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Shenshuaining Tablet combined with dapagliflozin in the treatment of stage III-IV diabetic kidney disease

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Abstract: Objective To explore the effect and safety of *Shenshuaining* Tablet combined with dapagliflozin in the treatment of patients with stage Ⅲ-Ⅳ type 2 diabetes mellitus (T2DM) complicated with diabetic kidney disease (DKD). **Methods** A total of 81 patients with stage Ⅲ-Ⅳ T2DM complicated with DKD who were treated at Anqing First People's Hospital of Anhui Medical University from August 2022 to January 2024 were prospectively selected as the research subjects and randomly divided into the control group (n=40) and the combination group (n=41). The control group was treated with dapagliflozin (10 mg/d). The combined group was treated with *Shenshuaining* Tablets (4 tablets each time, 3 times a day) combined with dapagliflozin (10 mg/d). The treatment course for both groups was 12 weeks. The effects of the two groups of patients after treatment were compared. The changes in renal function indicators (serum creatinine, cystatin C, blood urea nitrogen), blood lipids (total cholesterol, triglycerides), inflammatory indicators (interleukin-6, C-reactive protein, tumor necrosis factor-α) levels before and after treatment were compared, and the safety of medication during the treatment period was evaluated between the two groups. **Results** After treatment, the total effective rate of the combination group was higher than that of the control group (92.68% *vs* 72.50%, χ^2=5.769, P=0.016). After treatment, renal function indicators, blood lipid indicators, and inflammatory indicators in both groups decreased, and compared with the control group, the combination group showed more significant improvement (P<0.05). During the treatment period, there was no statistically significant difference in the incidence of side effects between the combination group and the control group (14.63% *vs* 10.00%, χ^2 =0.402, P= 0.526). **Conclusion** The combination of *Shenshuaining* Tablets and dapagliflozin has a good clinical efficacy in the treatment of stage Ⅲ-Ⅳ T2DM patients with DKD, and can further improve renal function, blood lipids, and inflammatory factor levels.

Keywords: *Shenshuaining* Tablet; Dapagliflozin; Diabetic kidney disease; Renal function; Blood lipid; Inflammatory indicator; Side effect; Type 2 diabetes mellitus

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Diabetic kidney disease (DKD) is the main cause of end-stage renal disease (ESRD) [1]. DKD has no obvious symptoms in the early stage. After entering the overt proteinuria stage, the rate of progression to ESRD is approximately 14 times that of other renal lesions. Once DKD progresses to ESRD, it will cause irreversible damage to renal function. Stage III-IV DKD is mainly characterized by progressive increase in microalbuminuria and progressive decrease in glomerular filtration rate. Timely intervention may reverse renal function damage, making it the optimal time for DKD treatment [2-3]. Clinically, sodium-glucose cotransporter 2 inhibitors are recommended as first-line medication for DKD. Dapagliflozin, as a representative drug among them, has not shown ideal therapeutic effect on DKD [4]. Traditional Chinese medicine holds that the pathogenesis of DKD is mainly qi-yin deficiency and blood stasis obstructing collaterals [5]. *Shenshuaining* Tablets is a Chinese patent medicine with good effects of promoting blood circulation and removing blood stasis, and replenishing qi and strengthening the spleen, but its efficacy in DKD has not been clarified [6]. This study investigates the efficacy and safety of *Shenshuaining* Tablets combined with dapagliflozin in the treatment of patients with stage III-IV type 2 diabetes mellitus complicated with DKD, and the results are reported as follows.

1 Materials and methods

1.1General information

The study subjects were 81 patients with stage III-IV type 2 diabetes mellitus complicated with DKD who were admitted to the Anqing First People's Hospital of Anhui Medical University. They were divided into a control group (n=40) and a combined group (n=41) using the random number method.

Inclusion criteria: (1) Met the diagnostic criteria for type 2 diabetes mellitus [7]; (2) Met the diagnostic criteria for DKD [8] with stage III-IV; (3) Aged ≥18 years; (4) Signed the informed consent form.

Exclusion criteria: (1) Psychiatric disorders; (2) Other kidney diseases; (3) Severe heart, liver, or lung dysfunction; (4) Pregnancy or lactation; (5) Other types of diabetes mellitus; (6) Received dialysis or related treatment for kidney disease in the past 3 months; (7) Malignant

tumors; (8) Hematological or immune system diseases.

