

Review Article

Therapeutic effect of YiQi HuoXue BuShen decoction combined with Western medicine on hypertensive nephropathy: a meta-analysis

Mingming Liu¹, Hong Wang², Ping Lv¹

¹Department of Traditional Chinese Medicine, Taizhou First People's Hospital, Taizhou 318020, Zhejiang, China;

²Department of Nephrology, Taizhou First People's Hospital, Taizhou 318020, Zhejiang, China

Received March 27, 2023; Accepted May 15, 2023; Epub June 15, 2023; Published June 30, 2023

Abstract: Objective: To comprehensively evaluate therapeutic effect of YiQi HuoXue BuShen decoction combined with Western medicine on hypertensive nephropathy. Methods: The CNKI, WanFang, VIP, Chinese Biomedical Database (CBM), PubMed, Embase and Cochrane Library databases were searched to collect the randomized controlled trials (RCTs) of YiQi HuoXue BuShen decoction combined with Western medicine on hypertensive nephropathy, which were published as of March 10, 2023. Then, these articles were screened to extract and evaluate the data. Revman 5.3 was applied for data analysis. Results: Eight RCTs involving 732 patients were included after screening. Comparing with Western medicine, YiQi HuoXue BuShen decoction combined with Western medicine enhanced the clinical effect [OR = 3.48, 95% CI: 2.12~5.73, $P < 0.00001$]; reduced 24-hour urine protein content [OR = -0.60, 95% CI: -0.92~-0.28, $P = 0.0003$], serum creatinine (Scr) [OR = -39.11, 95% CI: -44.72~-33.51, $P < 0.00001$], blood urea nitrogen (BUN) [OR = -2.51, 95% CI: -4.06~-0.95, $P = 0.002$], cystatin C (Cys-C) [OR = -0.30, 95% CI: -0.36~-0.25, $P < 0.00001$], Urine β 2-microglobulin [OR = -0.42, 95% CI: -0.87~-0.02, $P = 0.06$]; and enhanced creatinine clear rate (Ccr) [OR = 3.24, 95% CI: 1.85~4.64, $P < 0.00001$]. In addition, the combination treatment didn't increase the incidence of adverse reaction compared with western medicine [OR = 1.55, 95% CI: 0.61~3.95, $P > 0.05$]. Conclusions: The combination of YiQi Huoxue Bushen decoction and western medicine can effectively improve the clinical symptoms and renal function of patients with hypertensive nephropathy and provide more theoretical basis for clinical application.

Keywords: Yiqi Huoxue Bushen decoction, Western medicine, hypertensive nephropathy, effect

Introduction

Hypertensive nephropathy is a special type of renal disease that causes arteriosclerosis and glomerulosclerosis due to primary hypertension [1]. Patients experience arteriolar spasm and decreased blood perfusion at an early stage [2]. If not controlled in a timely manner, it may develop into nephron sclerosis, fibrosis, and even renal failure, posing a serious threat to a patient's life. In the early stages of hypertension, renal artery spasm occurs, leading to decreased blood flow, followed by progressive glomerulosclerosis, renal interstitial fibrosis, renal tubular atrophy, and even renal failure [3]. Its clinical manifestations are mainly acid-base imbalance, electrolyte disorder, retention of toxic metabolites, and damage to major organs

and systems of the whole body, which may further develop into irreversible end-stage renal failure [4]. However, due to the fact that the early clinical symptoms of the disease are insidious, many patients have already entered the stage of renal failure when the disease is discovered. At present, the incidence of hypertensive nephropathy in China is increasing annually. It ranked the third in the primary incidence of hemodialysis patients in China in 1999, accounting for the first cause of chronic renal failure in the elderly [5].

Currently, Western medicine is mainly used to treat renal failure caused by hypertensive nephropathy. Nifedipine is a commonly used antihypertensive drug in clinical practice, which can alleviate renal dysfunction by lowering

Combination of Chinese and Western medicine on hypertensive nephropathy

blood pressure in patients [6]. However, because Nifedipine does not directly affect the kidneys, its efficacy is slow, and it is prone to develop drug resistance, making it unsuitable for long-term treatment [7]. Irbesartan is an angiotensin II receptor antagonist, which can effectively inhibit the conversion of angiotensin I into angiotensin II, thereby inhibiting vasoconstriction and aldosterone release, reducing water and sodium retention, lowering blood pressure, and protecting target organ function [8]. This drug is particularly suitable for patients with hypertension and renal dysfunction. However, the efficacy of irbesartan alone in the treatment of hypertensive renal damage is not ideal. It can cooperate with methods such as blood purification and kidney transplantation [9]. Although these methods can effectively improve or treat clinical symptoms, blood purification requires long-term and regular treatment [10]. The cost is quite high, and there are strict requirements for professional personnel and medical equipment. Kidney transplantation is not only costly, but also subject to stringent transplant conditions.

According to traditional Chinese medicine, hypertension can be divided into liver yang hyperactivity syndrome, yin deficiency yang hyperactivity syndrome, phlegm dampness obstruction syndrome, and qi stagnation and blood stasis syndrome according to symptoms and signs [11]. The syndrome of hyperactivity of liver yang and syndrome of qi stagnation and blood stasis are more common. Hypertension can cause pathological damage to the heart, brain, kidneys, blood vessels, and other organs [12]. Traditional Chinese medicine can effectively prevent and reduce damage to target organs, with a certain organ protection effect. With the vigorous development of traditional Chinese medicine therapy in China, certain achievements have been achieved in the treatment of hypertensive nephropathy [13]. Yiqi Huoxue Bushen decoction has the medicinal effects of supplementing qi, nourishing yin, tonifying the kidney, promoting blood circulation and resolving blood stasis. It can improve clinical efficacy by promoting renal function [14]. Studies confirmed that the combination treatment of Yiqi Huoxue Bushen decoction and Western medicine shows better efficacy, and the clinical symptoms and renal function have obvious improvement [15]. However, the quality of existing research is inconsistent, and

each study has its own focus. In this study, we systematically evaluated the therapeutic effect of Yiqi Huoxue BuShen decoction combined with Western medicine on hypertensive nephropathy.

