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REVIEW

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Efficacy and Safety of Adding and Subtracting Decoction of Rehmanniae Combined with Western Medicine in the Treatment of Hypertension: A Systematic Review and Meta-analysis

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Competing interests

The authors declare no conflicts of interest.

Abbreviations

CNKI, Chinese National Knowledge Internet; CBM, China Biomedical Literature Service System; DBP, diastolic blood pressure; SBP, systolic blood pressure; RCTs, randomized controlled trials; TCM, Traditional Chinese Medicine; HBP, high blood pressure; MD, Mean difference; SMD, standardized mean difference; RR, relative risk; Qd, once a day; Bid, twice a day; RAS, renin angiotensin systems; SNS, sympathetic nervous system.

Citation

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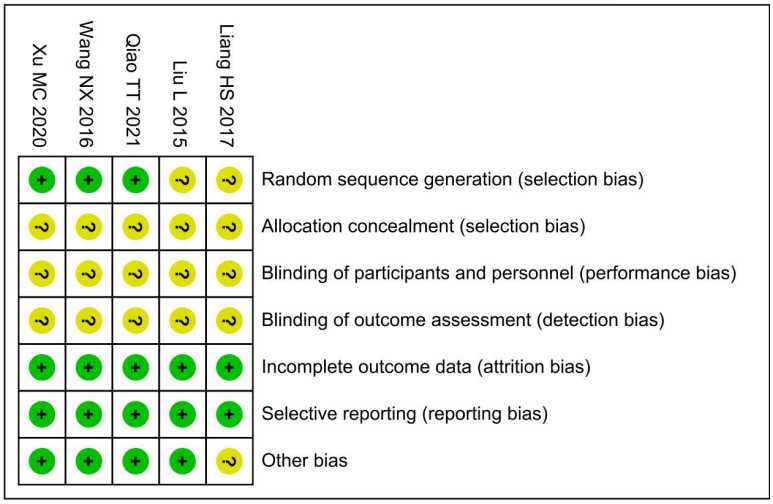
Abstract

Objective: Systematically evaluating the efficacy and safety of adding and subtracting decoction of rehmanniae combined with Western medicine in the treatment of hypertension. **Methods:** PubMed, The Cochrane Library, EMBASE, Web of Science, CNKI, Wanfang Database, VIP database and China Biomedical Literature Service System (CBM) were searched. All randomized controlled studies (RCTs) on adding and subtracting decoction ofrehmanniae combined with Western medicine in the treatment of hypertension were retrieved. The retrieval period is from the database construction to November 2021.Two investigators independently screened the literature, collected baseline data of patients and data on related indicators, and evaluated the risk of bias in the included randomized controlled trials. Meta-analysis was performed by RevMan5.3 software. **Results:** Five randomized controlled trials including 380 patients were obtained after screening by inclusing and exclusing criteria.Meta-analysis results showed that: In the experimental group, TCM syndrome score (MD＝-4.08, 95%CI: -5.32 to -2.84, $P<0.00001$), systolic blood pressure (SBP) (MD＝-7.77, 95%CI: -12.03 to -3.51, $P=0.0003$), diastolic blood pressure (DBP) (MD＝-6.76, 95%CI: -9.59 to -3.93, $P<0.00001$) were better than the control group, and the differences were statistically significant. **Conclusion:** The current evidence shows that compared with the simple use of Western medicine, adding and subtracting decoction of rehmanniae combined with Western medicine in the treatment of hypertension has more advantages in improving TCM syndromes and reducing systolic and diastolic blood pressure, and the conclusion is reliable. However, due to the limited number and low quality of included randomized controlled trials, more randomized, double-blind, large-sample clinical studies are needed to confirm the above conclusions.