There was no statistically significant difference in baseline data between the two groups (P>0.05), as shown in **Table 1.** This study was approved by the Ethics Committee of Anqing First People's Hospital.

Tab.1 Comparison of general data between two groups

Item	Combined group (n=41)	Control group (n=40)	χ^2/t value	P value
Gender (case)				
Male	25	28	0.729	0.393
Female	16	12	1.250	0.215
Age (years)	44.24±5.32	45.79±5.83	0.624	0.534
Disease stage (case)				
Stage III	30	23	2.198	0.138
Stage IV	11	17		

1.2 Treatment methods

Both groups received conventional treatments after admission, including maintaining water and electrolyte balance, regulating blood lipids, lowering blood pressure, anti-infection, etc. Additionally, both groups were given oral Dapagliflozin Tablets (manufactured by Beijing SL Pharm, specification: 10 mg, H20233316) at a dosage of 1 tablet/time, once daily. On this basis, the combined group was additionally given oral *Shenshuaining* Tablets (manufactured by Qinhuangdao Shanhaiguan Pharmaceutical, Z20060226) at a dosage of 4 tablets/time, three times daily. Both groups were treated for 12 weeks.

1.3 Observation indicators

(1) Clinical efficacy [9].

- Markedly effective: Urinary albumin excretion rate (UAER) decreased by ≥1/2, blood glucose returned to or approached normal levels, and clinical symptoms were significantly relieved;
- Effective: UAER decreased by 1/5 to 1/2, blood glucose levels decreased significantly, and clinical symptoms were alleviated;
- Ineffective: UAER decreased by ≤1/5, with basically no changes in blood glucose levels and clinical symptoms;
- Total effective rate = (Total cases - Ineffective cases)/Total cases × 100%.

(2) Detection indicators. Peripheral venous blood was collected from patients before and after treatment, and serum was separated. Automatic biochemical analyzer was used to determine serum creatinine, cystatin C, blood urea nitrogen, total cholesterol, and triglycerides. Enzyme-linked immunosorbent assay (ELISA) was used to measure interleukin (IL)-6, C-reactive protein (CRP), and tumor necrosis factor (TNF)-α.

(3) Safety analysis. Adverse reactions such as dizziness, headache, nausea and vomiting, skin allergy, and diarrhea during treatment were recorded.

1.4 Statistical methods

SPSS 24.0 statistical software was used to process the data. Measurement data conforming to normal distribution were expressed as $\bar{x} \pm s$ and analyzed by t-test; count data were expressed as cases (%) and analyzed by χ^2 test. A P value <0.05 indicated a statistically significant difference.

2 Results

2.1 Comparison of efficacy between two groups

After treatment, in the combined group, there were 21 cases of markedly effective, 17 cases of effective, and 3 cases of ineffective; in the control group, there were 20 cases of markedly effective, 9 cases of effective, and 11 cases of ineffective. The total effective rate of the combined group was higher than that of the control group, and the difference was statistically significant (92.68% *vs* 72.50%, χ^2=5.769, P=0.016).

2.2 Comparison of renal function before and after treatment between two groups

After treatment, the levels of serum creatinine, cystatin C, and blood urea nitrogen decreased in both groups, and compared with the control group, the combined group had lower levels (P<0.05). **[Table 2]**

Tab.2 Comparison of renal function levels between two groups ($\bar{x} \pm s$)

Group	Serum creatinine (μmol/L)		Cystatin C (mg/L)		Blood urea nitrogen (nmol/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Combined group(n=41)	141.81±23.23	68.63±14.79[a]	3.08±0.40	1.36±0.24[a]	13.80±2.01	7.53±1.25[a]
Control group(n=40)	140.64±23.59	86.35±16.84[a]	3.12±0.28	1.77±0.24[a]	12.65±2.33	9.49±1.64[a]
***t* value**	0.225	5.035	0.520	7.687	2.380	6.059
***P* value**	0.823	<0.001	0.604	<0.001	0.020	<0.001

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

2.3 Comparison of blood lipid levels before and after treatment between the two groups

After treatment, the blood lipid levels decreased in both groups (P<0.05). Compared with the control group, the combined group had lower blood lipid levels after treatment (P<0.05). **[Table 3]**