Methods

Literature retrieval strategy

The CNKI, WanFang, VIP, Chinese Biomedical Database (CBM), PubMed, Embase and Cochrane Library databases were searched to collect the randomized controlled trials (RCTs) of Yiqi Huoxue BuShen decoction combined with Western medicine on hypertensive nephropathy, which were published as of March 10, 2023. The key words included Yiqi Huoxue BuShen decoction, Western medicine, Nifedipine, Amlodipine besylate, enalapril maleate, Candesartan Cilexetil, hypertensive nephropathy. We use the search of PubMed as an example, the search formula was “((Yiqi Huoxue BuShen) and ((Western medicine) or (Nifedipine) or (Amlodipine besylate) or (Enalapril maleate) or (Candesartan Cilexetil)) and (“Hypertensive Nephropathy” [Supplementary Concept]))”.

Inclusion and exclusion criteria

Inclusion criteria: (1) Randomized controlled trial (RCT) published in China or abroad; (2) Patients with hypertensive nephropathy; (3) The control group was treated with western medicine, and the experimental group was given the combination treatment of Yiqi Huoxue BuShen decoction and western medicine; (4) Articles having at least one of the following indicators included: ① The total clinical effective rate; ② 24-hour urinary protein quantification; ③ Serum creatinine (Scr); ④ Blood urea nitrogen (BUN); ⑤ Cystatin C (Cys-C); ⑥ Urine β 2-microglobulin; ⑦ Enhanced creatinine clear rate (Ccr); ⑧ Adverse reaction.

Exclusion criteria: (1) Articles published repeatedly; (2) Articles that couldn't provide relevant or specific data for extraction; (3) Review, conference papers, animal/cell experiment articles.

Literature screening and data extraction

After removing the duplicate documents, two researchers (Mingming Liu, Hong Wang) independently examined the document's title and

Combination of Chinese and Western medicine on hypertensive nephropathy

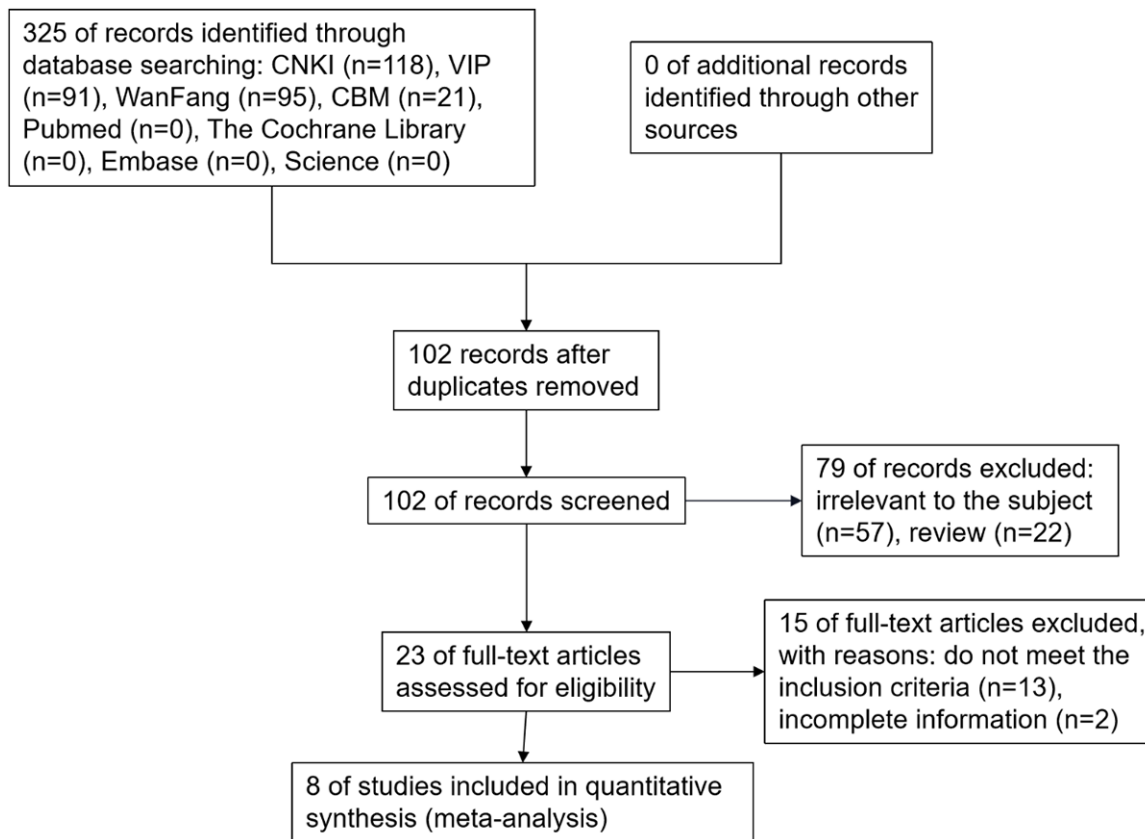


Figure 1. Literature screening process.

abstract and removed reviews, non-clinical studies, and other items that were blatantly irrelevant. Then the full text was read for further screening. Relevant information was extracted, including the number of cases, type of western medicine, course of treatment, and outcome indicators. Disputes were solved by consulting a third researcher (Ping Lv).

Risk assessment of bias

The items of bias risk assessment include: (1) Generation of random sequence (selective bias); (2) Distribution concealment (selective bias); (3) Implementation of blind method for researchers and subjects (implementation bias); (4) Results Implementation of evaluator blind method (measurement bias); (5) Integrity of result data (wear bias); (6) Report bias; (7) Bias from other sources.

Statistical analysis

Software RevMan 5.3 was employed for the meta-analysis. For binary variables, the odds

ratio (OR) was used for calculating the relationship between a variable and the likelihood of an event occurring, while the mean difference (MD), along with its 95% confidence interval (95% CI), was used for measuring the absolute difference between the mean value in two different groups. The Q test was used to examine the heterogeneity of the included research results. The fixed effect (FE) model was employed if the heterogeneity between the research outcomes was low ($P > 0.1$ and $I^2 < 50\%$); otherwise, the random effect (RE) model was applied. To determine whether there was publishing bias, a funnel map was created.