Keywords: Decoction of rehmanniae; High blood pressure; Meta analysis; Randomized controlled trial



Introduction

Hypertension, one of the most common chronic diseases, is a cardiovascular syndrome, and its main clinical manifestations of systemic arterial blood pressure continued to rise [1]. It can damage the structure and function of vital organs such as the heart, brain and kidneys, and eventually lead to the failure of these organs [2]. Hypertension is a worldwide cardiovascular disease and one of the major risk factors leading to premature death. It is estimated 1.39 billion adults worldwide had high blood pressure in 2010 [3]. By 2025, 1.5 billion people worldwide are expected to have high blood pressure [4]. The incidence of hypertension is increasing year by year in China, but the perception rate of hypertension patients,the treatment rate and control rate of hypertension are still at a low level [5]. High sodium and low potassium diet, old age, female , alcohol consumption, obesity, diabetes and cardiovascular disease are all risk factors for hypertension [6-8]. At present, the treatment of hypertension is mainly to take long-term western medicine to control blood pressure, and there are many adverse reactions, such as irritant dry cough, hyperkalemia, etc. these seriously affect the quality of life of patients, thus reducing medication compliance [9]. TCM treatment of hypertension emphasizes the holistic concept, comprehensive syndrome differentiation and multi-link conditioning, which has good curative effect and few side effects [10]. According to the comprehensive syndrome differentiation, hypertension was divided into 4 types: hyperactive syndrome of liver fire hyperactive syndrome of Yin deficiency and Yang, deficiency of both Yin and Yang syndrome, and excessive accumulation of phlegm and dampness syndrome [11], decoction of rehmanniae is often used for treatment of hypertension with deficiency of Yin and Yang [10]. Decoction of rehmanniae comes from the Shengji Zonglu in the Song dynasty [12], composed of cooked rehmannia officinalis, cornus officinalis, dendrobium, cistanche deserticola, aconite, schisandra fruit, cinnamon white poria, ophiopogon, calamus, polygala. The adding and subtracting decoction of rehmanniae is based on radix rehmanniae decoction, which is added and subtracted medicine according to the symptoms of patients. In recent years, there are more and more literatures on the treatment of hypertension by adding and subtracting decoction of rehmanniae combined with Western medicine, but the sample size is small, and the literature quality and efficacy have not been systematically evaluated. Therefore, this paper conducted a meta-analysis of randomized controlled trials of adding and subtracting decoction of rehmanniae combined with Western medicine in the treatment of hypertension, providing reliable evidence-based basis for clinicians to apply the addition and reduction of decoction of rehmanniae combined with Western medicine in the treatment of hypertension.

Research Methods

Inclusion Criteria

Study types Only Randomized controlled trials (RCTs) were included in this study, Whether or not Blinded trials is performed, and the languages were limited to Chinese and English.

Research object Patients diagnosed with hypertension according to the hypertension diagnostic criteria [13] and TCM syndrome type diagnostic criteria formulated by the Guidelines for Clinical Research of New Chinese Herbal Medicines [10].

Interventions test group: adding and subtracting decoction of rehmanniae combined with Western medicine was used, and there was no limit on the quantity, dosage, method and course of medicine; Control group: western medicine was used only, the frequency, dosage and course of treatment were not limited.

Outcome Indicators Main outcome indicators: TCM syndrome score, which was evaluated according to theGuiding Principles for Clinical Research of New TCM Drugs issued by the Ministry of Health in 2002 [11]; Secondary outcome measures: ① Diastolic blood pressure (DBP); ② Systolic blood pressure (SBP); ③ Adverse reactions.

Exclusion criteria

① When the literatures that were repeatedly published, we included studies with the most complete data and highest quality; ② The type of published papers is abstract or the relevant data in the papers is incomplete, but the relevant data cannot be obtained by contacting the author; ③ Literature review, basic research or animal experiments; ④Literature without relevant outcome indicators; ⑤ Studies with obvious data errors; ⑥ Research that does not meet the diagnostic criteria of TCM syndrome type; ⑦ Studies without relevant outcome indicators.

Retrieval Strategy

Research on the treatment of hypertension by Dihuang Yinzi was comprehensively searched in Both Chinese and English databases from the database construction to November 2021. Retrieval databases included CNKI, Wanfang Database, VIP Database, China Biomedical Literature Service system, PubMed, Web of Science, The Cochrane Library and EMBASE.The search words adopt the combination of subject words and free words, and the English search words include: HPLC of rehmanniae, Hypertension, Hypertension disease, High blood pressure, Radix Rehmannia Formulae, radix rehmanniae decoction, Decoction of Rehmanniae, Formulae of Rehmanniae, Dihuang Drink, Dihuang Yinzi, Rehmanniae Potion. Chinese search words include: Gaoxue Ya、Dihuang Yinzi.

