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CLINICAL STUDY

Efficacy of Shenzhuo formula on diabetic kidney disease: a retrospective study

Tian Jiaxing, Zhao Linhua, Zhou Qiang, Liu Wenke, Chen Xinyan, Lian Fengmei, Tong Xiaolin

Tian Jiaxing, Department of Endocrinology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing 100053, China; Department of Endocrinology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing 100053, China; Graduate School, Beijing University of Chinese Medicine, Beijing 100029, China

Zhao Linhua, Zhou Qiang, Liu Wenke, Chen Xinyan, Lian Fengmei, Tong Xiaolin, Department of Endocrinology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing 100053, China

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Correspondence to: Prof. Tong Xiaolin, Department of Endocrinology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing 100053, China. xiaolintong66@sina.com

Telephone: +86-10-88001166; +86-18810383272

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Abstract

OBJECTIVE: To observe the efficacy of a traditional Chinese medicine, Shenzhuo formula, on patients with diabetic kidney disease (DKD).

METHODS: Eighty-eight outpatients with DKD were enrolled. Changes in estimated glomerular filtration rate (eGFR), creatinine clearance, serum creatinine, blood-urea-nitrogen, albuminuria, glycosylated hemoglobin (Hb_{A1C}), blood pressure, and lipid profile were measured and analyzed before and after intervention with Shenzhuo formula for 1, 3, 6, 9, 12, and 18 months.

RESULTS: Compared with the baseline amounts, serum creatinine decreased, and eGFR and creatinine clearance increased, significantly after intervention for 1, 3, 6, 9, 12, and 18 months (all $P < 0.05$). Mean eGFR increased by 2.11 mL/min per 1.73 m^2/y after 18-month treatment. Urinary protein at 24 h decreased significantly after 1, 3, 9, and 12 months ($P < 0.05$). Hb_{A1C} decreased significantly ($P < 0.05$) after 3, 6, 9, 12, and 18 months, and systolic blood pressure decreased significantly ($P < 0.05$) after 1, 3, and 6 months. Total cholesterol decreased significantly ($P < 0.05$) after 1, 3, 6, and 18 months. Triglyceride and low-density lipoprotein-cholesterol decreased significantly ($P < 0.05$) after 1 and 3 months.

CONCLUSION: Shenzhuo formula can improve eGFR and possibly slow DKD progression. Shenzhuo formula can also lower Hb_{A1C}, lipid levels and blood pressure.

Key words: Diabetic nephropathies; Creatinine; Estimated glomerular filtration rate; Shenzhuo formula

INTRODUCTION

Diabetic kidney disease (DKD) is one of the most severe complications of diabetes mellitus (DM). The prevalence of DKD is increasing gradually because more people are suffering from DM. DKD is the primary cause of end-stage renal disease. The high incidence of DM and DKD results in considerable burdens upon medical resources and society. Thus, a number of DM- and DKD-preventative therapies have been advocated.[1-3]

According to international guidelines on DKD,[1] man-

aging indices such as serum creatinine (Scr), creatinine clearance (Ccr), and, albuminuria can postpone PKD progression. In fact, most DKD patients cannot achieve these goals. Thus, it is important to search for new candidate drugs for DKD for such patients.

Researchers have demonstrated the clinical benefit of tight glycemic control, which can prevent/postpone diabetic complications.[4] Because DKD patients usually have the complications of hypertension and dyslipidemia, optimal treatment involves controlling blood pressure (BP) and lipids. Such combined therapy can decrease the risk of cardiovascular events and aid kidney function.[5-7]

This retrospective analysis focused on DKD patients administered a traditional Chinese medicine, namely, Shenzhuo formula [Dahuang (*Radix Et Rhizoma Rhei Palmati*), Shuizhi (*Hirudo*), Huangqi (*Radix Astragali Mongolici*), Danshen (*Radix Salviae Miltiorrhizae*)]. We assessed the effects of Shenzhuo formula on kidney function, estimated glomerular filtration rate (eGFR), BP, and lipid profiles.

MATERIALS AND METHODS

General data

Subjects were outpatients from the Endocrine Department of Guang'anmen Hospital, China Academy of Chinese Medical Sciences (Beijing, China) from July 2007 to July 2012.

