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Study on the Intervention of Renal Yang Deficiency Hypertension by Combined External Therapies of Traditional Chinese Medicine Through Regulating the RASS System

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Abstract: *Objective*: This study explores the mechanism and clinical efficacy of combined external therapies of traditional Chinese medicine (such as moxibustion, acupoint application, etc.) in intervening renal Yang deficiency hypertension through regulating the renin-angiotensin-aldosterone system (RASS). *Methods*: Sixty-one patients with renal Yang deficiency hypertension admitted to the hospital were selected as the study subjects. They were divided into a Western medicine combined with external therapies of traditional Chinese medicine group (n=30) and a conventional Western medicine treatment group (n=31) based on a random number table method. The enrollment information, blood pressure changes, and differences in aldosterone, angiotensin II, and renin activity during follow-up were compared between the two groups. *Results*: There were no statistically significant differences in gender, past history, pre-study medication, hypertension grading, aldosterone, angiotensin II, renin activity levels, and blood pressure between the two groups at baseline ($P > 0.05$). Aldosterone, angiotensin II, and renin activity levels were significantly reduced in both groups after treatment compared to pre-treatment levels. Moreover, the aldosterone, angiotensin II, and renin activity levels in the Western medicine combined with external therapies of traditional Chinese medicine group were significantly lower than those in the conventional Western medicine treatment group, with statistically significant differences ($P < 0.05$). *Conclusion*: Western medicine combined with external therapies of traditional Chinese medicine may regulate the RASS system through multiple targets, restoring renal Yang Qi transformation function and providing a new strategy for the integrated treatment of renal Yang deficiency hypertension with Chinese and Western medicine.

Keywords: Combined external therapies of traditional Chinese medicine; RASS system; Renal Yang deficiency hypertension

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1. Introduction

Hypertension is one of the most common chronic diseases worldwide, with a complex pathogenesis involving imbalances in neuroendocrine, vasoactive substances, and renal regulatory systems [1]. The renin-angiotensin-aldosterone system (RASS), as a core pathway for blood pressure regulation, can lead to vasoconstriction, water-sodium retention, and oxidative stress responses when overactivated, further exacerbating the progression of hypertension [2]. In recent years, traditional Chinese medicine theories have demonstrated unique advantages in the prevention and treatment of hypertension, particularly the potential association between "renal Yang deficiency" as a critical pathogenesis of hypertension and dysfunction of the RASS system. Renal Yang, the root of Yang Qi in the body, is responsible for warmth and Qi transformation. Deficiency of renal Yang leads to abnormal water metabolism, which can trigger internal cold accumulation, blood vessel constriction, and ultimately elevated blood pressure [3]. Currently, Western medicine interventions targeting the RASS system rely mainly on drugs such as angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB), but long-term use may cause adverse reactions such as dry cough and hyperkalemia [4]. Traditional Chinese medicine therapies emphasize holistic regulation and may regulate the RASS system through multiple targets, improving clinical symptoms and long-term outcomes for patients with renal Yang deficiency hypertension. Additionally, external therapies (such as moxibustion, acupoint application, auricular acupressure, etc.) can stimulate specific meridians and acupoints, regulating Qi and blood circulation and synergistically enhancing the efficacy of internally administered Chinese medicine [5, 6]. However, research on the mechanism of combined external therapies of traditional Chinese medicine in regulating the RASS system to intervene in renal Yang deficiency hypertension remains scarce and urgently needs further exploration. This study intends to combine traditional Chinese medicine syndrome differentiation and treatment with modern biological techniques to investigate the regulatory effect of Western medicine combined with external therapies of traditional Chinese medicine on key RASS factors in patients with renal yang deficiency hypertension, providing a new theoretical basis and clinical strategy for the integrated prevention and treatment of hypertension with Chinese and Western medicine.

2. Research objects and methods

2.1. Research objects

Sixty-one patients with hypertension due to kidney Yang deficiency treated in the hospital are selected as the research subjects, including 31 male patients and 30 female patients.