Literature screening and data extraction

The first and second authors independently searched and read the relevant literature, collected and recorded the baseline data of the patients and the data of related indicators. The two authors cross-checked with each other, and negotiated with the corresponding author to resolve any differences.First, the title and abstract were read to conduct a preliminary screening of the literature. After excluding the literature that obviously did not meet the inclusion criteria, the full text was further read to conduct a secondary screening according to the inclusion criteria to determine the final inclusion of the literature.If there are missing data, the first author or corresponding author of the original study will be contacted by email and phone for relevant information and data.The information to be extracted includes: ① Basic information of included studies: first author, publication year, number of cases in treatment group and control group, baseline of patients in both groups, disease diagnostic criteria adopted in the original study, etc. ② TCM syndrome type, course of disease, treatment plan and course of treatment in the two groups;③ Outcome indicators included in this study.

Bias risk assessment of included studies

The risk of bias for included RCTs was assessed independently by the first and second authors and the results were cross-checked.If there is any discrepancy in the evaluation, discuss and resolve it with the corresponding author.The RCT bias risk assessment tool recommended by Cochrane Manual 5.1.0 was used to evaluate the risk of bias [14].

Statistical Analysis

Meta-analysis was performed by using RevMan5.3 software.For continuous variables, if the units of measurement indicators or tools are the same, Mean difference (MD) is used for analysis;If measurement tools or units are inconsistent, Standardized mean difference (SMD) is used for analysis.If the research data are dichotomous variables, Relative risk (RR) is used as the statistic $\chi 2$ test was used to test heterogeneity and was combined $I2$

Quantitative determination of heterogeneity. If $P>0.10$, $I2<50\%$, there was no significant heterogeneity between studies, and a fixed-effect model was used for meta-analysis. If $P<0.10$, $I2>50\%$, indicating significant heterogeneity between studies, the cause of heterogeneity needs to a further analyzed. After excluding the influence of obvious clinical and methodological heterogeneity, the random-effect model is used for Meta analysis.Sensitivity analysis was used to observe the influence of single study on the combined effect size and judge the stability of meta-analysis results. When the number of outcome indicators included exceeded 10 studies, publication bias was evaluated by using RevMan5.3 software to make funnel plots.

Results

Literature screening process and results

A total of 240 literatures were retrieved from the above 8 databases, and 180 literatures were obtained after cull.Preliminary screening excluded 165 reading titles and abstracts, 55 inconsistencies in research diseases, 103 inconsistencies in intervention measures, 4 reviews, and 3 animal experiments. The full text of 15 papers was read, including 10 papers excluded according to inclusion and exclusion criteria, 6 papers with inconsistent intervention measures, one repeatedly published paper, and one paper with obvious data errors. There was one study that did not meet the diagnostic criteria of TCM syndrome type and one literature that had no relevant outcome indicators, and 5 literatures were finally included [15-19]. The literature screening process is shown in Figure 1.