Diagnosis

A total of 88 subjects were enrolled for screening. Diagnostic criteria for DM was based on those set by the World Health Organization in 1999.[8] Diagnostic criteria for DKD were based on Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease set by the American Kidney Foundation in 2007.[1] These criteria were Scr > 106 μmol/L or Ccr < 80 mL/min or eGFR <90 mL/min per 1.73 m^2 or urinary protein of 300-3500/24 h. Diagnostic criteria for hypertension were based on guidelines for the prevention and treatment of hypertension in 2010 by Chinese and American organizations.[9,10] Diagnostic criteria for dyslipidemia were based on guidelines for the prevention and management of dyslipidemia set by the China Joint Commission 2007.[11]

Inclusion criteria

Subjects were included in the study if they met the diagnostic criteria described above and if they underwent examinations in Guang'anmen Hospital. The follow-up period was > 3 months and the Scr test was conducted more than twice.

Exclusion criteria

Patients in whom urinary levels of protein were caused by primary nephritis, who had drug-induced renal damage, or other secondary nephropathies were excluded. Patients were excluded if they had: diabetic ketoacidosis or severe inflammation within the previous month; complications of severe cardiovascular / cerebrovascular diseases; diseases of the liver or hematopoietic system; or mental illness. Women who were pregnant, planning to become pregnant, or who were breastfeeding could not participate in this study. Patients were also excluded if they: had allergies (or a history of allergies); were consuming alcohol and/or psychoactive substances; or participating in other clinical trials.

Intervention

DKD patients' levels of blood glucose, lipid, and BP were stabilized by oral medications or insulin injections. All patients were administered a modified Shenzhuo formula (200 mL, b.d.). Shenzhuo formula was taken 30 min before or after breakfast and supper. Treatment lasted ≥ 12 weeks.

Measurements

Measurements of Scr, blood-urea-nitrogen (BUN), 24-h urinary protein, glycosylated hemoglobin (HbA-IC) and lipids were carried out in a central laboratory in Guang'anmen Hospital after an overnight fast of 10-12 h. BP was taken (on the non-dominant arm, supported at heart level) by a physician. Levels of Scr and BUN were measured using an enzymatic method (UniCel DxC 800 Automatic Biochemical Analyzer; Beckman Coulter, Fullerton, CA, USA). Urinary levels of protein over 24 h were measured using the Pyrogallol Red method (Synchron Automatic Biochemical Analyzer; Beckman Coulter). Hb_{A1c} levels were measured by an enzymatic method (7020 Automatic Biochemical Analyzer; Hitachi, Tokyo, Japan). Levels of total cholesterol (TC) and triglycerides (TG) were measured by enzymatic methods (Beckman Coulter). Levels of high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were determined by immuno-inhibition methods (HDL-C, LDL-C Direct; Wako Pure Chemical Industries, Osaka, Japan).

Measurements of Scr, BUN, 24-h urinary protein, Hb_{A1C}, BP, and lipid profile for each patient were recorded at the first visit and 1, 3, 6, 9, 12, and 18 months after the first visit. eGFR, Ccr, and reciprocal serum creatinine (rScr) were calculated by Modification of Diet in Renal Disease formula. Adverse events were assessed using vital signs, clinical signs and symptoms.[12-15]

Statistical analyses

Statistical analyses were processed via SPSS v15.0 (IBM, Armonk, NY, USA). Measurement data were the mean ± standard deviation ($\bar{x} \pm s$). The paired *t*-test was used to compare baseline and after-intervention changes in the abovementioned characteristics. A

two-sample comparison of means was conducted by the independent samples *t*-test. Disaggregated data correlation was conducted by the χ^2 test. $P < 0.05$ was considered significant.

RESULTS

General characteristics

This retrospective study involved 88 patients, the baseline characteristics of which are shown in Table 1. In total, 73 patients suffered from hypertension and 64 suffered from dyslipidemia.

Indices of kidney function

Compared with the baseline (paired *t*-test), mean eGFR increased by 5.45, 7.66, 8.67, 9.84, and 9.93 mL/min per 1.73 m^2 after intervention for 1, 3, 6, 9, and 12 months, respectively. Mean Ccr increased by 4.86, 7.06, 8.00, 9.49, 9.50, and 9.91 mL/min, and mean Scr decreased by 7.48, 11.81, 16.65, 15.23, 14.50, and 17.76 μmol/L after 1, 3, 6, 9, 12, and 18 months, respectively. Mean 24-h urinary protein decreased by 136.93, 195.84, 231.58, and 311.81 mg/24 h after intervention for 1, 3, 9, and 12 months, respectively. All the results mentioned above exhibited significant differences ($P < 0.05$) (Table 2, Table 3).