2.4 Comparison of changes in inflammatory factor before and after treatment between two groups

After treatment, the inflammatory factor levels decreased in both groups, and the inflammatory factor levels in the combined group were lower than those in the control group after treatment (P<0.05). **[Table 4]**

2.5 Comparison of adverse reactions between two groups

During treatment, there were 6 cases of adverse reactions in the combined group (2 cases of dizziness and headache, 1 case of nausea and vomiting, 2 cases of diarrhea); and 4 cases in the control group (1 case of dizziness and headache, 2 cases of nausea and vomiting, 1 case of urinary tract infection, 1 case of diarrhea). There was no statistically significant difference in the incidence of adverse reactions between the combined group and the control group (14.63% *vs* 10.00%, χ^2=0.402, *P*=0.526).

Tab.3 Comparison of blood lipid levels between two groups ($\bar{x}\pm s$, mmol/L)

Group	Total cholesterol		Triglycerides	
	Before treatment	After treatment	Before treatment	After treatment
Combined group (*n*=41)	5.64±1.23	3.17±0.46[a]	2.98±0.44	1.14±0.18[a]
Control group (*n*=40)	5.37±1.30	4.08±0.29[a]	3.11±0.36	1.75±0.31[a]
t value	0.960	10.621	1.453	10.863
P value	0.340	<0.001	0.150	<0.001

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

Tab.4 Comparison of inflammatory indicator levels between two groups ($\bar{x}\pm s$)

Group	IL-6(pg/mL)		CRP(mg/L)		TNF-α(pg/mL)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Combined group(*n*=41)	13.72±2.56	4.82±0.32[a]	14.14±2.35	6.74±1.17[a]	51.36±6.77	32.76±4.42[a]
Control group(*n*=40)	11.59±1.64	7.58±1.24[a]	14.23±2.32	9.61±1.80[a]	51.81±6.25	44.28±5.49[a]
t value	4.446	13.741	0.173	8.529	0.311	10.415
P value	<0.001	<0.001	0.862	<0.001	0.757	<0.001

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

3 Discussion

In patients with diabetes, long-term hyperglycemia leads to impairment of the redox system, with massive reactive oxygen species (ROS) generated from renal tubule and glomerulus-related cells. This causes pathological expansion of the glomerular basement membrane, impairs renal microcirculation, induces proteinuria, and triggers DKD [10-11]. If DKD progresses to ESRD, it seriously threatens patients' life and health; thus, timely treatment is necessary [12].

Clinical Western medicine treatment for DKD mainly uses hypoglycemic drugs, but its efficacy needs to be improved [13]. With the development of modern traditional Chinese medicine (TCM), integrated traditional Chinese and Western medicine therapy has become a new approach for treating DKD [14]. In TCM theory, DKD is categorized under "Niaozhuo", "Shuizhong", "Xulao", and "Guange". Prolonged illness leads to qi and yin deficiency, blood stasis obstruction, further impairing qi and blood circulation and causing spleen-kidney deficiency, thereby forming blood stasis syndrome. Therefore, treatment should focus on invigorating the spleen and kidney, removing blood stasis, and draining turbidity [15-17].

This study showed that the total effective rate of the combined group was higher than that of the control group after treatment, indicating that *Shenshuaining* Tablets combined with dapagliflozin can enhance therapeutic efficacy. *Shenshuaining* Tablets are composed of multiple Chinese herbs. *Rhubarb* promotes blood circulation to remove stasis, unblocks meridians, and purges the bowels to drain turbidity; *Radix Pseudostellariae* replenishes qi and invigorates the spleen; Pinelliae Rhizoma dries dampness; *Coptidis Rhizoma* clears heat and detoxifies; *Pericarpium Citri Reticulatae* regulates qi and aids transportation; *Salviae Miltiorrhizae Radix et Rhizoma* and *Carthami Flos* resolve blood stasis, relieve pain, and activate blood circulation to unblock meridians; *Achyranthis Bidentatae Radix* promotes qi circulation and tonifies the kidney; *Poria* induces diuresis, excretes dampness, invigorates the spleen, and harmonizes the stomach. The combined action of these herbs enables blood circulation promotion, blood stasis resolution, qi replenishment, and spleen invigoration.