The inclusion criteria of the study are:

(1) Meet the diagnostic criteria for hypertension, classified as grade II hypertension

(2) Meet the dialectical standards of traditional Chinese medicine syndromes, with the syndrome type being kidney Yang deficiency, referring to the "Guiding Principles for Clinical Research of New Chinese Medicines"

(3) Aged 18–65 years old; comply with ethical principles and sign an informed consent form

(4) All research subjects and their families have signed informed consent forms

The exclusion criteria included:

(1) Patients with hypertensive emergencies or secondary hypertension

(2) Those with severe cardiac insufficiency (cardiac function grade III or above), abnormal liver function (ALT > 40 U/L, AST > 40 U/L, TBIL > 21 μmol/L), abnormal renal function (Cr > 133 μmol/L, BUN > 7.1 mmol/L), tumors, and other severe diseases

(3) Women during pregnancy or lactation
(4) Disabled or mentally abnormal individuals according to legal provisions
(5) Those participating in other clinical trials
(6) Those with swallowing dysfunction
(7) Those with allergic constitution or multiple drug allergies
(8) Those with ruptured skin, induration at treatment acupoints, or skin allergies to the test drugs
(9) Those in critical condition

2.2. Methods

2.2.1. Experimental grouping

Sixty-one subjects are divided into a Western medicine combined with external treatment of traditional Chinese medicine group and a conventional Western medicine treatment group according to the random number table method, with 30 cases in the Western medicine combined with external treatment of traditional Chinese medicine group and 31 cases in the conventional Western medicine treatment group.

The conventional Western medicine treatment group received standard Western medicine treatment for a period of 1 month, specifically using standard antihypertensive drugs (CCB antihypertensive drugs + diuretics).

The traditional Chinese medicine combined with external treatment group received auricular acupuncture, auricular point pressing with beans, and acupoint application as external treatments combined with antihypertensive drugs for a treatment period of 1 month. Auricular acupuncture involved the application of moxibustion to the ears, Baihui, and Fengchi acupoints, with one moxibustion stick used per acupoint for 20 minutes. Auricular point pressing with beans used "Wang Bu Liu Xing" seeds as the pressing material, selecting acupoints such as Jiangya groove, Shenmen, Jiaogan, cortical subregion, heart, brain, spleen, and stomach, which are pressed on one side of the ear. Patients are instructed to press four times a day, 20 presses each time, alternating between the two ears, changing every two days, and continuing for four weeks. Acupoint application involved the use of powdered Wu Zhu Yu and Rou Gui mixed with vinegar and applied to the Yongquan acupoint. The treatment course is four weeks.

2.2.2. Statistical analysis of patient information

Patient information, including gender, past medical history, medication use before the study, and hypertension grading, is collected and analyzed for both groups. Additionally, 5 mL of fasting elbow venous blood is collected, centrifuged at 3500 r/min for 10 minutes to separate the serum, and radioimmunoassay is used to detect aldosterone (ALD), angiotensin II (AngII), and plasma renin activity (PRA).

2.2.3. Blood pressure measurement and analysis

Blood pressure levels are measured using a blood pressure monitor after patients rested for more than 5 minutes before treatment, and at 1, 2, 3, and 4 weeks after treatment initiation.

2.2.4. Traditional Chinese medicine syndrome scoring

Based on the relevant content of vertigo in the "Guiding Principles for Clinical Research of New Chinese Medicines (Trial Implementation)", the traditional Chinese medicine syndrome grading scoring method is used to evaluate five main syndromes: headache and dizziness, cold sensation in limbs or back, frequent or involuntary urination at night, fatigue and laziness to speak, and shortness of breath and weakness. These syndromes are scored

on a scale of 0 to 3 (none, mild, moderate, and severe), with higher scores indicating more severe conditions. The total score ranged from 0 to 15.

2.2.5. Statistical analysis of follow-up information for two groups of patients

Blood samples of 5 mL are collected from the patients in both groups after fasting, taken from the elbow vein. The samples are centrifuged at 3500 r/min for 10 minutes to separate the serum. Radioimmunoassay is used to detect aldosterone (Aldosterone, ALD), angiotensin II (Angiotensin II, AngII), and plasma renin activity (PRA).

2.3. Statistical analysis

All data in this study are processed using SPSS 20.0 statistical analysis software (IBM Corporation, USA). Measurement data are expressed as "mean ± standard deviation" (±s), and independent sample t-tests are used for comparisons between groups. Count data are expressed as percentages (%), and chi-square ($\chi 2$) analysis is used for comparisons between groups. A *P*-value less than 0.05 indicated a statistically significant difference.

