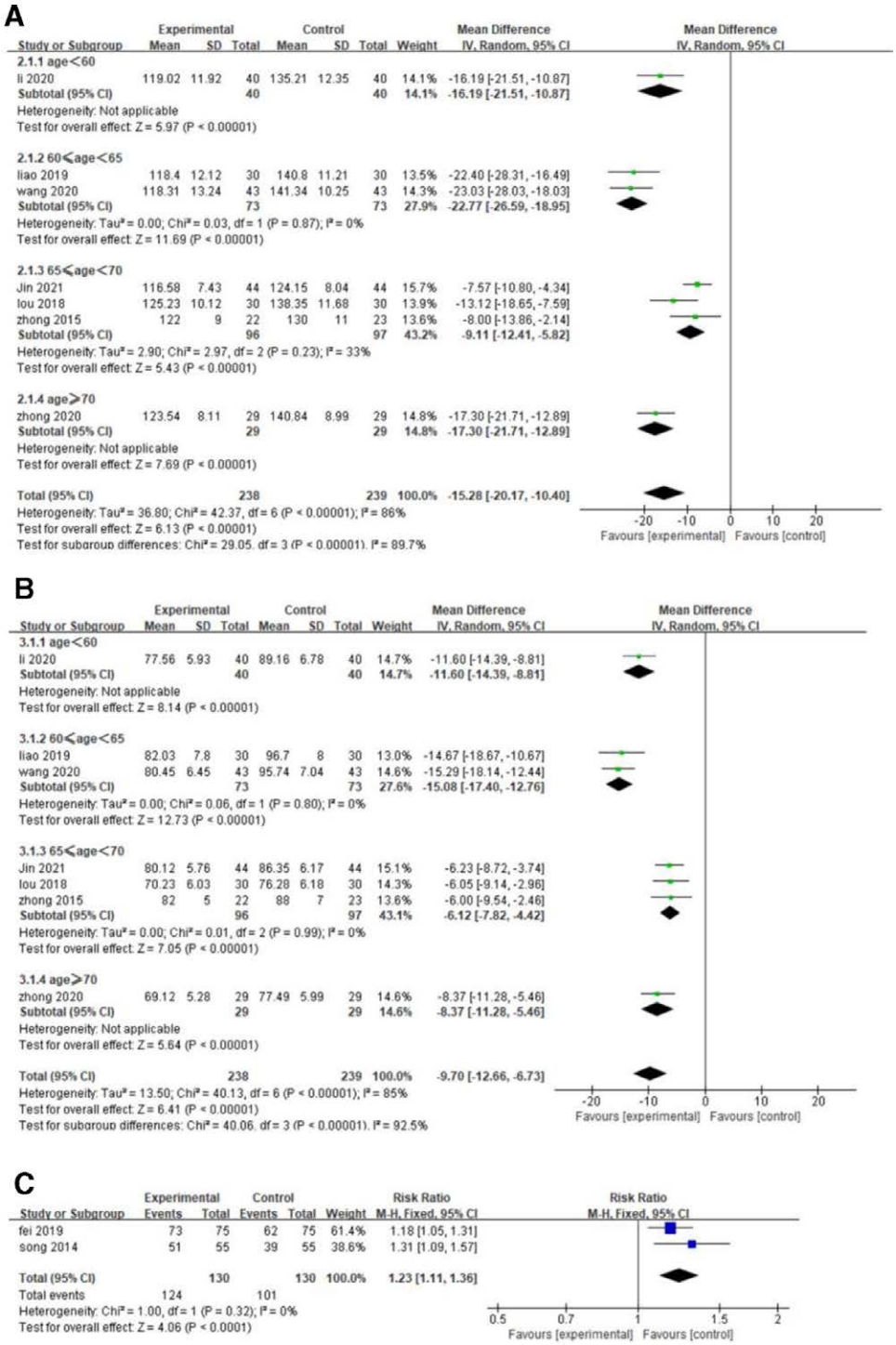

Figure 3. Forest plots of the comparison of THSWD versus antihypertensive drugs for the outcome of BP. A, SBP; B, DBP; C, categorical BP. BP = blood pressure, DBP = diastolic blood pressure, SBP = systolic blood pressure.