Results

Literature screening process and basic characteristics of inclusion research

At the time of the initial search, there were 325 relevant articles, as shown in **Figure 1**. Eight articles involving 732 hypertensive nephropathy patients were eventually included after a systematically review process. **Table 1** lists the

Combination of Chinese and Western medicine on hypertensive nephropathy

Table 1. The summarized information in each study

Study Year	Cases (n)		Kind of western medicine	Course of treatment (days)	Primary outcome
	Experimental group	Control group			
He 2018 [16]	40	40	Nifedipine	3 months	(1) (2) (3) (4)
Hu 2018 [17]	55	55	Amlodipine besylate and enalapril maleate	12 weeks	(1) (2) (3) (4) (5) (8)
Lan 2012 [18]	80	48	Candesartan Cilexetil	30 days * 3 times	(1) (2) (3) (4)
Nian 2019 [19]	52	52	Enalapril maleate tablets and amlodipine atorvastatin calcium tablets	12 weeks	(1) (6) (7) (8)
Sun 2021 [20]	25	25	Enalapril maleate and amlodipine besylate	3 months	(2) (4) (5)
Wang 2021 [21]	50	50	Irbesartan	12 weeks	(6) (7) (8)
Wei 2018 [22]	50	50	Benazepril Tablets	3 months	(1) (4) (6) (7)
Yu 2017 [23]	30	30	Nifedipine	3 months	(1) (2) (3) (4) (5)

Note: (1) The total clinical effective rate; (2) 24-hour urinary protein quantification; (3) Serum creatinine (Scr); (4) Blood urea nitrogen (BUN); (5) Cystatin C (Cys-C); (6) Urine β 2-microglobulin; (7) Creatinine clear rate (Ccr); (8) Adverse reaction.

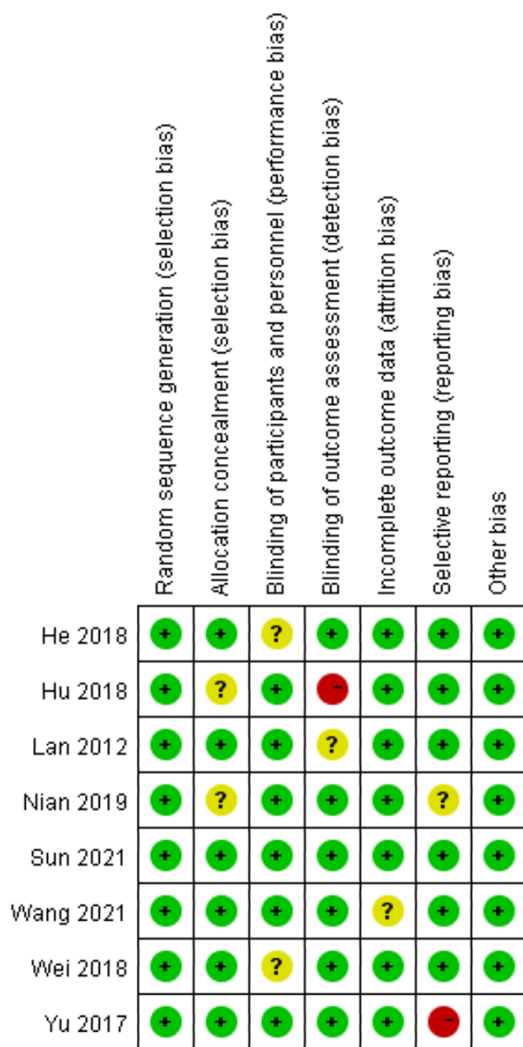


Figure 2. The scale for assessing the quality of clinical trials.

number of cases, kind of western medicine, course of treatment, and outcome measures for each study.

Bias risk assessment

The selection bias of 8 studies was “low risk” since they described the specific random classification method, in which 7 studies used a random number table method, and 1 study used the paper bag method. Two publications didn’t mention the allocation concealment and were therefore evaluated as “unclear”. Two studies didn’t explain the blinding of participants and personnel and was evaluated as “unclear”. In addition, one article didn’t meet the blinding of outcome assessment, which was decided as “high risk”, and one article didn’t mention it, which was regarded as “unclear”. For the incomplete outcome data, there was one publication evaluated as “low risk”. For the selective reporting, one was “unclear”, the other was “high risk”. See **Figures 2 and 3**.

Meta-analysis results

The clinical effective rate: As shown in **Figure 4**, there were 6 studies which evaluated the clinical effective rate. The result obtained by FE model ($I^2 = 0\%$) showed that the combination treatment of YiQi HuoXue BuShen decoction and western medicine enhanced the curative effect compared with western medicine alone [OR = 3.48, 95% CI: 2.12~5.73, $P < 0.00001$].

24-hour urinary protein quantification: There were 4 studies that evaluated the 24-hour urinary protein quantification. The results obtained by RE model ($I^2 = 89\%$) showed that the combination treatment of YiQi HuoXue BuShen decoction and western medicine decreased more in the 24-hour urinary protein compared with western medicine alone [OR = -0.60, 95% CI: -0.92~-0.28, $P = 0.0003$] (**Figure 5**).