Hb_{A1C}, BP, and lipids

Compared with baseline (paired *t*-test), after intervention for 3, 6, 9, 12, and 18 months, mean Hb_{A1C} decreased by 0.39, 0.36, 0.56, 0.59, and 0.63%, respectively. Mean BP decreased by 4.67, 5.60, and 7.21 mm Hg after 1, 3, and 6 months, respectively. Mean TC decreased by 0.30, 0.51, 0.66, and 0.52 mmol/L after 1, 3, 6, and 18 months, respectively. Mean TG decreased by 0.34 and 0.54 mmol/L after 1 and 3 months, respectively. Mean LDL-C decreased by 0.33 mmol/L after 3 months. All the changes mentioned above were significant ($P < 0.05$) (Table 4).

Kidney function and relevant indices

We found that 64 out of 88 DKD patients had improved/non-worsened kidney function and relevant indices, whereas 24 patients had worse kidney function and relevant indices. We analyzed the general data and found that those patients whose kidney function worsened had a longer duration and a younger age at diag-

Table 1 Baseline of patients with DKD

Parameter		Mean (standard deviation) (range) or *n* (%)
Age (years)		57.79 (13.59) (22-89)
Male sex (*n*)		56 (63.78)
Known duration of DM (years)		11.64 (7.30) (1-40)
Known duration of nephropathy (years)		3.22 (2.85) (1-15)
Age at diagnosis of DM (years)		47.14 (13.77) (17-76)
Age at diagnosis of nephropathy (years)		55.71 (13.50) (26-77)
Known duration of follow-up (years)		13.69 (10.67) (1-48)
Glucose-lowering treatment	Oral hypoglycemic agents (*n*)	42 (47.72)
	Insulin (*n*)	63 (71.59)
	eGFR (mL/min)	41.76 (14.65) (6.77-67.36)
	Ccr (mL/min)	43.65 (17.28) (8.57-88.31)
	Scr (μmmol)	169.98 (87.95) (108-575.4)
	BUN (mmol/L)	11.48 (3.20) (4.17-24.41)
	Albuminuria (mg)	1066.79 (849.46) (300.2-3440.00)
	Hb_{A1C} (%)	7.41 (1.30) (5.2-10.8)
Dyslipidemia	TC (mmol/L)	6.44 (1.47) (4.21-12.31)
	TG (mmol/L)	2.78 (1.39) (1.59-9.60)
	HDL-C (mmol/L)	1.06 (0.23) (0.62-1.79)
	LDL-C (mmol/L)	4.48 (0.78) (3.40-6.57)
Blood pressure	SBP (mm Hg)	141.90 (19.73) (105-190)
	DBP (mm Hg)	80.59 (12.44) (60-110)

Notes: DKD: diabetic kidney disease; eGFR: estimated glomerular filtration rate; DM: diabetes mellitus; Ccr: creatinine clearance; Scr: serum creatinine; BUN: blood-urea-nitrogen; Hb_{A1C}: glycosylated hemoglobin; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 2 Variations in kidney function in patients with DKD after intervention ($\bar{x} \pm s$)