Compared with the control group, renal function indicators in the combined group improved more significantly, suggesting that combined *Shenshuaining* Tablets with dapagliflozin can further improve renal function compared with dapagliflozin monotherapy. Modern pharmacological studies have confirmed that *Carthami Flos* and *Salviae Miltiorrhizae Radix et Rhizoma* can promote local renal blood perfusion and increase glomerular filtration rate; *Radix Pseudostellariae* contains vitamins, polysaccharides, saponins, and other active substances that improve renal function; polysaccharide components in *Poria* enhance cellular immune function and repair glomerular basement membrane damage; *Rhubarb* inhibits mesangial proliferation and delays glomerulosclerosis. The combined use of these herbs effectively improves renal function.

Dyslipidemia exists in DKD patients, leading to massive production of intrarenal vasoconstrictive substances, which easily increases glomerular blood viscosity, induces glomerulosclerosis, and further impairs renal function [18]. In this study, compared with the control group, the combined group had lower blood lipid levels after treatment, confirming that *Shenshuaining* Tablets combined with dapagliflozin can regulate blood lipid levels. This may be attributed to the blood lipid-regulating or lowering effects of *Rhubarb, Salviae Miltiorrhizae Radix et Rhizoma*, and *Achyranthis Bidentatae Radix*.

Inflammatory response plays an important role in the progression of DKD. Glucose metabolism disorder

increases ROS, promotes the expression of inflammatory factors, thereby damaging renal tissues, accelerating renal fibrosis, and aggravating the condition [19]. This study found that compared with the control group, the combined group had lower blood lipid indicators, suggesting that *Shenshuaining* Tablets combined with dapagliflozin can inhibit inflammatory response. Rhubarb extract can inhibit the expression of inflammatory factors; *Radix Pseudostellariae, Achyranthis Bidentatae Radix*, and *Poria* enhance immune function and exert anti-inflammatory effects; *Salviae Miltiorrhizae Radix et Rhizoma* also has certain anti-inflammatory effects. During treatment, there was no significant difference in the incidence of adverse effects between the two groups, indicating that *Shenshuaining* Tablets do not increase drug adverse effects and have good safety.

In conclusion, for patients with stage III-IV type 2 diabetes mellitus complicated with DKD, *Shenshuaining* Tablets combined with dapagliflozin can enhance therapeutic efficacy, improve renal function, reduce blood lipids and inflammatory response, and have good safety, making it a promising treatment option.

Conflict of interest None

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·论　著·

肾衰宁片联合达格列净治疗Ⅲ~Ⅳ期糖尿病肾病

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摘要：目的　探讨在Ⅲ~Ⅳ期2型糖尿病合并糖尿病肾病患者中使用肾衰宁片联合达格列净治疗的疗效及安全性。**方法**　前瞻性选取2022年8月至2024年1月在安徽医科大学附属安庆第一人民医院就诊的81例Ⅲ~Ⅳ期2型糖尿病合并糖尿病肾病患者为研究对象，随机分为对照组（n=40）和联合组（n=41），对照组采用达格列净（10 mg/d）治疗，联合组采用肾衰宁片（4 片/次，3 次/d）联合达格列净（10 mg/d）治疗。两组疗程均为12周。比较两组患者治疗效果。对两组治疗前后肾功能指标（血肌酐、胱抑素C、尿素氮）、血脂（总胆固醇、三酰甘油）、炎症指标（白细胞介素-6、C-反应蛋白、肿瘤坏死因子-α）水平的变化进行比较，并评估治疗期间的用药安全性。**结果**　治疗后，联合组总有效率高于对照组（92.68% *vs* 72.50%，χ^2=5.769，P=0.016）；治疗后，肾功能指标、血脂指标、炎症指标两组均降低，且与对照组比较，联合组改善更明显（P<0.05）；治疗期间，联合组与对照组副作用发生率差异无统计学意义（14.63% *vs* 10.00%，χ^2=0.402，P=0.526）。**结论**　相较于单独使用达格列净，肾衰宁片联合达格列净治疗对Ⅲ~Ⅳ期2型糖尿病合并糖尿病肾病患者的临床疗效更显著，改善肾功能、血脂和炎症因子水平的效果更好。

关键词：肾衰宁片；达格列净；糖尿病肾病；肾功能；血脂；炎症指标；副作用；2型糖尿病
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Shenshuaining Tablet combined with dapagliflozin in the treatment of stage Ⅲ-Ⅳ diabetic kidney disease

