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Efficacy of *Huoxue Huayu* Decoction combined with renin-angiotensin-aldosterone system inhibitors in diabetic nephropathy and its effects on oxidative stress indicators

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Abstract: Objective To investigate the clinical efficacy of *Huoxue Huayu* Decoction combined with renin-angiotensin- aldosterone system (RAAS)inhibitors in the treatment of diabetic nephropathy (DN), and to observe its impact on oxidative stress-related indicators. **Methods** Eighty DN patients admitted to Lianyungang Hospital of Chinese medicine Affiliated to Nanjing University of Chinese Medicine from June 2023 to March 2025 were selected and divided into two groups via random number table： the RAAS inhibitor group (n=40)was given basic diabetes treatment and RAAS inhibitors, and the combined group (n=40)was given *Huoxue Huayu* Decoction on top of the treatment for the RAAS inhibitor group. The following indexes were compared between the two groups, including clinical efficacy, Chinese medicine syndrome scores, renal function indicators [24-hour urinary protein quantification, urinary albumin/creatinine ratio (UACR), serum creatinine (Scr), blood urea nitrogen (BUN), glomerular filtration rate (GFR)] , and oxidative stress indicators [activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH -Px), malondialdehyde (MDA) level]. **Results** The total effective rate of the combined group was higher than that of the RAAS inhibitor group (92.50% *vs* 75.00%, χ^2=4.501, P<0.05). After treatment, the scores of primary and secondary syndromes in both groups were lower than those before treatment, and the scores in the combined group were lower than those in the RAAS inhibitor group (P<0.05). After treatment, the 24 -hour urinary protein quantification, UACR, Scr, and BUN in both groups decreased compared with pre-treatment, while GFR increased, and the combined group had lower 24-hour urinary protein quantification , UACR , Scr , and BUN , and higher GFR than the RAAS inhibitor group, with statistically significant differences (P<0.05). After treatment, the serum SOD and GSH-Px activities in both groups were higher than those before treatment, while the MDA level was lower, and the combined group had higher SOD and GSH-Px activities and lower MDA level than the RAAS inhibitor group, with statistically significant differences (P<0.05). **Conclusion** *Huoxue Huayu* Decoction combined with RAAS inhibitors has a significant clinical effect in the treatment of DN, which can effectively improve patients, renal function and reduce the level of oxidative stress.

Keywords: *Huoxue Huayu* Decoction: Renin-angiotensin-aldosterone system inhibitor; Oxidative stress; Renal function: Traditional Chinese medicine syndrome score

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Diabetic nephropathy (DN), the most common and severe microvascular complication of diabetes, has been on a continuous rise in incidence and has become the primary cause of end-stage renal disease [1]. In modern medicine, pharmacological intervention remains the main strategy for managing DN at the current stage. Inhibitors of the renin-angiotensin-aldosterone system (RAAS) are commonly used in the clinical treatment of DN. Angiotensin-converting enzyme inhibitors represented by benazepril and angiotensin II receptor antagonists represented by valsartan effectively reduce the state of intraglomerular hypertension, hyperperfusion, and hyperfiltration by inhibiting excessive RAAS activation, thereby delaying the progression of renal lesions [2-3]. However, for some patients, monotherapy fails to achieve the expected therapeutic effect. Chinese medicine categorizes DN into the realms of "edema," "kidney exhaustion," and "wasting-thirst," believing that the disease is located in the kidney, with collateral stasis running through its entire course, often involving the lung, spleen, and other zang-fu organs. The treatment should focus on promoting blood circulation to remove blood stasis and tonifying kidney qi [4]. Against this background, this study aims to investigate the clinical efficacy of a blood-activating and stasis-resolving prescription combined with RAAS inhibitors in the treatment of DN patients, and observe its effects on oxidative stress-related indicators, hoping to provide a reference for the comprehensive treatment plan of DN.