Variable	Intervention period (months)	*n*	Baseline	Intervention	*t* value	*P* value
Scr (μmol/L)	1	88	170.0±88.0	162.6±97.1	− 2.52	0.01[a]
	3	57	167.8±84.6	156.0±94.6	− 3.01	0.00[b]
	6	51	159.9±76.2	143.4±78.3	− 3.62	0.00[b]
	9	36	156.0±55.3	141.6±69.0	− 2.30	0.03[a]
	12	32	153.3±52.5	138.8±71.2	− 2.22	0.03[a]
	18	16	140.8±25.0	123.1±32.9	− 2.37	0.03[a]
GFR (mL/min per 1.73 m^2)	1	88	41.8±14.7	47.2±20.4	5.00	0.00[b]
	3	57	42.5±14.1	50.2±21.5	4.53	0.00[b]
	6	51	42.3±13.1	51.0±19.0	5.15	0.00[b]
	9	36	42.5±13.9	52.3±22.4	4.16	0.00[b]
	12	32	43.7±13.3	53.6±21.9	3.40	0.00[b]
	18	16	44.4±12.5	54.7±23.9	2.10	0.05
Ccr (mL/min)	1	88	43.7±17.3	48.5±22.4	4.98	0.00[b]
	3	57	44.2±16.8	51.3±24.5	4.46	0.00[b]
	6	51	43.6±15.7	51.6±21.9	5.12	0.00[b]
	9	36	44.8±16.4	54.3±25.9	4.14	0.00[b]
	12	32	46.1±16.3	55.6±25.8	3.36	0.00[b]
	18	16	46.9±14.9	56.8±25.0	2.22	0.04[a]
Albuminuria (mg/24 h)	1	71	1066.8±849.5	929.9±844.9	− 2.24	0.03[a]
	3	43	1153.0±883.1	957.1±906.7	− 2.30	0.03[a]
	6	39	1215.1±933.9	1064.7±1108.4	− 1.56	0.13
	9	34	1229.5±864.5	997.9±841.3	− 2.48	0.02[a]
	12	28	1326.8±914.5	1014.9±996.6	− 2.63	0.01[a]
	18	13	1462.8±883.6	1083.1±887.6	− 1.94	0.08
BUN (mmol/L)	1	85	11.5±3.2	11.3±4.0	− 0.58	0.56
	3	55	11.8±3.6	11.2±4.4	− 1.65	0.10
	6	41	11.4±3.1	10.8±4.4	− 1.15	0.26
	9	34	11.7±3.2	10.5±4.1	− 2.03	0.05
	12	29	11.5±3.0	10.5±4.0	− 1.62	0.12
	18	17	10.9±2.4	14.0±4.5	0.67	0.51

Notes: all patients took a modified Shenzhuo formula (200 mL, b.d.). Shenzhuo formula was taken 30 min before or after breakfast and supper. Scr: serum creatinine; eGFR: estimated glomerular filtration rate; Ccr: creatinine clearance; BUN: blood-urea-nitrogen. Compared with baseline, [a]$P < 0.05$, [b]$P < 0.01$.

Table 3 Rate of decrease in estimated glomerular filtration rate and slope of reciprocal serum creatinine in patients with DKD after intervention ($\bar{x} \pm s$)

Intervention period (months)	*n*	Rate of GFR decrease (mL/min per 1.73 m^2/y)	Slope of reciprocal Scr ($\times 10^6$ L·μmol^{-1}·d^{-1})
1	88	5.44	6.07
3	57	2.8	5.04
6	51	1.53	2.85
9	36	1.17	4.26
12	32	0.98	5.96
18	16	0.72	6.02

Notes: all patients took a modified Shenzhuo formula (200 mL, b.d.). Shenzhuo formula was taken 30 min before or after breakfast and supper. Scr: serum creatinine; eGFR: estimated glomerular filtration rate; Ccr: creatinine clearance.

Table 4 Variations in indices in patients with DKD after intervention ($\bar{x} \pm s$)

Variable	Intervention period (months)	*n*	Baseline	Intervention	*t* value	*P* value
Hb_{A1C} (%)	3	73	7.41±1.30	7.03±1.17	− 2.67	0.01[a]
	6	40	7.35±1.09	7.00±1.03	− 2.19	0.03[a]
	9	30	7.54±1.14	6.99±1.12	− 2.53	0.02[a]
	12	26	7.36±1.15	6.78±1.01	− 2.67	0.01[a]
	18	23	7.64±1.26	7.01±1.48	− 2.35	0.03[a]
SBP (mm Hg)	1	86	141.90±19.73	136.42±17.88	− 2.28	0.03[a]
	3	53	143.56±20.76	137.96±15.69	− 2.56	0.01[a]
	6	48	142.35±18.97	135.15±18.90	− 2.25	0.03[a]
	12	28	143.67±19.53	139.07±19.53	− 1.17	0.25
	18	14	143.07±25.11	134.00±14.73	− 1.40	0.18
DBP (mm Hg)	1	86	80.59±12.44	78.22±10.09	− 1.34	0.18
	3	53	80.73±12.21	78.32±11.95	− 1.49	0.14
	6	48	81.68±14.10	78.56±10.96	− 1.69	0.10
	12	28	81.07±13.63	76.96±9.26	− 1.76	0.09
	18	14	80.00±14.14	76.79±8.46	− 0.84	0.42
TC (mmol/L)	1	70	6.44±1.47	6.13±1.52	− 2.15	0.04[a]
	3	40	6.51±1.61	6.00±1.52	− 2.59	0.01[a]
	6	25	6.74±1.56	6.09±1.33	− 2.65	0.01[a]
	12	22	6.57±1.63	6.05±1.85	− 1.83	0.08
	18	15	6.63±0.89	6.11±1.12	− 2.28	0.04[a]
TG (mmol/L)	1	70	2.78±1.39	2.44±1.14	− 2.27	0.03[a]
	3	40	2.90±1.34	2.36±0.97	− 2.82	0.01[a]
	6	25	3.20±1.88	2.87±2.13	− 1.43	0.16
	12	22	3.43±2.01	3.01±1.67	− 1.37	0.19
	18	15	3.28±1.66	2.85±1.53	− 1.21	0.25
HDL-C (mmol/L)	1	45	1.06±0.23	1.15±0.30	2.02	0.05
	3	32	1.03±0.23	1.13±0.26	1.67	0.10
	6	18	0.99±0.17	1.03±0.21	0.67	0.52
	12	13	0.97±0.19	1.06±0.14	1.39	0.18
	18	12	0.99±0.21	1.07±0.18	1.17	0.27
LDL-C (mmol/L)	1	61	4.48±0.78	4.35±0.96	− 1.38	0.17
	3	33	4.24±0.62	3.91±0.77	− 2.54	0.02[a]
	6	19	4.34±0.79	4.08±1.13	− 1.05	0.31
	12	18	4.20±0.67	4.02±1.05	− 1.04	0.31
	18	13	4.24±0.51	4.17±0.87	− 0.43	0.68