Combination of Chinese and Western medicine on hypertensive nephropathy

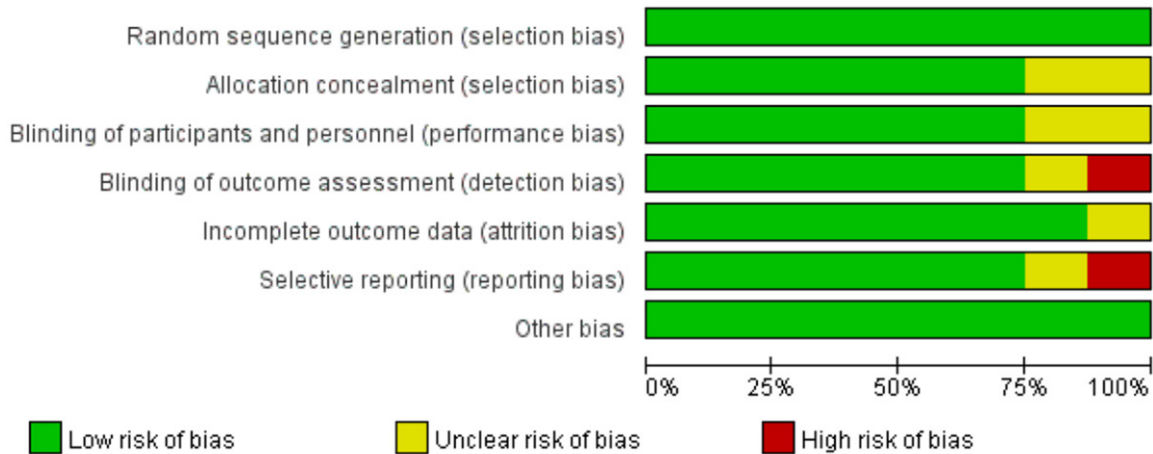


Figure 3. Summary chart of the risk bias assessment.

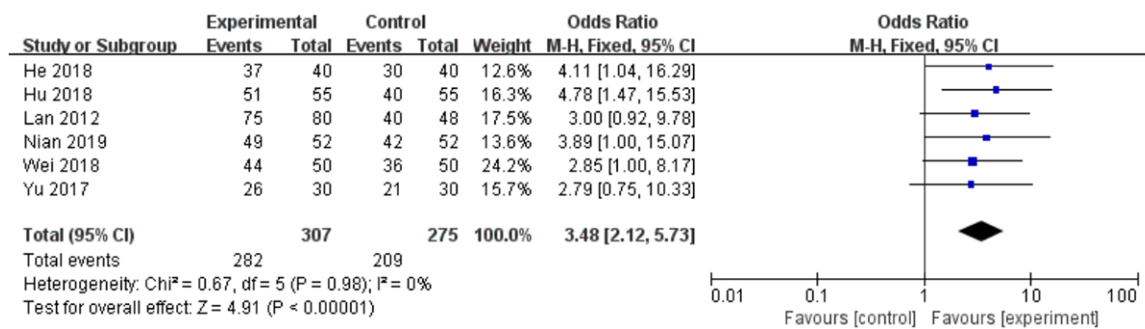


Figure 4. The comparison of total effective rate between two groups.

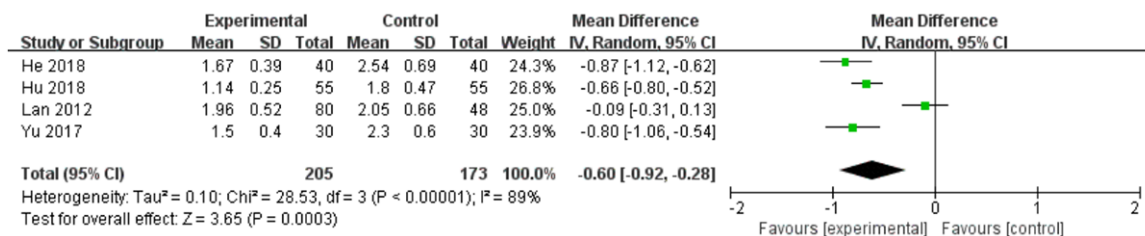


Figure 5. The comparison of 24-hour urinary protein quantification between two groups.

Serum creatinine: There were 5 articles that detected the Scr level. The heterogeneity was evaluated as $I^2 = 0\%$, so the FE model was performed. The result showed that there was a lower Scr level when the patients received combination treatment of YiQi HuoXue BuShen decoction and western medicine [OR = -39.11, 95% CI: -44.72~-33.51, $P < 0.00001$] (Figure 6).

Blood urea nitrogen: There were 6 studies that investigated the BUN level. The result obtained

by RE model ($I^2 = 88\%$) showed that the combination treatment of Yiqi Huoxue Bushen decoction and western medicine resulted in a lower BUN level compared with western medicine alone [OR = -2.51, 95% CI: -4.06~-0.95, $P = 0.002$] (Figure 7).

Cystatin C: There were 3 articles that detected the Cys-C level. The heterogeneity was evaluated as $I^2 = 48\%$, so the FE model was performed. The result showed that there was a lower Cys-C when the patients carrying on com-

Combination of Chinese and Western medicine on hypertensive nephropathy

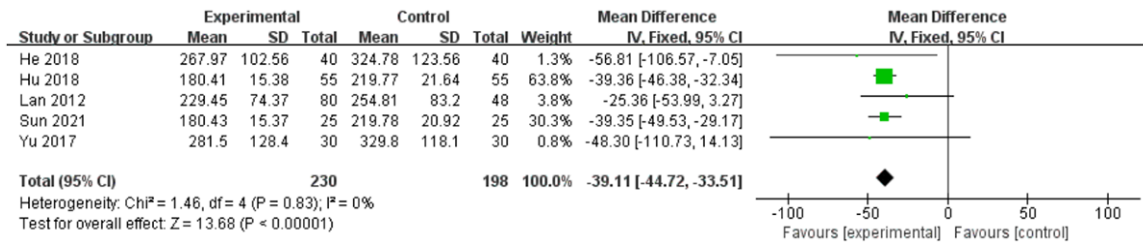


Figure 6. The comparison of serum creatinine (Scr) between two groups.

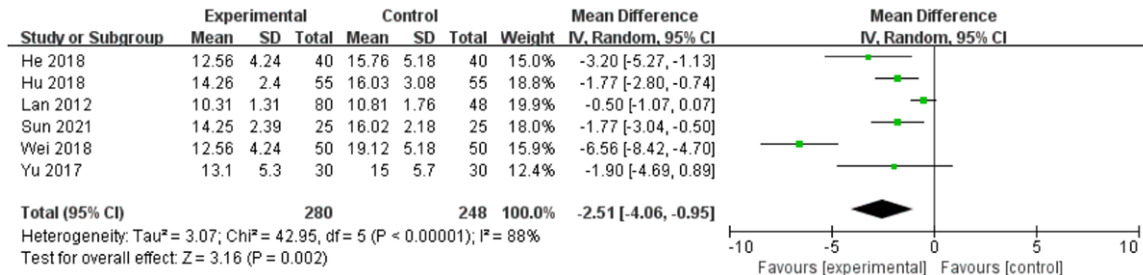


Figure 7. The comparison of blood urea nitrogen (BUN) between two groups.