1 Materials and Methods

1.1 General Data

A total of 80 DN patients treated at Lianyungang Hospital of Chinese medicine Affiliated to Nanjing University of Chinese Medicine from June 2023 to March 2025 were prospectively enrolled. **Inclusion criteria:** (1) Conformed to the diagnostic criteria for DN [5]. (2) Differentiated as the pattern of spleen-kidney yang deficiency with blood stasis according to Chinese medicine theory, with main symptoms

including lassitude and disinclination to speak, soreness and weakness of the waist and knees, cold hands and feet, frequent nocturia or clear and profuse urine, loose stools or five-watch diarrhea, or numbness of the finger tips; secondary symptoms including pale and dark complexion, cold pain in the lower abdomen, edema, or excessive sweating; tongue and pulse manifestations: pale and swollen tongue, thin white or white slippery tongue coating, deep, thready and weak pulse. (3) Signed informed consent was provided by the patients or their family members. **Exclusion criteria:** (1) Renal diseases caused by other etiologies; (2) Complicated with severe organ diseases; (3) Hypersensitivity to the study drugs; (4) Complicated with malignant tumors. The patients were divided into the RAAS inhibition group (40 cases, treated with basic diabetes treatment plus RAAS inhibitors) and the combination group (40 cases, treated with blood-activating and stasis-resolving prescription on the basis of the RAAS inhibition group) using a random number table method. There were no statistically significant differences in general data between the two groups ($P > 0.05$), indicating comparability. See **Table 1**.

Tab.1 Comparison of general data between the two groups（n=40)

Group	Gender (n)		Age (years, $\bar{x}\pm s$)	Duration of diabetes (years, $\bar{x}\pm s$)	Postprandial blood glucose on admission (mmol/L, $\bar{x}\pm s$)
	Male	Female			
Combination group	22	18	56.84±7.22	7.58±1.21	15.03±3.12
RAAS inhibition group	24	16	57.18±7.37	7.82±1.52	14.68±3.16
χ^2/t value	0.205		0.208	0.781	0.498
P value	0.651		0.835	0.437	0.620

1.2 Methods

Both groups received basic diabetes management measures, including dietary control, moderate exercise, blood glucose monitoring, and effective blood glucose regulation. Patients in the RAAS inhibition group were treated with RAAS inhibitors: Valsartan [Tian Da Pharmaceutical (Zhuhai) Co., Ltd., National Medicine Approval Number H20030777], 80 mg once daily; or Benazepril [Shanghai Xinya Pharmaceutical Minhang Co., Ltd., National Medicine Approval Number H20044840], 10 mg once daily. The dosage was adjusted reasonably based on the patient's blood pressure status and drug tolerance to ensure treatment safety and efficacy. Patients in the combination group received the blood-activating and stasis-resolving prescription on top of the RAAS inhibition group's treatment. The prescription composition was as follows: Danshen (Salvia miltiorrhiza) 30 g, Chuanxiong (Ligusticum chuanxiong) 15 g, Taoren (Prunus persica) 12 g, Honghua (Carthamus tinctorius) 12 g, Chishao (Paeonia lactiflora) 15 g, Danggui (Angelica sinensis) 15 g, Yimucao (Leonurus japonicus) 30 g, Dilong (Pheretima aspergillum) 12 g. Prepared using traditional Chinese medicine decoction methods, 1 dose was decocted daily to obtain 400 mL of medicinal liquid, which was administered warm in two divided doses (morning and evening). The treatment course for both groups was 12 weeks.

1.3 Observation indicators

(1)Clinical efficacy

① Marked improvement: Serum creatinine (Scr) decreased by ≥15%, 24-hour urinary protein quantitation decreased by ≥30%, glomerular filtration rate (GFR) increased by ≥10%, and Chinese medicine syndrome score reduced by ≥70%.

② Improvement: Scr decreased by 5%–15%, 24-hour urinary protein quantitation decreased by 15%–30%, GFR increased by 5%–10%, and Chinese medicine syndrome score reduced by 30%–70%.

③ No improvement or deterioration: Failed to meet the above improvement criteria or the condition worsened.

(2)Chinese medicine syndrome score [6]

Before and after treatment, primary and secondary symptoms were scored according to severity. Primary symptoms: 0 points for no symptoms, 2 points for mild, 4 points for moderate, 6 points for severe. Secondary symptoms: 0 points for no symptoms, 1 point for mild, 2 points for moderate, 3 points for severe.

(3)Renal function indicators

24-hour urinary protein quantitation, urinary albumin/creatinine ratio (UACR), Scr, blood urea nitrogen (BUN), and GFR were measured before and after treatment.

(4)Oxidative stress indicators

Fasting venous blood samples were collected before and after treatment. The activities of serum superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), as well as the level of malondialdehyde (MDA), were detected using enzyme-linked immunosorbent assay (ELISA).

(5)Adverse reactions

The occurrence of adverse reactions in both groups was recorded.

1.4 Statistical Analysis

Data were analyzed using SPSS 27.0 software. Measurement data with normal distribution are expressed as $\bar{x}\pm s$, and comparisons were performed using paired t-test and independent samples t-test. Enumeration data are expressed as n (%), and comparisons were performed using $\chi 2$ test. A P value < 0.05 was considered statistically significant.