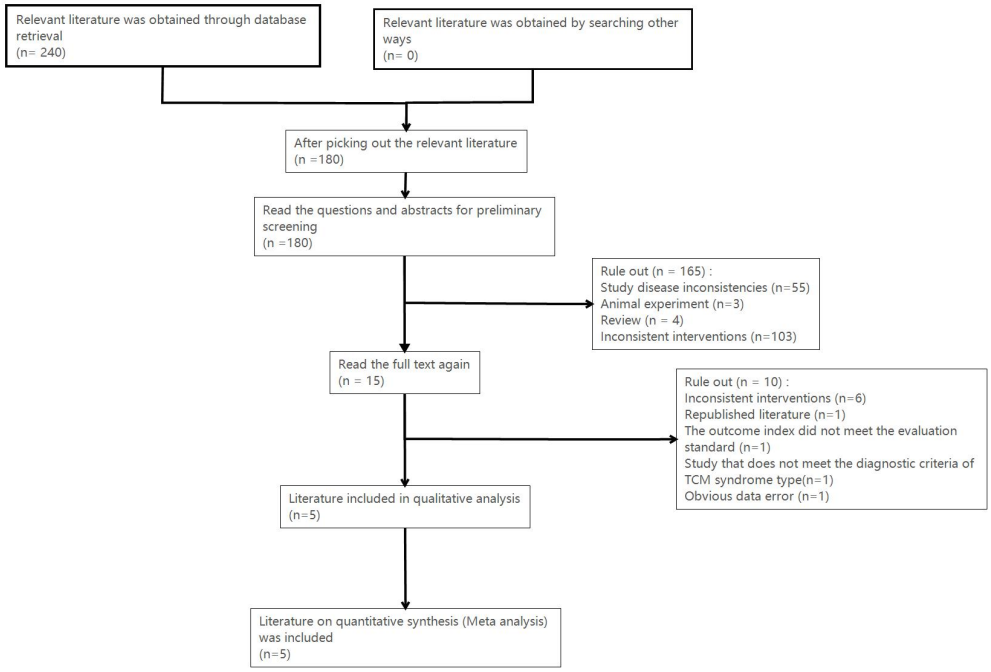


Figure1 Literature screening process and results

Basic features of the included study

The basic characteristics of the included study were shown in Table 1. The composition of decoction of rehmanniae in experimental group was different more or less. The characteristics of intervention measures were in Table 2. The treatment period was 14 days and a month. 4 studies were reported TCM syndrome score [15-18], 5 studies were reported SBP [15-19]. Two studies were reported on DBP adverse reactions were reported [15,17].

Table 1 Included basic characteristics of the study

Included in the study	Cases (T/C)	Gender (Male/female)		age (years old)		Course of the disease (year)		Period of treatment	Outcome indicators	High blood pressure Diagnostic criteria of disease	High blood pressure Diagnostic criteria of curative effect
		T	C	T	C	T	C				
Liang HS 2017 [15]	20/20	8/12	9/11	72.1±2.3	71.3±2.1	NA	NA	14 (days)	①②③④	⑤	⑤
Liu L 2015 [16]	30/30	16/14	17/13	73.50±5.28	74.8± 5.67	13.4±7.63	15.7±8.41	14 (days)	①②③	⑤⑥	⑤
Qiao TT 2021 [17]	29/29	15/14	13/16	51.±9.59	52.± 11.01	5.4±3.05	5.4±3.22	14 (days)	①②③④	⑤⑥⑦	⑤⑦
Wang NX 2016 [18]	75/75	46/29	43/32	74.5± 7.8	74.3± 7.6	12.3 ±2.5	12.4± 2.2	14 (days)	①②③	⑥	⑤
Xu MC 2020 [19]	36/36	19/17	18/18	74.5±8.56	74.7± 8.12	11.2±5.23	11.6±5.48	A month	②③	⑤	⑤

Note: T: test group;C: control group; NA: Not mentioned; ①TCM syndrome score; ②SBP; ③DBP; ④Adverse reactions; ⑤Refer to guiding Principles for Clinical Research of New Chinese Medicine [11]; ⑥Refer to Chinese Hypertension Prevention and Treatment Guidelines (2010 edition); ⑦Refer to Sweat law clinical hair micro.