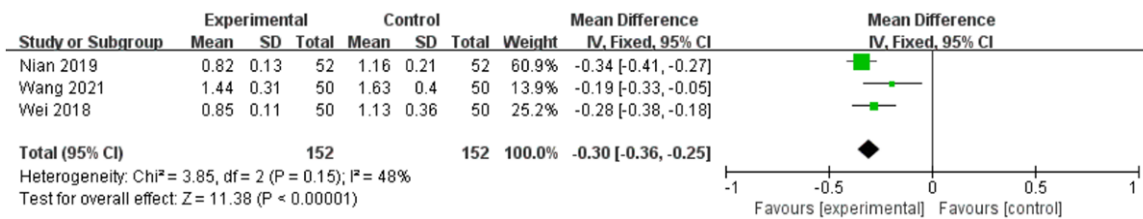


Figure 8. The comparison of cystatin C (Cys-C) between two groups.

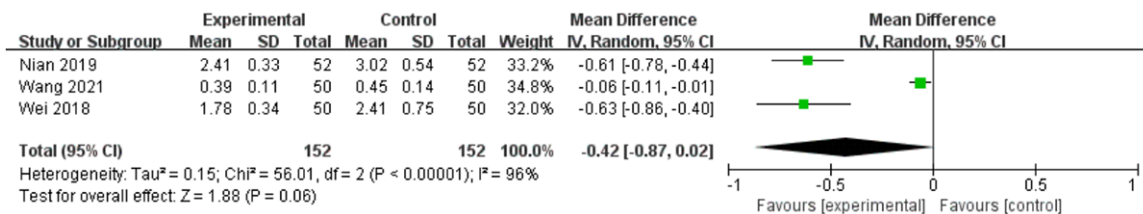


Figure 9. The comparison of Urine β 2-microglobulin between two groups.

combination treatment of Yiqi Huoxue Bushen decoction and western medicine [OR = -0.30, 95% CI: -0.36~-0.25, P < 0.00001] (Figure 8).

Urine β 2-microglobulin: As shown in Figure 9, the detection of urine β 2-microglobulin were included in 3 studies. The result obtained by RE model (I² = 96%) showed that the combination treatment of Yiqi Huoxue Bushen decoction and western medicine decrease the level of Urine β 2-microglobulin compared with western

medicine alone [OR = -0.42, 95% CI: -0.87~-0.02, P = 0.06].

Creatinine clear rate: There were 3 articles that detected the Ccr level. The heterogeneity was evaluated as I² = 0%, so the FE model was performed. The result showed that there was a higher Ccr level when the patients carrying on combination treatment of Yiqi Huoxue Bushen decoction and western medicine [OR = 3.24, 95% CI: 1.85~4.64, P < 0.00001] (Figure 10).

Combination of Chinese and Western medicine on hypertensive nephropathy

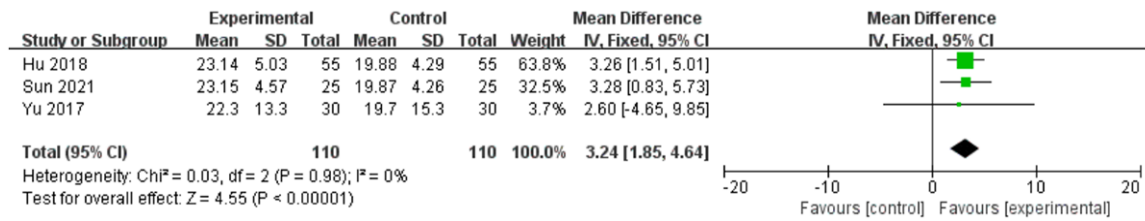


Figure 10. The comparison of creatinine clear rate (Ccr) between two groups.

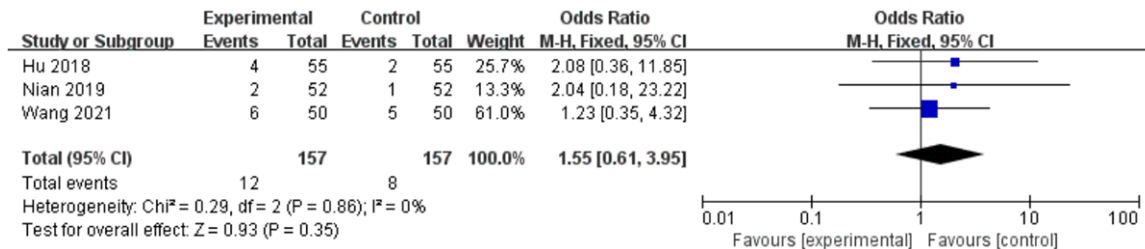


Figure 11. The comparison of adverse reaction between two groups.

Adverse reaction: In the analysis of adverse reaction, three publications were included. As shown in **Figure 11**, the heterogeneity was low ($I^2 = 0\%$), so the FE model was performed. The result showed that there was no obvious difference in the incidence of adverse reaction between two groups [$OR = 1.55$, 95% CI: 0.61~3.95, $P > 0.05$].

Publication bias

The funnel graphic of each outcome was created to assess publication bias. The dispersed distribution of included studies regarding each outcome index is asymmetrical, suggesting publication bias, which may be connected to the sample size of included research (**Figure 12**). In addition, the western medicines used in these 8 publications are not the same, including Nifedipine, Amlodipine besylate and enalapril maleate, Candesartan Cilexetil, Enalapril maleate tablets and amlodipine atorvastatin calcium tablets, Irbesartan, and Benazepril Tablets, which might also cause bias in conclusions to some extent.