2 Results

2.1 Comparison of Clinical Efficacy Between the Two Groups

The total effective rate of the combination group was significantly higher than that of the RAAS inhibition group ($P < 0.05$). See **Table 2**.

2.2 Comparison of Chinese medicine Syndrome Scores Between the Two Groups

After treatment, the scores of primary and secondary symptoms in both groups were significantly lower than those before treatment, and the scores in the combination group were lower than those in the RAAS inhibition group ($P < 0.05$). See **Table 3**.

2.3 Comparison of Renal Function Indices Between the Two Groups

After treatment, the 24-hour urinary protein quantification, UACR, Scr and BUN in both groups were decreased compared with those before treatment, while GFR was increased ($P < 0.05$); moreover, the 24-hour urinary protein quantification, UACR, Scr and BUN in the combination group were lower than those in the RAAS inhibition group, and GFR was higher than that in the RAAS inhibition group ($P < 0.05$). See **Table 4**.

2.4 Comparison of Oxidative Stress Indices Between the Two Groups

After treatment, the serum SOD and GSH-Px levels in both groups were increased compared with those before treatment, while the MDA level was decreased ($P < 0.05$); additionally, the SOD and GSH-Px levels in the combination group were higher than those in the RAAS inhibition group, and the MDA level was lower than that in the RAAS inhibition group ($P < 0.05$). See **Table 5**.

2.5 Comparison of Adverse Reactions Between the Two Groups

No severe adverse reactions occurred in either group during the treatment period.

Tab.2 Comparison of clinical efficacy between the two groups [case(%)]

Group	*n*	Marked improvement	Improvement	No improvement	Total effective
Combination group	40	18 (45.00)	19 (47.50)	3 (7.50)	37 (92.50)
RAAS inhibition group	40	8 (20.00)	22 (55.00)	10 (25.00)	30 (75.00)
χ^2 value					4.501
P value					0.034

Tab.3 Comparison of Chinese medicine syndrome scores between the two groups (point, $\bar{x}\pm s$)

Group	*n*	Primary symptoms		Secondary symptoms	
		Before Treatment	After Treatment	Before Treatment	After Treatment
Combination group	40	31.40±1.28	19.20±2.45[a]	4.12±0.89	2.46±0.84[a]
RAAS inhibition group	40	31.45±1.24	23.40±2.48[a]	4.14±0.86	3.10±0.87[a]
t value		0.177	7.620	0.102	3.347
P value		0.860	<0.001	0.919	0.001

Note: Compared with the same group before treatment, [a]$P < 0.05$.

Tab.4 Comparison of renal function indexes between the two groups (n=40,$\bar{x}\pm s$)

Group	24-hour Urinary Protein (g)		UACR（mg/g）		Scr（μmol/L）		BUN（mmol/L）		GFR（mL/min）	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Combination group	2.35±0.48	0.98±0.21[a]	1 256.32±156.78	668.45±89.32[a]	135.24±18.76	98.76±12.34[a]	8.95±1.23	6.23±0.85[a]	52.34±6.57	68.56±7.89[a]
RAAS inhibition group	2.38±0.51	1.56±0.32[a]	1 262.45±162.34	895.67±112.45[a]	136.57±19.23	115.67±15.43[a]	9.02±1.18	7.56±1.02[a]	51.89±6.72	58.67±7.23[a]
t value	0.271	9.584	0.172	10.007	0.313	5.413	0.260	6.335	0.303	5.845
P value	0.787	<0.001	0.864	<0.001	0.755	<0.001	0.800	<0.001	0.763	<0.001

Note: Compared with the same group before treatment, [a]$P < 0.05$.

Tab.5 Comparison of oxidative stress indexes between the two groups (n=40, $\bar{x}\pm s$)

Group	SOD（U/mL）		GSH-Px（U/mL）		MDA（nmol/mL）	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Combination group	85.67±10.23	145.67±15.43[a]	120.34±15.67	185.67±20.34a	4.89±0.54	2.13±0.32[a]
RAAS inhibition group	86.23±9.87	110.34±12.56[a]	121.02±16.23	150.23±18.76a	4.95±0.62	3.25±0.45[a]
t value	0.249	11.231	0.191	8.100	0.462	12.828
P value	0.804	<0.001	0.849	<0.001	0.646	<0.001

Note: Compared with the same group before treatment, [a]$P < 0.05$.