Table 2 Characteristics of intervention measures

Included in the study	The doctor of traditional Chinese medicine syndrome types	The experimental group			The control group
		The formulas	Traditional Chinese medicine composition	Western medicine	Western medicine
Liang HS 2017 [15]	Yin-yang deficiency	Add and subtract decoction of rehmanniae	20g cooked rehmannia and Poria, 15g fructus schisandrae, Radix polygala, Acorus gladiolis, Corni officinalis, Euphorbia officinalis, Cistanche deserticola, Ophiopogonis, Dendrobium, 10g cinnamon, peppermint and Fructus aconiti, decocted with ginger and jujube. At the same time, adding and subtracting drugs according to syndrome differentiation	Nifedipine sustained-release tablet 10mg bid	Nifedipine sustained-release tablet 10mg bid
Liu L 2015 [16]	Yin-yang deficiency	Add and subtract decoction of rehmanniae	Cooked rehmannia glutinosa 20g, Corni officinalis 15g, Dendrobium 15g, Maimendong 15g, Schisandra fruit 15g, Acorus gladiolus 15 g, Polygala polygala 15g, Tuckahoe 20g, Cistanche deserticola 15g, Aconite fruit 10 g, cinnamon 10g, Morinda officinalis 15g, menthol 10g, ginger 3 pieces, 4 dates; At the same time, adding and subtracting drugs according to syndrome differentiation	Nifedipine sustained-release tablet 20mg Qd	Nifedipine sustained-release tablet 20mg Qd
Qiao TT 2021 [17]	Yin and Yang are both empty and cold	Add and subtract decoction of rehmanniae	Cooked rehmannia 20g, Corni 15g Cistanche 9g, Morinda of ficinalis 9g,Dendrobium 10g, Ophiopogon 10g, Schisandra fruit 10g, Aconite fruit 6g, (decoct first) Tuckahoe 9g, menthol 9g.	Enalapril maleate tablet 5mg Qd	Enalapril maleate tablet 5mg Qd
Wang NX 2016 [18]	Yin-yang deficiency	Add and subtract decoction of rehmanniae	Cooked rehmannia 20g, menthol 10g, Tuckahoe 20g, Schisandrae 15g, Acorus gladiolus 15g, Polygala polygala 15g, Corni officinalis 15g, Morinda officinalis 15g, Maimendong 15g, Dendrobium officinale 15g, Aconite aconite 10g, cinnamon 10g, deserticola 15g, ginger 3 pieces, jujube 4 pieces; At the same time, adding and subtracting drugs according to syndrome differentiation	Nifedipine sustained-release tablet 20mg Qd	Nifedipine sustained-release tablet 20mg Qd
Xu MC 2020 [19]	Yin-yang deficiency	Add and subtract decoction of rehmanniae	Cooked Rehmannia rehmanniae 20g, Tuckahoe 20g, Morinda officinalis 15g, Schisandra fruit 15g, Ophiopogon japonicus 15g, Calamus acorus 15g, Deserticola deserticola 15g, Dendrobium officinale 15g, Cornus officinalis 15g, Polygala polygala 15g, Menthol menthol 10g, Aconite aconite 10g, cinnamon 10g, ginger 6g, 4 dates; At the same time, adding and subtracting drugs according to syndrome differentiation	Nifedipine sustained-release tablet 20mg Qd	Nifedipine sustained release, 20mg Qd

Note: Qd: once a day;Bid: Twice a day.

Bias risk evaluation results of included studies

The five included papers were evaluated using the RCT bias risk assessment tool recommended in Cochrane Manual 5.1.0 [15-19]. The method of random sequence generation is used correctly in 3 literatures [17-19]; None of the literature mentioned allocation concealment, and was rated as unclear; None of the literature mentioned blind method; All studies were rated as low risk of bias on incomplete outcome data; The literature was rated as low risk of bias in selective reporting. In other aspects of bias,one of the literatures was evaluated as having uncertain risk of bias due to uncertain baseline situation [15], while the other literatures were evaluated as having low risk of bias. The results of bias risk assessment are shown in Figure 2.