Author contributions

The authors would like to thank all members in this study. PCX conducted the conception and design of the study, analysis and interpretation of data, writing of the article and final approval of the version to be published. LKL and WQT collected and analyzed the data. QEL and TX contributed to the writing of the manuscript. LGC and LKL revised the manuscript. All authors reviewed and agreed the final manuscript.

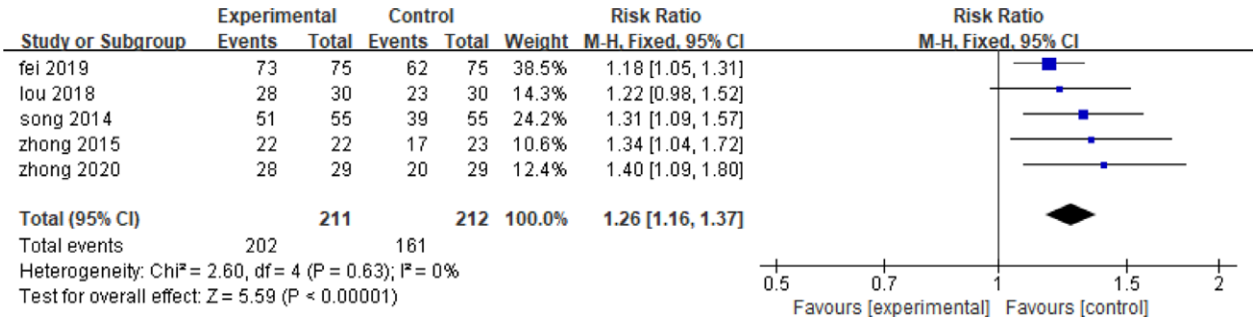

Figure 4. Forest plot of the comparison of THSWD versus THSWD combined with antihypertensive drugs for the outcome of symptoms.

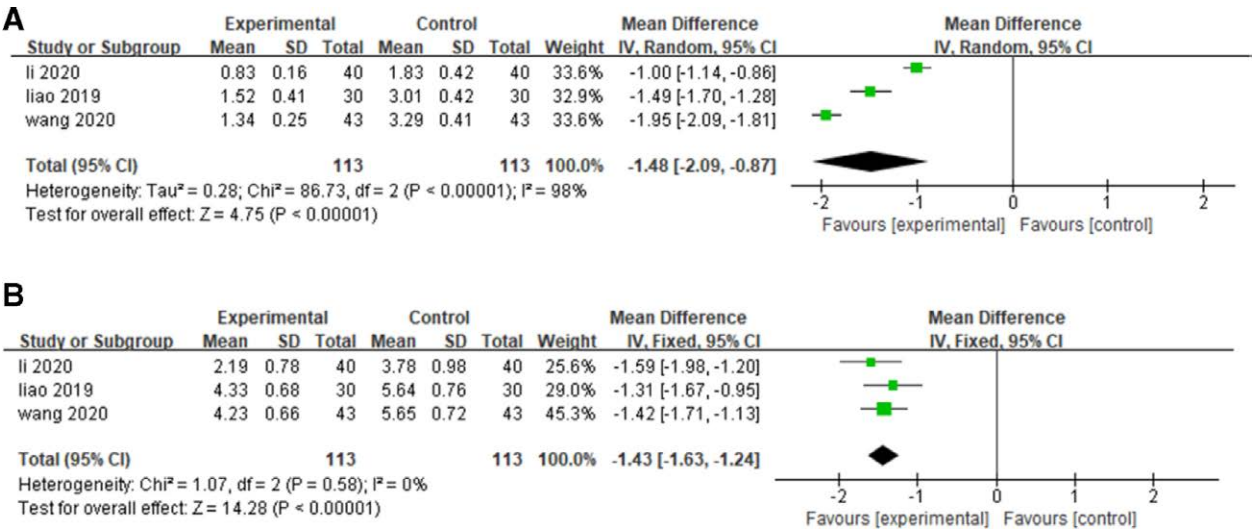

Figure 5. Forest plot of the comparison of THSWD versus antihypertensive drugs for the outcome of TG and TC. A, TG; B, TC. TG = triglyceride; TC = total cholesterol.