3 Discussion

DN has a complex pathogenesis involving multiple aspects such as glucose metabolism disorder, oxidative stress, inflammatory response, and excessive activation of the RAAS [7-8]. As commonly used drugs in DN treatment, RAAS inhibitors mainly inhibit the production of angiotensin II, thereby dilating efferent arterioles, effectively reducing intraglomerular pressure, decreasing proteinuria, and delaying renal fibrosis progression. However, clinical practice shows that long-term use of RAAS inhibitors has certain limitations, and it is difficult to effectively control the condition of some patients with this single drug.

In Chinese medicine, the spleen governs transportation and transformation, while the kidney governs storing essence. In cases of yang deficiency of the spleen and kidney, the transportation and transformation function of the spleen becomes abnormal, leading to internal accumulation of water dampness, obstruction of qi and blood circulation, and subsequent formation of blood stasis. Blood stasis blocks renal collaterals, disrupts the normal physiological function of the kidney, and causes a series of clinical symptoms such as proteinuria and edema [9-10]. Therefore, the blood-activating and stasis-resolving method is of great significance in DN treatment. The results of this study showed that the total effective rate of the combined group was significantly higher than that of the RAAS inhibition group. After treatment, the

scores of primary and secondary symptoms were significantly lower in the combined group than in the RAAS inhibition group; 24-hour urinary protein quantification, UACR, Scr, and BUN were significantly lower, while GFR was significantly higher in the combined group. These findings indicate that the blood-activating and stasis-resolving recipe combined with RAAS inhibitors has a definite curative effect in DN treatment, effectively improving clinical symptoms and renal function. Analysis of the blood-activating and stasis-resolving recipe used in this study shows that: *Salvia miltiorrhiza* (Danshen) has the effects of activating blood circulation, removing blood stasis, unblocking meridians, and relieving pain; *Ligusticum chuanxiong* (Chuanxiong) can activate blood circulation, promote qi movement, dispel wind, and relieve pain; *Prunus persica* (Taoren) and *Carthamus tinctorius* (Honghua) work together to activate blood circulation and resolve stasis; *Angelica sinensis* (Danggui) nourishes blood while activating circulation; *Paeonia lactiflora* (Chishao) clears heat, cools blood, dissipates stasis, and relieves pain; *Leonurus japonicus* (Yimucao) activates blood circulation, regulates menstruation, promotes diuresis, and reduces swelling; *Pheretima* (Dilong) is effective in unblocking meridians and activating collaterals. The combination of these herbs achieves the therapeutic goals of activating blood circulation, resolving stasis, promoting diuresis, and reducing swelling [11-12]. From the perspective of modern pharmacology, the components of these herbs play multiple roles in DN treatment. Salvianolic acid B in *Salvia miltiorrhiza* can reduce extracellular matrix deposition, thereby effectively delaying renal fibrosis progression [13]. Amygdalin in *Prunus persica* has anti-inflammatory and antioxidant properties, which can reduce oxidative stress damage to renal cells [14]. Hydroxysafflor yellow A in *Carthamus tinctorius* can inhibit apoptosis of renal tubular epithelial cells and protect renal tubular function [15]. Therefore, the combined application of the blood-activating and stasis-resolving recipe and RAAS inhibitors significantly enhances the therapeutic effect of DN.

Oxidative stress plays an important role in the occurrence and development of DN. When the body is in a diabetic pathological state, the dynamic balance of the oxidation-antioxidation system is disrupted, which in turn causes damage to renal tissue cells [16]. SOD and GSH-Px are important antioxidant enzymes in the body, which can scavenge excessive reactive oxygen species through catalytic reactions. MDA is the terminal metabolite of lipid peroxidation, and its level can be used as a direct indicator to evaluate the degree of oxidative stress in the body [17-18]. The results of this study showed that SOD and GSH-Px levels in the combined group were significantly higher than those in the RAAS inhibition group, while MDA level was significantly lower. This indicates that the blood-activating and stasis-resolving recipe combined with RAAS inhibitors can more effectively regulate the oxidative stress state of the body and reduce oxidative stress damage to the kidney, which is closely related to the antioxidant effects of multiple Chinese herbal components in the recipe [19].

This study has certain limitations: limited by the small sample size and short observation period, it is difficult to comprehensively and accurately present long-term therapeutic effects and potential adverse reactions. Therefore, large-sample, multi-center long-term follow-up clinical studies need to be carried out in the future to further verify the conclusions of this study.