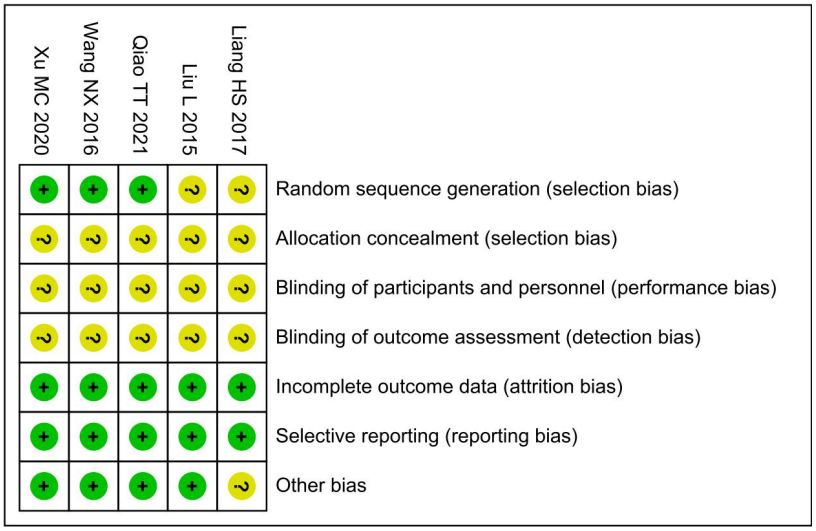


Figure 2 bias risk assessment of included studies

Meta-analysis results

TCM syndrome score

TCM syndrome score is used to evaluate the improvement of TCM syndrome as the main outcome index. A total of 4 RCTs were included, including 308 patients [15-18] .There was heterogeneity among studies (P=0.010, $I2$= 74%), literature characteristics of four studies reporting TCM syndrome score were analyzed. Heterogeneity analysis was performed by using one-by-one elimination method, and Qiao TT 2021 was excluded [17]. Heterogeneity disappeared after the original study. Analysis of the original study with Qiao TT 2021 revealed that patients with an average age of 50+ years [17], and the TCM syndrome type was deficiency of Yin and Yang combined with cold coagulation syndrome. Enalapril maleate tablets were used in the Qiao TT 2021 study [17]. The average age of the other three groups was 70+ years old. Nifedipine sustained release tablet was used in combination with western medicine, and the TCM syndrome type was deficiency of Yin and Yang. Therefore, the heterogeneity was considered to be caused by age, TCM syndrome type and type of combined use of Western drugs. Random effects model is used. Meta-analysis results showed that the experimental group was superior to the control group in improving TCM syndromes (MD= -4.08, 95%CI: -5.32 to -2.84, P<0.00001), and the difference was statistically significant (P<0.05, Figure 3).

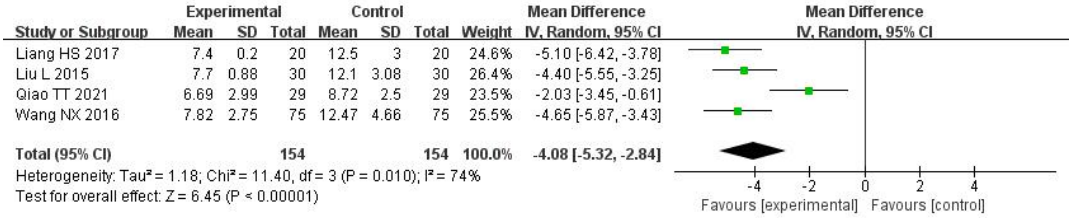


Figure 3 TCM syndrome integral

Systolic blood pressure (SBP)

A total of 5 RCTs were included, including 380 patients.There was heterogeneity among studies (P<0.00001, I^2=86%) [15-19] . The literature characteristics of 5 studies reporting systolic blood pressure were analyzed, and sensitivity analysis was performed by using the one-by-one elimination method. Heterogeneity still existed when any study was excluded.However, the analysis of the original study found no other significant clinical heterogeneity, so statistical heterogeneity was considered and the random effect model was adopted. Meta-analysis results showed that after treatment, the experimental group was superior to the control group in reducing systolic blood pressure (MD = -7.77, 95%CI: -12.03 to -3.51, P = 0.0003), and the difference was statistically significant (P < 0.05, Figure 4).

Diastolic blood pressure (DBP)

A total of 5 RCTs were included [15-19], including 380 patients. There was heterogeneity among studies (P< 0.00001, I^2=88%). The literature characteristics of five studies reporting diastolic blood pressure were analyzed, and the heterogeneity was analyzed by one-by-one elimination method. When any study was excluded, the heterogeneity still existed. However, the analysis of the original study found no other significant clinical heterogeneity, so statistical heterogeneity was considered and the random effect model was adopted. Meta-analysis results showed that after treatment, the experimental group was superior to the control group in reducing diastolic blood pressure (DBP) (MD = -6.76, 95%CI: -9.59 to -3.93, P <0.00001), and the difference in systolic blood pressure between the experimental group and the control group was statistically significant (P<0.05, Figure 5).

Adverse reactions

Among the 5 included papers [15-19], 380 patients were included in total, and only 2 papers were clear reports on drug safety,

accounting for 40% of the total number of included papers [15,17]. And it was clearly stated that no adverse reactions were observed in the experimental group and the control group after treatment. The remaining 3 papers (accounting for 60% of the total included literatures) did not mention adverse reactions. Due to the limited number of included randomized controlled trials and lack of sample data, the adverse reactions of decoction of rehmanniae combined with Western medicine in the treatment of hypertension could not be accurately evaluated. More randomized, double-blind, large-sample clinical studies are needed to investigate the incidence of adverse reactions.