Notes: all patients took a modified Shenzhuo formula (200 mL, b.d.). Shenzhuo formula was taken 30 min before or after breakfast and supper. Hb_{A1C}: glycosylated hemoglobin; SBP: systolic pressure; DBP: diastolic pressure; TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol. Compared with baseline, [a]$P < 0.05$.

nosis for DM and DKD than those whose kidney function improved/did not worsen. DM course was (12.49 ± 6.34) versus (11.61 ± 8.63) years, respectively. The diagnostic age of DM and DKD was (48 ± 13) versus (47 ± 13) and (58 ± 12) versus (53 ± 15) years, respectively. The relationships among kidney function, age, course of DM, and age at diagnosis is shown in Figure 1.

Scr, lipids, and BP at first visit tended to be higher in patients whose kidney function worsened than in those in which it improved/did not worsen after interven-

tion. Urinary protein and Hb_{A1C} levels were not significantly different compared with those at the first visit. The relationships among kidney damage and glycemia, BP, and lipids at the first visit is shown in Figure 2. Final-visit eGFR was significantly higher among those with improved/non-worsened kidney function compared with those with worsened kidney function. The rate of eGFR decrease was significantly lower among those with non-worsened kidney function compared with those with worsened kidney function. Patients with improved/non-worsened kidney function had better-controlled urinary protein, Hb_{A1C}, and BP (Table 5). The prevalence of uncontrolled blood glucose in patients with worsened kidney function was higher than in those with improved/non-worsened kidney function, whereas the prevalence of uncontrolled lipids and BP was not significantly different (Table 6).

rScr and relevant indices

The relationships among rScr and percentage change in urinary protein, glycemia, BP, and lipid profile is shown in Figure 3. An obvious relationships among rScr and percentage change in urinary protein was observed.

Safety analyses

The liver function and routine blood test of all the participants indicated no significant changes after intervention compared with baseline. No severe adverse events were reported.

DISCUSSION

Reversal of DKD is usually difficult once micro-albuminuria has become established. eGFR declines gradually when overt proteinuria appears. Researchers have reported decreases in eGFR of 2-10 mL/min per 1.73 m^2/y.[16-19] In this retrospective study using Shenzhuo formula to treat DKD, mean eGFR increased by 2.11 mL/min per 1.73 m^2/y, and rScr showed a declining trend (4.71 after 6 months, 10.03 after 12 months). The treatment could postpone commencement of dialysis for ≈ 5 years.[15] These results suggest that TCM could provide a new, alternative therapy for DKD.