In conclusion, the blood-activating and stasis-resolving recipe combined with RAAS inhibitors has significant clinical efficacy in the treatment of DN, which can effectively improve renal function and reduce oxidative stress levels in patients.

Conflict of Interest No

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·论　著·

活血化瘀方联合肾素-血管紧张素-醛固酮系统抑制剂对糖尿病肾病的疗效及对氧化应激指标的影响

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摘要：目的　探究活血化瘀方联合肾素-血管紧张素-醛固酮系统（RAAS）抑制剂对糖尿病肾病（DN）的临床疗效，并观察其对氧化应激相关指标的影响。**方法**　前瞻性选取2023年6月至2025年3月南京中医药大学附属连云港医院收治的80例DN患者，按随机数字表法分为RAAS抑制组（40例，给予糖尿病基础治疗及RAAS抑制剂治疗）和联合组（40例，在RAAS抑制组基础上给予活血化瘀方）。比较两组临床疗效、中医证候积分、肾功能指标[24 h尿蛋白定量、尿白蛋白/肌酐比值（UACR）、血肌酐（Scr）、血尿素氮（BUN）、肾小球滤过率（GFR）]、氧化应激指标[超氧化物歧化酶（SOD）、谷胱甘肽过氧化物酶（GSH-Px）活性、丙二醛（MDA）]。**结果**　联合组总有效率高于RAAS抑制组（92.50% *vs* 75.00%，χ^2=4.501，*P*<0.05）。治疗后，两组主症及次症积分均较治疗前降低，且联合组低于RAAS抑制组（*P*<0.05）。治疗后，两组24 h尿蛋白定量、UACR、Scr及BUN均较治疗前降低，GFR均较治疗前升高，且联合组24 h尿蛋白定量、UACR、Scr及BUN低于RAAS抑制组，GFR高于RAAS抑制组，差异有统计学意义（*P*<0.05）。治疗后，两组血清SOD、GSH-Px较治疗前升高，MDA水平较治疗前降低，且联合组SOD、GSH-Px高于RAAS抑制组，MDA低于RAAS抑制组，差异有统计学意义（*P*<0.05）。**结论**　活血化瘀方联合RAAS抑制剂治疗DN具有显著临床疗效，可有效改善患者的肾功能，降低氧化应激水平。

关键词：活血化瘀方；肾素-血管紧张素-醛固酮系统抑制剂；氧化应激；肾功能；中医证候积分
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Abstract: Objective　To investigate the clinical efficacy of *Huoxue Huayu* Decoction combined with renin-angiotensin-aldosterone system (RAAS) inhibitors in the treatment of diabetic nephropathy (DN), and to observe its impact on oxidative stress-related indicators. **Methods**　Eighty DN patients admitted to Lianyungang Hospital of TCM Affiliated to Nanjing University of Chinese Medicine from June 2023 to March 2025 were selected and divided into two groups via random number table: the RAAS inhibitor group (*n*=40) was given basic diabetes treatment and RAAS inhibitors, and the combined group (*n*=40) was given *Huoxue Huayu* Decoction on top of the treatment for the RAAS inhibitor group. The following indexes were compared between the two groups, including clinical efficacy, TCM syndrome scores, renal function indicators [24-hour urinary protein quantification, urinary albumin/creatinine ratio (UACR), serum creatinine (Scr), blood urea nitrogen (BUN), glomerular filtration rate (GFR)], and oxidative stress indicators [activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), malondialdehyde (MDA) level].

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Results　The total effective rate of the combined group was higher than that of the RAAS inhibitor group (92.50% *vs* 75.00%, χ^2=4.501, P<0.05). After treatment, the scores of primary and secondary syndromes in both groups were lower than those before treatment, and the scores in the combined group were lower than those in the RAAS inhibitor group (P<0.05). After treatment, the 24-hour urinary protein quantification, UACR, Scr, and BUN in both groups decreased compared with pre-treatment, while GFR increased, and the combined group had lower 24-hour urinary protein quantification, UACR, Scr, and BUN, and higher GFR than the RAAS inhibitor group, with statistically significant differences (P<0.05). After treatment, the serum SOD and GSH-Px activities in both groups were higher than those before treatment, while the MDA level was lower, and the combined group had higher SOD and GSH-Px activities and lower MDA level than the RAAS inhibitor group, with statistically significant differences (P<0.05).
Conclusion　*Huoxue Huayu* Decoction combined with RAAS inhibitors has a significant clinical effect in the treatment of DN, which can effectively improve patients' renal function and reduce the level of oxidative stress.