Discussion

Hypertensive nephropathy is a common complication of hypertension. Currently, the pathogenesis of renal failure caused by hypertensive nephropathy has not been fully elucidated in the academic community, which may be related to metabolic product excretion disorders, acid-

base imbalance, electrolyte disorders, and so on [24]. Currently, Western medicine can only alleviate some symptoms of renal failure caused by hypertensive nephropathy, with high treatment costs and many adverse reactions [25]. Enalapril maleate is a widely used angiotensin converting enzyme inhibitor in clinical practice, while amlodipine besylate is a widely used calcium antagonist. The combination of the two can effectively control the amount of urine protein in patients, help reduce blood pressure levels, and have certain advantages in improving quality of life [26]. However, after long-term use, its efficacy shows a progressive downward trend. Therefore, it is particularly important to seek effective treatment methods to control the development of the disease.

According to traditional Chinese medicine, renal failure caused by hypertensive nephropathy belongs to the category of “dizziness, edema, and depression”. The disease is located in the kidney, and can be induced by irregular lifestyle, deficiency of the body, and invasion of external pathogens [27]. The pathogenesis can be summarized as dampness, turbidness, poisoning, spleen and kidney deficiency, etc. Therefore, traditional Chinese medicine treatment should focus on tonifying kidney yin, dredging blood vessels, and strengthening spleen [28]. In this study, on the basis of Western medicine treatment, the effect of supplementing qi, activating blood circulation, and tonifying the kidney prescription is relatively

Combination of Chinese and Western medicine on hypertensive nephropathy

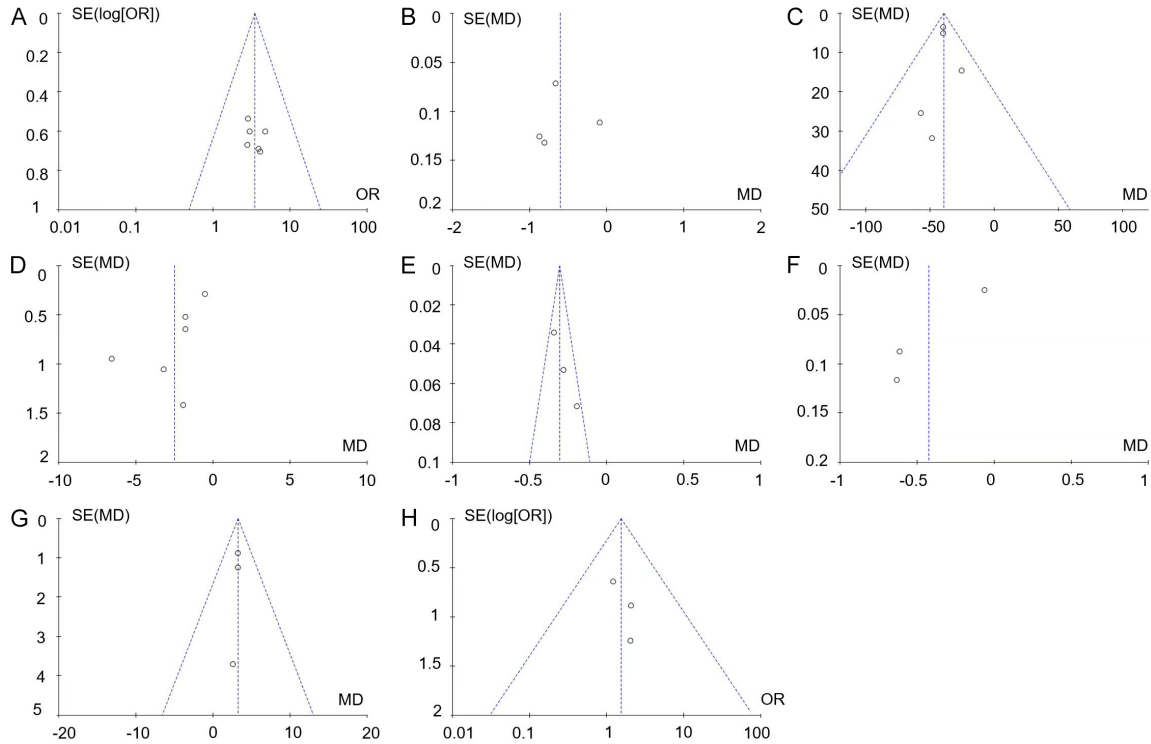


Figure 12. Assessment of publication bias. A. The total clinical effective rate; B. 24-hour urinary protein quantification; C. Serum creatinine (Scr); D. Blood urea nitrogen (BUN); E. Cystatin C (Cys-C); F. Urine β 2-microglobulin; G. Creatinine clear rate (Ccr); H. Adverse reaction.

significant. In the prescription, orange peel regulates qi, strengthens spleen, and promotes the circulation of the five internal organs [29]; *Achyranthes bidentata* can remove blood stasis and dredge meridians, diuresis and drench; *Pueraria root* relieves external heat, elevates yang, and stops diarrhea; *Fructus aurantii* can regulate qi in a broad range [11]; diuresis and detumescence can tonify qi to anti perspiration; *Salvia miltiorrhiza* can promote blood circulation and remove blood stasis, clear the heart and remove irritation; *Rehmannia glutinosa* can nourish yin and promote fluid production, clear heat and cool blood [30]; diuresis and detumescence, heat clearing and detoxification; Chinese wolfberry nourishes the liver and kidney, replenishes blood and calms the nerves; *Epimedium* can tonify the kidney and strengthen yang, dispel wind and remove dampness; *Radix Pseudostellariae* generates fluid to moisten the lungs, replenish qi and strengthen the spleen; *Licorice* can clear heat and detoxify, replenish spleen and replenish qi [31]. The combination of various drugs have the efficacy of removing dampness and blood stasis, nourishing the kidney and strengthening the spleen. Modern pharmacological studies

have shown that *Fructus Aurantii* can effectively relax vascular smooth muscle, promote peripheral arteriolar relaxation, and help reduce peripheral blood flow resistance [12]; *Salvia miltiorrhiza* can play a good role in improving the internal environment of renal microcirculation and enhancing fibrinolytic activity in patients, helping to reduce blood viscosity, thereby reversing or delaying renal function damage; *Rehmannia glutinosa* can effectively enhance the patient's immune system, increase blood perfusion, improve lipid metabolism and protein levels, and effectively alleviate glomerular oxygen free radical damage [32].