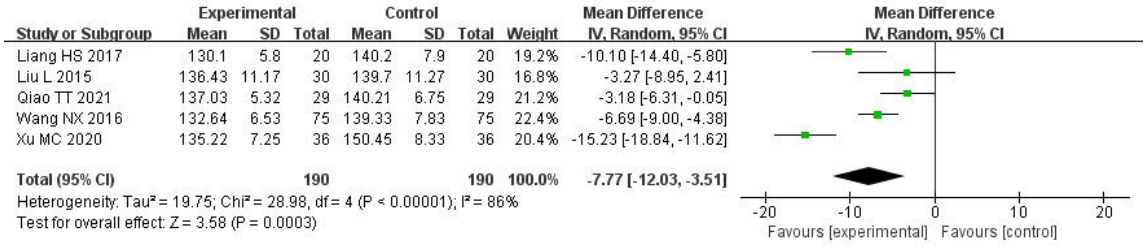


Figure 4 Systolic blood pressure (SBP)

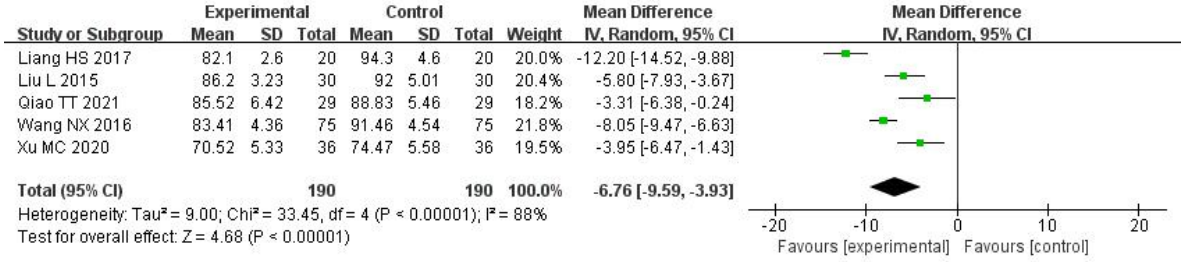


Figure 5 Diastolic blood pressure (DBP)

Sensitivity analysis

The sensitivity analysis of the above the outcome indicators was carried out by using the one-by-one elimination method, and the effect size and p-value changes were observed after the exclusion. When analyzing the TCM syndrome score, excluding the original Qiao TT2021 study [17], the meta-analysis result was $P=0.73$, indicating that the results were unstable in terms of TCM syndrome score and influenced by a single study.Other indicators, such as systolic blood pressure (SBP) and diastolic blood pressure (DBP), showed no significant change in the effect size and P value of outcome indicators excluding any of the included studies ($P<0.05$), indicating that the meta-analysis results of these indicators were stable.

Publication bias

The number of studies included in the TCM syndrome score integral outcome index was 4, and the number of studies was $4<10$, so the funnel plot can not be used to evaluate publication bias.

Discussion

Hypertension has many pathogenesis mechanisms, according to Braunwald's account of heart disease,i t including neural mechanisms (mainly SNS), renal mechanisms (mainly sodium and water retention), vascular mechanisms (mainly endothelial and vascular smooth muscle mechanisms), and hormonal mechanisms (mainly renin angiotensin system (RAS)[20]. According to Chinese medicine theory analysis, hypertension belongs to vertigo, headache category [21]. One of its common disease mechanism is affection maladjusted, liver stagnation qi is stagnant, then liver stagnation changes fire to send liver fire to go up phlogistic or liver Yang go up hyperactive, further development sends Yin deficiency Yang hyperactive, liver kidney Yin deficiency, the loss of Yin affect Yang, finally Yin and Yang two loss [22]. Hypertension can be treated with rehmannia decoction, a supplement of Yin and Yang. Rehmannia sinensis and cornus officinalis can nourish kidney Yin and fill kidney essence, cistanche deserticola and Euphorbia officinalis can nourish kidney and warm Yang. The four herbs, suppling Yin and Yang, are all junyao; Radix Ophiopogon, fructus schisandrae, Dendrobium nourishing Yin;aconite, cinnamon sent the fire return to kidney, and then accompanied by Polygala, stone calamus, Poria cohoe kaiqiao phlegm, heart and kidney intersection;Mint light clear evacuation, ginger jujube adjustable fill Yin and Yang qi and blood.The whole formula takes into account all aspects of the body, regulating the function of the whole body, so as to treat hypertension [23]. Modern pharmacological studies show that rehmannia glutinis has an improvement effect on cardiovascular diseases such as myocardial strain and left ventricular hypertension caused by hypertension, and has an anti-hypertensive effect [24-26]. Cornus can enhance myocardial contractility and enhance the pumping function of the heart [27]. Meanwhile, rehmannia glutinosa combined with cornus officinalis can induce angiogenesis and promote vascular remodeling [28]. Morinda officinalis has the function of protecting cardiovascular and anti-oxidation [29]; Cistanche has the function of relaxing blood vessels [30]. Decoction of rehmanniae can achieve the exact therapeutic effect by anti-oxidation, anti-aging, protection of vascular endothelium, alleviation of inflammation and injury, improvement of cerebral blood circulation, alleviation of brain tissue damage during recovery, and promotion of neuron repair [31].