3. Results

3.1. Statistical analysis of enrollment information for two groups of patients

There were no statistically significant differences in gender, past medical history, pre-study medication use, hypertension grading, aldosterone, angiotensin II, and plasma renin activity levels between the two groups ($P > 0.05$), as shown in **Table 1**.

Table 1. Statistical analysis of enrollment information for two groups of patients ($\bar{x}$±s)

Grouping	TCM + external therapy (*n*=30)	Conventional Western medicine (*n*=31)	t/χ^2 value	*P* value
Gender (Male/Female)	13/17	18/13	0.111	0.930
Past medical history			1.200	0.356
Hypertension	28(93.34)	29(93.54)		
Hypertension, Hyperlipidemia, Diabetes	1(3.33)	1(3.23)		
Hypertension, Hyperlipidemia	1(3.33)	1(3.23)		
Pre-study medication			0.382	0.298
CCB	23(76.67)	20(64.52)		
ARB	0(0.00)	3(9.68)		
CCB + ARB	7(23.33)	6(19.35)		
None	0(0.00)	2(6.45)		
Hypertension grade			0.535	0.687
Grade I	16(53.33)	16(51.61)		
Grade II	14(46.67)	15(48.39)		
Aldosterone (pg/mg)	137.84 ± 10.59	115.94 ± 7.95	0.790	0.436
Angiotensin II (pg/mg)	48.99 ± 2.08	52.00 ± 8.41	0.669	0.509
Renin (μIU/mL)	58.93 ± 1.67	21.65 ± 2.48	1.248	0.222

3.2. Blood pressure measurement analysis for two groups of patients

There were no statistically significant differences in blood pressure measurements between the two groups ($P > 0.05$), as shown in **Table 2**.

Table 2. Blood pressure measurement analysis for two groups of patients ($\bar{x}\pm s$)

Time point	TCM + external therapy (n=30) (mmHg, Systolic/Diastolic)	Conventional Western medicine (n=31) (mmHg, Systolic/Diastolic)	t/χ^2 value	P value
First	136.10/83.60	143.03/88.13	4.775	0.131
Second	139.70/86.90	136.84/84.87	5.892	0.107
Third	141.10/88.20	134.20/82.50	10.500	0.060
Fourth	136.50/85.50	134.40/82.40	5.200	0.121

3.3. Comparison of TCM syndrome scores between two groups of patients

The external treatment group of traditional Chinese medicine scored significantly better than the control group in terms of TCM syndromes such as headache and dizziness, cold extremities or back chill, frequent or involuntary urination at night, fatigue and laziness, shortness of breath, and lack of strength ($P < 0.05$). The difference was statistically significant, as shown in **Table 3**.

Table 3. Comparison of TCM syndrome scores between two groups of patients [$\bar{x}\pm s$, points]

Group	Headache/ Dizziness (score)	Cold limbs/ Back Sensation (score)	Frequent nocturia/ Incontinence (score)	Lassitude with reluctance to speak (score)	Shortness of breath/ Fatigue (score)
TCM external therapy (n=30)	1.35 ± 0.66	1.20 ± 0.90	1.88 ± 0.53	1.99 ± 0.75	1.13 ± 0.92
Western medicine (n=31)	2.12 ± 0.71	2.55 ± 0.75	2.64 ± 0.69	2.46 ± 0.80	2.03 ± 1.01
t	4.326	3.127	5.220	2.542	3.875
P	0.000	0.002	0.000	0.013	0.000

3.4. Statistical analysis of follow-up information for two groups of patients

The levels of aldosterone, angiotensin II, and plasma renin activity in both groups were significantly lower than before treatment. Moreover, the levels of aldosterone, angiotensin II, and plasma renin activity in the integrated traditional Chinese and external treatment group were significantly lower than those in the conventional Western medicine treatment group. The differences were statistically significant ($P < 0.05$), as shown in **Table 4**.