Keywords: *Huoxue Huayu* Decoction; Renin-angiotensin-aldosterone system inhibitor; Oxidative stress; Renal function; Traditional Chinese medicine syndrome score

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糖尿病肾病(diabetic nephropathy,DN)作为糖尿病最常见且严重的微血管并发症,其发病率持续攀升,已成为终末期肾病的首要病因[1]。在现代医学中,药物干预仍是现阶段应对DN的主要策略。肾素-血管紧张素-醛固酮系统(renin-angiotensin-aldosterone system,RAAS)抑制剂为临床治疗DN的常用药。以贝那普利为代表的血管紧张素转换酶抑制剂和以缬沙坦为代表的血管紧张素Ⅱ受体拮抗剂,通过抑制RAAS过度激活,有效降低肾小球内高压、高灌注及高滤过状态,延缓肾脏病变进展[2-3]。然而,对于部分患者,单一用药未能达到预期的治疗效果。中医将DN归属于"水肿""肾劳""消渴"等范畴,认为该病病位在肾,络脉瘀阻贯穿始终,常累及肺、脾等脏腑,治疗应以活血化瘀、补益肾气为主[4]。基于上述背景,本研究旨在探讨活血化瘀方联合RAAS抑制剂治疗DN患者的临床疗效,并观察其对氧化应激相关指标的影响,期望为DN的综合治疗方案提供参考。

1　资料与方法

1.1　一般资料　前瞻性纳入2023年6月至2025年3月于南京中医药大学附属连云港医院就诊的80例DN患者。纳入标准:(1)符合DN诊断标准[5]。(2)依据中医理论,辨证为脾肾阳虚兼血瘀型,主症为神疲懒言,腰膝酸软,手足畏寒,夜尿频或小便清长,大便不成形、稀软或五更泄泻,或指端麻木。次症为面色淡暗,下腹冷痛或浮肿或多汗。舌脉:舌淡体胖,舌苔薄白或白滑,脉象沉细无力。(3)患者或家属签署知情同意书。排除标准:(1)因其他原因导致的肾脏疾病;(2)合并严重脏器疾病;(3)对研究药物过敏;(4)合并恶性肿瘤者。按随机数字表法将患者分为RAAS抑制组(40例,给予糖尿病基础治疗及RAAS抑制剂治疗)和联合组(40例,在RAAS抑制组基础上给予活血化瘀方治疗),两组一般资料比较差异无统计学意义(P>0.05),具有可比性。见表1。

表1　两组一般资料比较　(n=40)

Tab.1　Comparison of general data between the two groups (n=40)

组别	性别(例)		年龄	糖尿病病程	入院时餐后血糖
	男	女	(岁, $\bar{x}\pm s$)	(年, $\bar{x}\pm s$)	(mmol/L, $\bar{x}\pm s$)
联合组	22	18	56.84±7.22	7.58±1.21	15.03±3.12
RAAS抑制组	24	16	57.18±7.37	7.82±1.52	14.68±3.16
χ^2/t值	0.205		0.208	0.781	0.498
P值	0.651		0.835	0.437	0.620

1.2　方法　两组患者均实施糖尿病基础治疗措施,涵盖饮食调控、适度运动、血糖监测以及血糖水平的有效控制等多个方面。RAAS抑制组患者接受RAAS抑制剂治疗:缬沙坦[天大药业(珠海)有限公司,国药准字H20030777],每次80 mg,每日1次,或者贝那普利(上海新亚药业闵行有限公司,国药准字H20044840),每次10 mg,每日1次,并依据患者的血压状况以及对药物的耐受程度,对用药剂量进行合理调整,以确保治疗的安全性与有效性。联合组在RAAS抑制组治疗的基础上联合运用活血化瘀方进行治疗,组成如下:丹参30 g,川芎15 g,桃仁12 g,红花12 g,赤芍15 g,当归15 g,益母草30 g,地龙12 g。按照传统中药煎制方法,每日煎煮1剂,煎取药汁400 mL,分为早晚2次,以温服的方式给药。两组疗程均为12周。

1.3　观察指标　(1)临床疗效:显效为血肌酐(serum creatinine,Scr)下降≥15%,24 h尿蛋白定量下降≥30%,肾小球滤过率(glomerular filtration rate,GFR)升高≥10%,中医证候积分减少≥70%。有效为