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Abstract: Objective　To explore the effect and safety of *Shenshuaining* Tablet combined with dapagliflozin in the treatment of patients with stage Ⅲ-Ⅳ type 2 diabetes mellitus (T2DM) complicated with diabetic kidney disease (DKD). **Methods**　A total of 81 patients with stage Ⅲ-Ⅳ T2DM complicated with DKD who were treated at Anqing First People's Hospital of Anhui Medical University from August 2022 to January 2024 were prospectively selected as the research subjects and randomly divided into the control group (n=40) and the combination group (n=41). The control group was treated with dapagliflozin (10 mg/d). The combined group was treated with *Shenshuaining* Tablets (4 tablets each time, 3 times a day) combined with dapagliflozin (10 mg/d). The treatment course for both groups was 12 weeks. The effects of the two groups of patients after treatment were compared. The changes in renal function indicators (serum creatinine, cystatin C, blood urea nitrogen), blood lipids (total cholesterol, triglycerides), inflammatory indicators (interleukin-6, C-reactive protein, tumor necrosis factor-α) levels before and after treatment were compared, and the safety of medication during the treatment period was evaluated between the two groups. **Results**　After treatment, the total effective rate of the combination group was higher than that of the control group (92.68% *vs* 72.50%, χ^2=5.769, P=0.016). After treatment, renal function indicators, blood lipid indicators, and inflammatory indicators in both groups decreased, and compared with the control group, the combination group showed

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more significant improvement (P<0.05). During the treatment period, there was no statistically significant difference in the incidence of side effects between the combination group and the control group (14.63% *vs* 10.00%, χ^2=0.402, P=0.526). **Conclusion** The combination of *Shenshuaining* Tablets and dapagliflozin has a good clinical efficacy in the treatment of stage Ⅲ-Ⅳ T2DM patients with DKD, and can further improve renal function, blood lipids, and inflammatory factor levels.

Keywords: *Shenshuaining* Tablet; Dapagliflozin; Diabetic kidney disease; Renal function; Blood lipid; Inflammatory indicator; Side effect; Type 2 diabetes mellitus

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糖尿病肾病(diabetic kidney disease,DKD)是引起终末期肾病(end-stage renal disease,ESRD)的主要原因[1]。DKD早期无明显症状,进入显性蛋白尿期后,进展至ESRD的速度大约为其他肾脏病变的14倍,一旦进展为ESRD,会对肾功能造成不可逆的损害。而Ⅲ~Ⅳ期DKD主要表现为微量白蛋白尿不断加重和肾小球滤过率进行性下降,及时干预有逆转肾功能损害的可能,是治疗DKD的最佳时机[2-3]。临床推荐钠-葡萄糖共转运蛋白2抑制剂作为治疗DKD的一线用药,达格列净作为其中的代表药物,治疗DKD效果并不理想[4]。中医学认为,DKD病机主要为气阴两虚,瘀血阻络[5]。肾衰宁片属于中成药,具有较好的活血化瘀、益气健脾作用,但在DKD中的疗效尚未明确[6]。本研究探讨肾衰宁片联合达格列净治疗Ⅲ~Ⅳ期2型糖尿病合并DKD患者疗效及安全性,现报道如下。

1　资料与方法

1.1　一般资料　研究对象来自安徽医科大学附属安庆第一人民医院就诊的81例Ⅲ~Ⅳ期2型糖尿病合并DKD患者,按数字随机法分为对照组(n=40)和联合组(n=41)。纳入标准:(1)符合2型糖尿病的的诊断标准[7];(2)符合DKD的诊断标准[8],且分期为Ⅲ~Ⅳ期;(3)年龄≥18周岁;(4)签署知情同意书。排除标准:(1)精神类疾病;(2)其他肾脏疾病;(3)严重心、肝、肺功能障碍;(4)妊娠或哺乳期;(5)其他类型糖尿病;(6)近3个月内因肾病接受透析等相关治疗;(7)恶性肿瘤;(8)血液、免疫系统疾病。两组患者的基础资料比较差异无统计学意义(P>0.05),见表1。本研究通过安庆市第一人民医院伦理委员会审查。

1.2　治疗方法　两组患者入院后均予以维持水与电解质平衡、调节血脂、降压、抗感染等常规治疗,并采用达格列净片(北京双鹭药业,10 mg,国药准字H20233316)口服,片/次,1次/d。在此基础上,联合组加用肾衰宁片(秦皇岛市山海关药业,国药准字Z20060226)口服,4片/次,3次/d。两组均治疗12周。