In this study, 8 RCTs involving 732 patients were included after screening. Comparing with Western medicine alone, *YiQi HuoXue BuShen* decoction combined with Western medicine enhanced the clinical effect, reduced 24-hour urine protein content, serum creatinine (Scr), blood urea nitrogen (BUN), cystatin C (Cys-C), Urine β 2-microglobulin, and elevated creatinine clear rate (Ccr). It shows that *Yiqi Huoxue Bushen* Formula combined with western medicine can effectively delay and alleviate renal function damage while providing basic treat-

Combination of Chinese and Western medicine on hypertensive nephropathy

ment for hypertensive nephropathy and adding no extra adverse reactions, making it safe and reliable. It is consistent with the results in Yu et al [23]. Yiqi Huoxue Bushen decoction can improve blood microcirculation in patients, increase blood flow, inhibit free radical production, and promote kidney recovery [20]. Western medicine can relax vascular smooth muscle by inhibiting Ca^{2+} influx, thereby expanding blood vessels, increasing blood flow, and expanding peripheral arterioles, alleviating peripheral vascular resistance, reducing heart load, and lowering blood pressure, thereby reducing the exudation of protein in the blood, reducing damage to the renal filter system, and assisting traditional Chinese medicine in achieving better efficacy [27].

Although this study has developed tight inclusion and exclusion criteria, it still has certain limitations: (1) There are currently few RCTs for the combination treatment of Yiqi Huoxue Bushen decoction on hypertensive nephropathy, and the sample size is small, which lowers the test efficiency; (2) The quality of methodology included in the study varies, and there is a certain bias in random method, blinding method, etc.; (3) There are few reports on the safety of Yiqi Huoxue Bushen decoction in the included studies; (4) Different Western medicines used in the included articles may lead to greater heterogeneity in the analysis. The findings need to be supported by additional research by gathering more studies. Confounding influences can be detected and controlled using a more stringent multi-center, randomized, double-blind trial procedure to raise the reliability of the study.

Acknowledgements

This work was supported by 2023 Zhejiang Provincial Science and Technology Program of Traditional Chinese Medicine (2023ZF057) and 2021 Zhejiang Basic Public Welfare Research Plan Project (LQ21H050001).

Disclosure of conflict of interest

None.

Address correspondence to: Ping Lv, Department of Traditional Chinese Medicine, Taizhou First People's Hospital, No. 218, Hengjie Road, Huangyan District, Taizhou 318020, Zhejiang, China. Tel: +86-0576-84016757; E-mail: lvpingclub@126.com

References

- [1] Lucero CM, Prieto-Villalobos J, Marambio-Ruiz L, Balmazabal J, Alvear TF, Vega M, Barra P, Retamal MA, Orellana JA and Gómez GI. Hypertensive nephropathy: unveiling the possible involvement of hemichannels and pannexons. *Int J Mol Sci* 2022; 23: 15936.
- [2] Chen Z, Peng Y, Yang F, Qiang X, Chen Y, Chen Y, Cao L, Liu C and Zhang J. Traditional Chinese medicine injections combined with antihypertensive drugs for hypertensive nephropathy: a network meta-analysis. *Front Pharmacol* 2021; 12: 740821.
- [3] Carriazo S, Vanessa Perez-Gomez M and Ortiz A. Hypertensive nephropathy: a major roadblock hindering the advance of precision nephrology. *Clin Kidney J* 2020; 13: 504-509.
- [4] Mennuni S, Rubattu S, Pierelli G, Tocci G, Fofi C and Volpe M. Hypertension and kidneys: unraveling complex molecular mechanisms underlying hypertensive renal damage. *J Hum Hypertens* 2014; 28: 74-79.
- [5] Jialiken D, Qian L, Ren S, Wu L, Xu J and Zou C. Combined therapy of hypertensive nephropathy with ginkgo leaf extract and dipyridamole injection and antihypertensive drugs: a systematic review and meta-analysis. *Medicine (Baltimore)* 2021; 100: e25852.
- [6] Cavalcante PAM, Alenina N, Budu A, Freitas-Lima LC, Alves-Silva T, Agudelo JSH, Qadri F, Camara NOS, Bader M and Araújo RC. Nephropathy in hypertensive animals is linked to M2 macrophages and increased expression of the YM1/Chi3l3 protein. *Mediators Inflamm* 2019; 2019: 9086758.
- [7] Mocker A, Hilgers KF, Cordasic N, Wachtveitl R, Menendez-Castro C, Woelfle J, Hartner A and Fahlbusch FB. Renal chemerin expression is induced in models of hypertensive nephropathy and glomerulonephritis and correlates with markers of inflammation and fibrosis. *Int J Mol Sci* 2019; 20: 6240.
- [8] Wang Z, Zhai J, Zhang T, He L, Ma S, Zuo Q, Zhang G, Wang Y and Guo Y. Canagliflozin ameliorates epithelial-mesenchymal transition in high-salt diet-induced hypertensive renal injury through restoration of sirtuin 3 expression and the reduction of oxidative stress. *Biochem Biophys Res Commun* 2023; 653: 53-61.
- [9] Vettoretti S, Caldiroli L, Zanoni F, Azzini V, Villarini A, Meazza R and Messa P. Patients with hypertensive nephropathy and chronic kidney disease might not benefit from strict blood pressure control. *Kidney Blood Press Res* 2018; 43: 1706-1715.
- [10] Hung MH, Huang CC, Chung CM and Chen JW. 24-h ambulatory blood pressure variability and hypertensive nephropathy in Han Chinese hy-