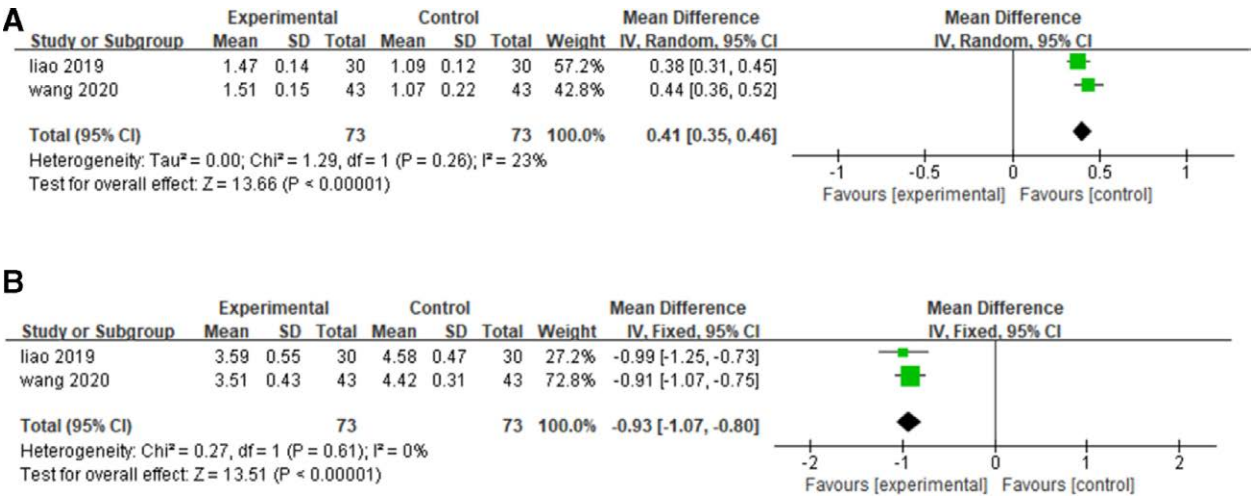

Figure 6. Forest plot of the comparison of THSWD versus antihypertensive drugs for the outcome of HDL-C and LDL-C. A, HDL-C; B, LDL-C. HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol.

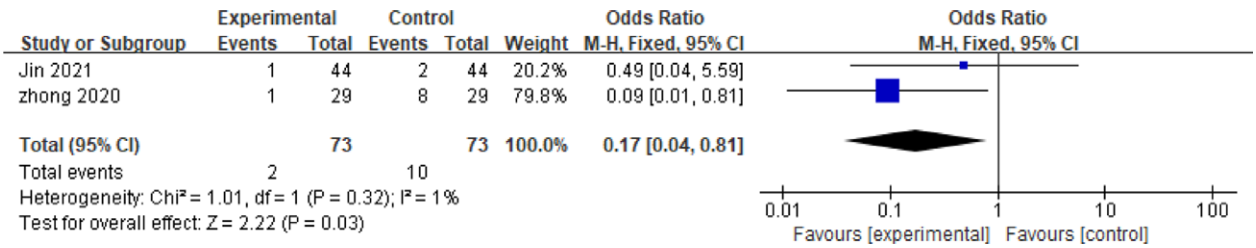

Figure 7. Forest plot of the incidence of adverse events.

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