Five randomized controlled trials of adding and subtracting decoction of rehmanniae combined with western medicine in the treatment of hypertension were systematically evaluated in this paper. .Meta-analysis results showed that : (1) Compared with western medicine alone, adding and subtracting decoction of rehmanniae combined with western medicine can better improve the main symptoms such as vertigo, headache, Lumbar genu sour soft , chills and limb cold, as well as the minor symptoms such as tinnitus, palpitations, shortness of breath, nocturnal frequent urination, and has outstanding curative effect in improving TCM symptoms of hypertension. (2) In terms of systolic blood pressure (SBP) control. Among the 5 RCTS included [15-19], the mean systolic blood pressure of all studies in the

experimental group was reduced within the normal range after treatment; After treatment, the mean systolic blood pressure of the control group was only controlled to the higher level of the normal range in 2 studies [15,18], and the mean systolic blood pressure of the patients in the other 3 studies was still higher than 140mmHg [16,17,19], and the hypotensive effect of the experimental group was significantly better than that of the control group. It indicated that the combination of rehmanniae decoction and Western medicine had a more significant effect in reducing systolic blood pressure than western medicine alone, and the sensitivity analysis was stable, indicating reliable efficacy. (3) In terms of controlling the diastolic blood pressure (DBP).Among the 5 included RCTS [15-19], the mean diastolic blood pressure of the experimental group was reduced to the normal range after treatment, while the mean diastolic blood pressure of the control group was only reduced to the normal range in 2 studies [17,19] after treatment, nd the mean diastolic blood pressure of the patients in the other 3 studies was higher than 90mmHg [15,16,18]. It indicated that dihuang Yinzi combined with Western medicine had a more significant effect in reducing diastolic blood pressure, and the sensitivity analysis was stable, indicating reliable efficacy. (4) On the opposite side of adverse reactions, only 2 studies proved that neither the experimental group nor the control group had adverse reactions [15,17], which could not accurately assess the occurrence of adverse reactions.

The results of this study has certain limitations: (1) The quality of the included studies is low, some literature is mentioned random two words, not say specific random methods, also did not say allocation concealment and Blinded trials concrete operation, there may be a selective bias, implementation bias and measurement bias, etc.,it has a certain impaction on the reliability of results ; (2) The sample size of the included studies was small and of low quality, which requires more randomized, double-blind, large-sample clinical studies to confirm; (3) The included studies were all from China, with regional limitations and poor universality; (4) Follow-up after treatment was not reported in all studies, which is insufficient to judge the long-term efficacy and safety of drugs; (5) Due to the particularity of TCM dialectics and TCM decoction, the composition and dosage of rehmanniae decoction used in different studies are different to some extent, which affects the authenticity of the results when evaluating the effect of intervention measures; (6) Adverse reactions were not mentioned in some studies, which lacked safety basis.

Current evidence proves that the decoction of rehmanniae (which is addited or subtracted) combined with Western medicine in the treatment of hypertension can significantly improve the traditional Chinese syndrome of hypertension patients such as vertigo, headache, Lumbar genu sour soft, chills and cold limbs within 2-4 weeks, effectively reduce systolic and diastolic blood pressure indicators, and the efficacy is better than the use of western medicine alone. However, due to the limited number and low quality of included randomized controlled trials, more randomized, double-blind, large-sample clinical studies are needed to confirm the above conclusions.

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