Combination of Chinese and Western medicine on hypertensive nephropathy

- pertensive patients. *J Clin Hypertens (Greenwich)* 2021; 23: 281-288.
- [11] Xu Z, Qian L, Niu R, Yang Y, Liu C and Lin X. Efficacy of Huangqi injection in the treatment of hypertensive nephropathy: a systematic review and meta-analysis. *Front Med (Lausanne)* 2022; 9: 838256.
- [12] Du H, Xiao G, Xue Z, Li Z, He S, Du X, Zhou Z, Cao L, Wang Y, Yang J, Wang X and Zhu Y. QiShenYiQi ameliorates salt-induced hypertensive nephropathy by balancing ADRA1D and SIK1 expression in Dahl salt-sensitive rats. *Biomed Pharmacother* 2021; 141: 111941.
- [13] Guo F, Zhang W, Su J, Xu H and Yang H. Prediction of drug positioning for Quan-Du-Zhong capsules against hypertensive nephropathy based on the robustness of disease network. *Front Pharmacol* 2019; 10: 49.
- [14] Xie M, Deng L, Yu Y, Xie X and Zhang M. The effects of Bushen Yiqi Huoxue prescription and its disassembled prescriptions on a diabetic retinopathy model in Sprague Dawley rats. *Biomed Pharmacother* 2021; 133: 110920.
- [15] Li Z, Meng L, Qin Y, Xiao L and Gao B. Effect of Yiqi Huoxue Fang on the life quality of hypertension patients with chronic kidney disease. *J Tradit Chin Med* 2016; 44: 5.
- [16] He L and Che Q. Effects of Yiqi Huoxue Bushen decoction combined with Nifedipine on urinary protein, Scr, BUN and clinical efficacy in patients with renal failure due to hypertensive nephropathy. *Medical Innovation of China* 2018; 15: 4.
- [17] Hu X. Clinical observation on the effect of Yiqi Huoxue Bushen decoction combined with western medicine in treating renal failure caused by hypertensive nephropathy. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 2018; 27: 4.
- [18] Lan C. Yiqi Bushen decoction combined with western medicine in the treatment of 80 cases of renal proteinuria. *Shaanxi Traditional Chinese Medicine* 2012; 1583-1584.
- [19] Nian S, Feng L and Zhao Y. Effect of Yiqi Huoxue Bushen Granule on CysC, IMD, FGF23, APN, ET-1, CGRP in peripheral blood of patients with early renal injury in essential hypertension. *Journal of Chinese Medicinal Materials* 2019; 42: 4.
- [20] Sun H. Observation on the therapeutic effect of Yiqi Huoxue Bushen recipe combined with conventional western medicine on renal failure caused by hypertensive nephropathy. *Practical Clinical Practice of Integrating Traditional Chinese and Western Medicine* 2021; 21: 2.
- [21] Wang X, Zhao L and Huang Y. Protective effect of Yiqi Huoxue Bushen formula combined with irbesartan on renal function in patients with hypertensive renal damage. *Shaanxi Traditional Chinese Medicine* 2021; 42: 4.
- [22] Wei X. Clinical observation on the therapeutic effect of Bushen Yiqi Huoxue recipe combined with benazepril tablets on hypertensive nephropathy and its effect on renal function. *China Traditional Chinese Medicine Technology* 2018; 25: 2.
- [23] Yu L, Lu M, Dai Y and Fang J. Observation on the therapeutic effect of Yiqi Huoxue Bushen recipe combined with Nifedipine on renal failure caused by hypertensive nephropathy. *Introduction to Traditional Chinese Medicine* 2017; 23: 3.
- [24] Wu L, Liu M and Fang Z. Combined therapy of hypertensive nephropathy with breviscapine injection and antihypertensive drugs: a systematic review and a meta-analysis. *Evid Based Complement Alternat Med* 2018; 2018: 2958717.
- [25] Xu Q, Shen Y, Zhao J and Shen J. Salvianolate injection for hypertensive nephropathy patients who were using valsartan: a systematic review and meta-analysis. *Front Pharmacol* 2023; 14: 1119150.
- [26] Wang Z, Wang S, Zhao J, Yu C, Hu Y, Tu Y, Yang Z, Zheng J, Wang Y and Gao Y. Naringenin ameliorates renovascular hypertensive renal damage by normalizing the balance of renin-angiotensin system components in rats. *Int J Med Sci* 2019; 16: 644-653.
- [27] Dong Z, Dai H, Feng Z, Liu W, Gao Y, Liu F, Zhang Z, Zhang N, Dong X, Zhao Q, Zhou X, Du J and Liu B. Mechanism of herbal medicine on hypertensive nephropathy (Review). *Mol Med Rep* 2021; 23: 234.
- [28] Fu H, Hou W, Zhang Y and Hu X. Alprostadil for hypertensive nephropathy: a systematic review and meta-analysis of randomized controlled trials. *PLoS One* 2022; 17: e0269111.
- [29] Li M, Lie B, Duan T, Chen D, Xia T, Xie H, Lin G, Yang J and Li Z. The protective effect of Bajijiasu on the treatment of hypertensive nephropathy in rats. *Curr Mol Pharmacol* 2022; 16: 751-758.
- [30] Zheng YW, Wu LF, Zhao YH, Wu LH and Li J. Network meta-analysis of Huoxue Huayu Chinese medicine injections on hypertensive nephropathy. *Zhongguo Zhong Yao Za Zhi* 2020; 45: 4997-5007.
- [31] Huan JM, Su WG, Li W, Gao C, Zhou P, Fu CS, Wang XF, Wang YM and Wang YF. Summarizing the effective herbs for the treatment of hypertensive nephropathy by complex network and machine learning. *Evid Based Complement Alternat Med* 2021; 2021: 5590743.
- [32] Yang X, Zhou B, Zhou L, Cui L, Zeng J, Wang S, Shi W, Zhang Y, Luo X, Xu C, Xue Y, Chen H, Chen S, Wang G, Guo L, Jose PA, Wilcox CS, Wu S, Wu G and Zeng C. Development and validation of prediction models for hypertensive nephropathy, the PANDORA study. *Front Cardiovasc Med* 2022; 9: 794768.