1.3　观察指标　(1)临床疗效[9]。显效:尿白蛋白排泄率(urinary albumin excretion rate,UAER)降低≥1/2,血糖恢复或接近正常水平,临床症状显著减轻;有效:1/5≤UAER降低≤1/2,血糖水平显著下降,临床症状有所减轻;无效:UAER降低≤1/5,血糖水平和临床症状基本无变化;总有效率=(总例数-无效例数)/总例数×100%。(2)检测指标。于治疗前后采集患者的外周静脉血,分离血清,采用全自动生化分析仪测定血肌酐、胱抑素C、血尿素氮、总胆固醇、三酰甘油;采用酶联免疫法测定白细胞介素(interleukin,IL)-6、C-反应蛋白(C-reactive protein,CRP)、肿瘤坏死因子(tumor necrosis factor,TNF)-α。(3)安全性分析。记录治疗期间头晕、头痛、恶心呕吐、皮肤过敏、腹泻等副作用。

1.4　统计学方法　使用SPSS 24.0统计软件处理数据。符合正态分布的计量资料以$\bar{x}\pm s$表示,采用t检验;计数资料以例(%)表示,采用χ^2检验。P<0.05表示差异有统计学意义。

2　结　果

2.1　两组疗效比较　治疗后,联合组显效21例,有效17例,无效3例。对照组显效20例,有效9例,无效11例。联合组总有效率高于对照组,差异有统计学意义(92.68% *vs* 72.50%,χ^2=5.769,P=0.016)。

2.2　两组治疗前后肾功能水平比较　治疗后,两组血肌酐、胱抑素、尿素氮水平均下降,且与对照组对比,联合组更低(P<0.05)。见表2。

2.3　两组治疗前后血脂水平比较　治疗后,两组血脂水平均下降(P<0.05)。与对照组比较,联合组治疗后血脂水平更低(P<0.05)。见表3。

表1　两组一般资料比较　($\bar{x}\pm s$)

Tab.1　Comparison of general data between two groups　($\bar{x}\pm s$)

组别	例数	性别(例)		年龄(岁)	病程(d)	疾病分期(例)	
		男	女			Ⅲ期	Ⅳ期
联合组	41	25	16	44.24±5.32	6.34±1.26	30	11
对照组	40	28	12	45.79±5.83	6.51±1.19	23	17
χ^2/t值		0.729		1.250	0.624	2.198	
P值		0.393		0.215	0.534	0.138	

表2　两组肾功能水平比较　($\bar{x}\pm s$)

Tab.2　Comparison of renal function levels between two groups　($\bar{x}\pm s$)

组别	血肌酐(μmol/L)		胱抑素C(mg/L)		血尿素氮(mmol/L)	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
联合组(n=41)	141.81±23.23	68.63±14.79[a]	3.08±0.40	1.36±0.24[a]	13.80±2.01	7.53±1.25[a]
对照组(n=40)	140.64±23.59	86.35±16.84[a]	3.12±0.28	1.77±0.24[a]	12.65±2.33	9.49±1.64[a]
t值	0.225	5.035	0.520	7.687	2.380	6.059
P值	0.823	<0.001	0.604	<0.001	0.020	<0.001

注：与同组治疗前比较，[a]P<0.05。

表3　两组血脂水平对比　(mmol/L, $\bar{x}\pm s$)

Tab.3　Comparison of blood lipid levels between two groups　(mmol/L, $\bar{x}\pm s$)

组别	总胆固醇		三酰甘油	
	治疗前	治疗后	治疗前	治疗后
联合组(n=41)	5.64±1.23	3.17±0.46[a]	2.98±0.44	1.14±0.18[a]
对照组(n=40)	5.37±1.30	4.08±0.29[a]	3.11±0.36	1.75±0.31[a]
t值	0.960	10.621	1.453	10.863
P值	0.340	<0.001	0.150	<0.001