Scr 下降 5%~15%，24 h 尿蛋白定量下降 15%~30%，GFR 升高 5%~10%，中医证候积分减少 30%~70%。无效为未达到上述有效标准或病情加重。(2) 中医证候积分[6]：治疗前后对主症和次症按严重程度分级计分，主症无症状 0 分，轻度 2 分，中度 4 分，重度 6 分；次症无症状 0 分，轻度 1 分，中度 2 分，重度 3 分。(3) 肾功能指标：检测治疗前后 24 h 尿蛋白定量、尿白蛋白/肌酐比值(urinary albumin/creatinine ratio，UACR)、Scr、血尿素氮(blood urea nitrogen，BUN)及 GFR 等肾功能指标。(4) 氧化应激指标：在治疗前后，采集患者空腹状态下的静脉血样本，运用酶联免疫吸附法检测血清中的超氧化物歧化酶(superoxide dismutase，SOD)、谷胱甘肽过氧化物酶(glutathione peroxidase，GSH-Px)活性以及丙二醛(malondialdehyde，MDA)水平。(5) 记录两组不良反应发生情况。

1.4　统计学方法　采用 SPSS 27.0 软件分析数据。符合正态分布的计量资料用 $\bar{x}\pm s$ 表示，比较采用配对 t 检验和独立样本 t 检验；计数资料用例(%)表示，采用 χ^2 检验。$P<0.05$ 为差异有统计学意义。

2　结　果

2.1　两组临床疗效比较　联合组总有效率显著高于 RAAS 抑制组($P<0.05$)。见表 2。

2.2　两组中医证候积分比较　治疗后，两组主症及次症积分均较治疗前显著降低，且联合组低于 RAAS 抑制组($P<0.05$)。见表 3。

2.3　两组肾功能指标比较　治疗后，两组 24 h 尿蛋白定量、UACR、Scr 及 BUN 均较治疗前降低，GFR 均较治疗前升高($P<0.05$)；且联合组 24 h 尿蛋白定量、UACR、Scr 及 BUN 低于 RAAS 抑制组，GFR 高于 RAAS 抑制组($P<0.05$)。见表 4。

2.4　两组氧化应激指标比较　治疗后，两组血清 SOD、GSH-Px 较治疗前升高，MDA 水平较治疗前降低($P<0.05$)，且联合组 SOD、GSH-Px 高于 RAAS 抑制组，MDA 低于 RAAS 抑制组($P<0.05$)。见表 5。

2.5　两组不良反应发生情况比较　两组治疗期间未出现严重不良反应。

表 2　两组临床疗效比较　[例(%)]

Tab.2　Comparison of clinical efficacy between the two groups　[case(%)]

组别	例数	显效	有效	无效	总有效
联合组	40	18(45.00)	19(47.50)	3(7.50)	37(92.50)
RAAS 抑制组	40	8(20.00)	22(55.00)	10(25.00)	30(75.00)
χ^2 值					4.501
P 值					0.034

表 3　两组中医证候积分比较　(分，$\bar{x}\pm s$)

Tab.3　Comparison of Chinese medicine syndrome scores between the two groups　(point，$\bar{x}\pm s$)

组别	例数	主症		次症	
		治疗前	治疗后	治疗前	治疗后
联合组	40	31.40±1.28	19.20±2.45[a]	4.12±0.89	2.46±0.84[a]
RAAS 抑制组	40	31.45±1.24	23.40±2.48[a]	4.14±0.86	3.10±0.87[a]
t 值		0.177	7.620	0.102	3.347
P 值		0.860	<0.001	0.919	0.001

注：与本组治疗前比较，[a]$P<0.05$。

表 4　两组肾功能指标比较　(n=40，$\bar{x}\pm s$)

Tab.4　Comparison of renal function indexes between the two groups　(n=40，$\bar{x}\pm s$)

组别	24 h 尿蛋白定量(g)		UACR(mg/g)		Scr(μmol/L)		BUN(mmol/L)		GFR(mL/min)	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
联合组	2.35±0.48	0.98±0.21[a]	1 256.32±156.78	668.45±89.32[a]	135.24±18.76	98.76±12.34[a]	8.95±1.23	6.23±0.85[a]	52.34±6.57	68.56±7.89[a]
RAAS 抑制组	2.38±0.51	1.56±0.32[a]	1 262.45±162.34	895.67±112.45[a]	136.57±19.23	115.67±15.43[a]	9.02±1.18	7.56±1.02[a]	51.89±6.72	58.67±7.23[a]
t 值	0.271	9.584	0.172	10.007	0.313	5.413	0.260	6.335	0.303	5.845
P 值	0.787	<0.001	0.864	<0.001	0.755	<0.001	0.800	<0.001	0.763	<0.001