Table 4. Statistical analysis of follow-up information for two groups of patients ($\bar{x}\pm s$)

Group	TCM + External therapy (n=30)	Conventional Western medicine (n=31)	t/χ^2-value	P-value
Aldosterone (pg/mg)	100.28 ± 4.35	116.92 ± 5.25	12.530	0.003
Angiotensin II (pg/mg)	40.15 ± 1.76	47.28 ± 2.91	10.972	0.001
Renin (μIU/mL)	27.36 ± 2.99	32.66 ± 4.52	13.716	0.003

4. Discussion

This study observed the intervention effect of combined traditional Chinese medicine (TCM) and external therapies (including auricular point pressing with beans, moxibustion, and acupoint application) on patients with kidney-Yang deficiency hypertension. The results showed that after treatment, patients' levels of aldosterone (ALD), angiotensin II (AngII), and plasma renin activity (PRA) were significantly reduced, while blood pressure (both systolic and diastolic) was effectively controlled. These findings suggest that the combined TCM and external therapies may improve the pathological state of kidney-Yang deficiency hypertension and exert antihypertensive effects by regulating the overactivation of the renin-angiotensin-aldosterone system (RASS).

In the theory of TCM, kidney-Yang deficiency hypertension belongs to the categories of "dizziness" and "headache". Its pathogenesis is mainly attributed to kidney yang deficiency, which leads to impaired Qi transformation, internal retention of water and dampness, and subsequently, poor circulation of Qi and blood and imbalance of Yin and Yang. Modern medical research has shown that the overactivation of the RASS system is closely related to the occurrence and development of hypertension [7]. Specifically, the elevation of AngII and ALD can cause vasoconstriction, water and sodium retention, and oxidative stress reactions, further exacerbating the progression of hypertension. According to TCM theory, kidney Yang has the functions of warming, promoting, and controlling. Kidney Yang deficiency results in the loss of Qi transformation and disordered water metabolism, which highly corresponds to the water and sodium metabolism mechanism regulated by the RASS system. The results of this study indicate that the combined TCM and external therapies can reduce the levels of AngII, ALD, and PRA, suggesting that they may inhibit the abnormal activation of the RASS system by warming and nourishing kidney yang and regulating water metabolism, thereby improving hypertension.

This study found that patients' PRA, AngII, and ALD levels significantly decreased after treatment, indicating that the combined TCM and external therapies may intervene in the RASS system through the following pathways: The warming yang method in TCM (such as moxibustion on auricular points like the kidney and subcortex) may improve renal blood flow and reduce renin secretion caused by renal ischemia. External therapies in TCM (such as auricular point pressing with beans, moxibustion, and acupoint application) can stimulate specific meridians (such as the Foot Shaoyin Kidney Meridian and Du Meridian), improve microcirculation, and enhance vasodilation function. Additionally, warming and nourishing kidney Yang herbs (such as aconite and cinnamon bark) may regulate endothelial function, promote the release of nitric oxide (NO), and antagonize vasoconstriction induced by AngII, thereby synergistically lowering blood pressure [8].

Recent studies have shown that TCM has the advantage of multi-target regulation in the treatment of hypertension [9, 10]. For example, certain kidney-Yang-tonifying prescriptions (such as JinKui ShenQi Pill) have been proven to reduce AngII levels and improve endothelial function. This study further confirms that the combined TCM and external therapies can not only regulate the RASS system but also holistically improve the symptoms of kidney Yang deficiency, such as aversion to cold, soreness and weakness of waist and knees, and frequent nocturia. This reflects the advantages of "syndrome differentiation and treatment" and "holistic regulation" in TCM. Compared with pure Western medications (such as ACEI/ARB drugs), the combined TCM and external therapies focus not only on lowering blood pressure but also on restoring the body's Yin-Yang balance and reducing the side effects (such as dry cough and hyperkalemia) caused by long-term medication use. Furthermore, the non-drug characteristics of external therapies (such as moxibustion and acupoint application) make them safer for long-term interventions.

5. Conclusion

In summary, the combined TCM and external therapies may lower AngII and ALD levels and improve blood pressure and clinical symptoms in patients with kidney-Yang deficiency hypertension by inhibiting the overactivation of the RASS system. This therapeutic approach embodies the characteristic of "treating both the manifestation and root cause" in TCM and provides a new theoretical basis and practical direction for the integrated treatment of hypertension with both Western and TCM methods. Future research should focus on conducting large-sample, multi-center studies to optimize treatment regimens and promote clinical application.

Disclosure statement

The authors declare no conflict of interest.

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