注：与同组治疗前比较，[a]P<0.05。

2.4　两组治疗前后炎症因子水平变化比较　治疗后，两组炎症因子水平均下降，且联合组治疗后炎病因子水平低于对照组(P<0.05)。见表4。

2.5　两组副作用比较　治疗期间，联合组6例存在副作用(头晕头痛2例，恶心呕吐1例，腹泻2例)，对照组有4例(头晕头痛1例，恶心呕吐2例，泌尿系统感染1例，腹泻1例)。联合组和对照组副作用发生率差异无统计学意义(14.63% *vs* 10.00%，χ^2=0.402，P=0.526)。

表4　两组炎症因子水平比较　($\bar{x}\pm s$)

Tab.4　Comparison of inflammatory indicator levels between two groups　($\bar{x}\pm s$)

组别	IL-6(pg/mL)		CRP(mg/L)		TNF-α(pg/mL)	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
联合组(n=41)	13.72±2.56	4.82±0.32[a]	14.14±2.35	6.74±1.17[a]	51.36±6.77	32.76±4.42[a]
对照组(n=40)	11.59±1.64	7.58±1.24[a]	14.23±2.32	9.61±1.80[a]	51.81±6.25	44.28±5.49[a]
t值	4.446	13.741	0.173	8.529	0.311	10.415
P值	<0.001	<0.001	0.862	<0.001	0.757	<0.001

注：与同组治疗前比较，[a]P<0.05。

3　讨　论

糖尿病患者长期处于高糖状态下，会导致机体氧化还原系统损伤，大量活性氧从肾小管和肾小球相关细胞中生成，引起肾小球基底膜病理性扩张，影响肾脏微循环，产生蛋白尿，引发DKD[10-11]。DKD病情如果进展到ESRD，严重威胁患者生命健康，因此需及时治疗[12]。临床西医治疗DKD主要采用降糖药物，但其疗效还有待改善[13]。伴随现代中医的发展，中西医结合疗法成为治疗DKD的新方案[14]。中医认为，DKD归属于“尿浊”“水肿”“虚劳”“关格”等范畴，由于久病导致气阴损伤，瘀血阻滞，进而气血运行不畅、脾肾两虚，形成血瘀证。因此，治疗应以健脾益肾、祛瘀泄浊为主[15-17]。

本研究显示，治疗后联合组总有效率高于对照组，说明肾衰宁片联合达格列净治疗可以提高疗效。肾衰宁片由多味中药制成，其中，大黄逐瘀通经、通腑泄浊；太子参益气健脾；半夏燥湿；黄连子清热解毒；陈皮理气助运；丹参和红花化瘀止痛、活血通经；牛膝行气补肾；茯苓利水渗湿、健脾和胃；诸药共用，可活血化瘀、益气健脾。与对照组比较，联合组肾功能指标改善更明显，提示相比达格列净单药治疗，联合肾衰宁片能够进一步改善肾功能。现代药理学研究证实，红花和丹参能促进肾脏局部血液灌注，提高肾小球清除率；太子参含有维生素、多糖、皂苷等多种有效物质，可以改善肾功能；茯苓中多糖体成分可以促进细胞免疫功能，修复肾小球基底膜损伤；大黄可以抑制系膜增生，延缓肾小球硬化。以上药物合用，能有效改善肾功能。

DKD患者体内存在血脂紊乱，导致肾内缩血管活性物质大量生成，易增加肾小球血液黏度，引起肾小球硬化，进一步损伤肾功能[18]。本研究中，与对照组比较，联合组治疗后血脂更低，证实肾衰宁片联合达格列净治疗可以调节血脂水平。这可能是由于中药大黄、丹参和牛膝均有调节或降低血脂的作用。

炎症反应在DKD病情发展中起重要作用，糖代谢紊乱会增加活性氧，促进炎症因子表达，从而损伤肾脏组织，加速肾纤维化，加重病情[19]。本研究发

现，与对照组比较，联合组炎症因子水平更低，提示肾衰宁片联合达格列净治疗可以抑制炎症反应。大黄提取物能够抑制炎症因子表达；太子参可以增强机体免疫力，发挥抗炎效果；丹参具有一定的抗炎作用。治疗期间，两组副作用发生率比较无明显差异，提示肾衰宁片治疗不会增加药物副作用，安全性好。

综上所述，对于Ⅲ~Ⅳ期2型糖尿病合并DKD患者，采用肾衰宁片联合达格列净治疗能增强疗效、改善肾功能、降低血脂和减轻炎症反应，且安全性好，是一种较好的治疗方案。

利益冲突　无

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