注：与本组治疗前比较，[a]$P<0.05$。

表 5　两组氧化应激指标比较　(n=40，$\bar{x}\pm s$)

Tab.5　Comparison of oxidative stress indexes between the two groups　(n=40，$\bar{x}\pm s$)

组别	SOD(u/mL)		GSH-Px(u/mL)		MDA(nmol/mL)	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
联合组	85.67±10.23	145.67±15.43[a]	120.34±15.67	185.67±20.34[a]	4.89±0.54	2.13±0.32[a]
RAAS 抑制组	86.23±9.87	110.34±12.56[a]	121.02±16.23	150.23±18.76[a]	4.95±0.62	3.25±0.45[a]
t 值	0.249	11.231	0.191	8.100	0.462	12.828
P 值	0.804	<0.001	0.849	<0.001	0.646	<0.001

注：与本组治疗前比较，[a]$P<0.05$。

3　讨　论

DN 发病机制复杂，涉及糖代谢紊乱、氧化应激、炎症反应、RAAS 过度激活等多个方面[7-8]。RAAS 抑制剂作为 DN 治疗中常用的药物，主要是通过抑制血管紧张素Ⅱ生成，进而扩张出球小动脉，有效降低肾

小球内压力，减少蛋白尿的产生，同时延缓肾脏纤维化进程。然而，临床实践表明，长期应用RAAS抑制剂存在一定局限性，部分患者的病情难以通过该单一药物得到有效控制。

脾主司运化，肾主封藏精气。若脾肾阳虚，脾之运化功能失常，水湿内生，气血运行受阻，瘀血由此内生；瘀血阻滞肾络，干扰肾脏正常生理功能，出现蛋白尿、水肿等一系列临床症状[9-10]。因此，活血化瘀法在DN的治疗中具有重要意义。本研究结果显示，联合组总有效率显著高于RAAS抑制组，治疗后主症及次症积分显著低于RAAS抑制组，24 h尿蛋白定量、UACR、Scr及BUN显著低于RAAS抑制组，GFR显著高于RAAS抑制组，表明活血化瘀方联合RAAS抑制剂治疗DN疗效确切，能有效改善临床症状和肾功能。分析可知，本研究使用的活血化瘀方中，丹参具有活血祛瘀、通经止痛之功效；川芎可活血行气、祛风止痛；桃仁与红花共奏活血化瘀之功；当归兼具补血活血之能；赤芍可清热凉血、散瘀止痛；益母草活血调经、利尿消肿；地龙善于通经活络；众药配伍，合力达成活血化瘀、利水消肿的治疗目的[11-12]。从现代药理学角度来看，该方中的药物成分在DN治疗中发挥着多种作用。丹参中的丹酚酸B能够减少细胞外基质的沉积，从而有效延缓肾脏纤维化进程[13]。桃仁中的苦杏仁苷具有抗炎、抗氧化特性，能够减轻肾脏细胞所遭受的氧化应激损伤[14]。红花中的羟基红花黄色素A可抑制肾小管上皮细胞的凋亡，对肾小管功能起到保护作用[15]。故活血化瘀方与RAAS抑制剂联合应用，使得DN的治疗效果得以显著提升。

氧化应激在DN的发生、发展中起重要作用。当机体处于糖尿病病理状态时，体内氧化-抗氧化系统的动态平衡被打破，进而引发肾脏组织细胞的损伤[16]。SOD和GSH-Px作为体内重要的抗氧化酶类，可通过催化反应清除过量活性氧；而MDA是脂质过氧化反应的终末代谢产物，其水平可作为评估机体氧化应激程度的直观指标[17-18]。本研究结果显示，联合组SOD、GSH-Px显著高于RAAS抑制组，MDA显著低于RAAS抑制组，说明活血化瘀方联合RAAS抑制剂能够更为有效地调节机体氧化应激状态，减轻氧化应激对肾脏的损伤，而这一作用与活血化瘀方中多种中药成分所具备的抗氧化作用密切相关[19]。

本研究存在一定局限性：受限于样本量较小且观察周期较短，难以全面准确地呈现长期治疗效果及潜在不良反应。因此，后续需开展大样本、多中心的长期随访临床研究，以进一步验证本研究结论。

综上所述，活血化瘀方联合RAAS抑制剂治疗DN具有显著临床疗效，可有效改善患者的肾功能，降低氧化应激水平。

利益冲突 无

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