Our data suggested that the rate of eGFR decrease, longer course of DKD, younger age at diagnosis, as well as higher levels of Scr, lipids, and BP at the first visit were

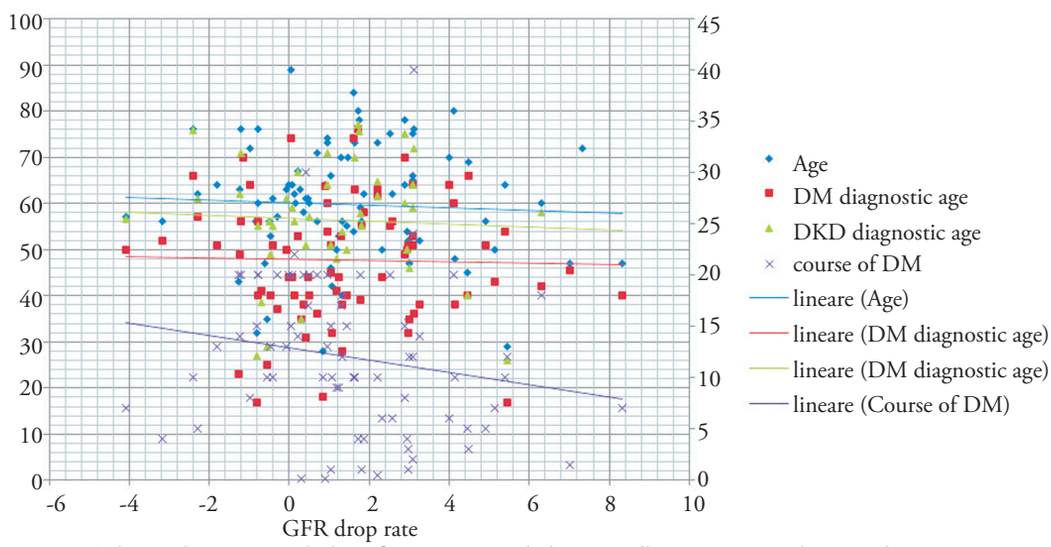

Figure 1 Relationships among kidney function, age, diabetes mellitus course, and age at diagnosis
DM: diabetes mellitus; DKD: diabetic kidney disease.

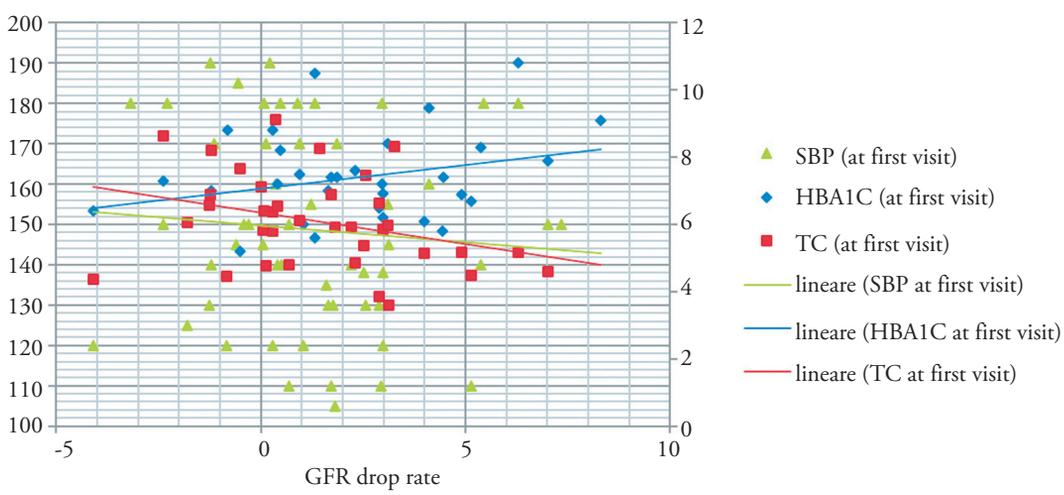

Figure 2 Relationships among kidney function and glycemia, blood pressure, and lipid profile at the first visit
SBP: systolic blood pressure; Hb_{A1C}: glycosylated hemoglobin; TC: total cholesterol.

Table 5 Analyses of related factors between patients with DKD whose kidney function worsened and those with improved/non-worsened kidney function after intervention

	Worsened		*P* value, (baseline *vs* follow-up)	Improved/non-worsened		*P* value		
	baseline	Follow-up		baseline	Follow-up	baseline *vs* follow-up	Baseline *vs* baseline	Follow-up *vs* follow-up
Male/female (*n*)	18/6		-	42/22		-	-	-
Duration of DM [*n* (%)]	12.49 (6.34)		-	11.61 (8.63)		0.656	-	-
Scr [*n* (%)]	197.64 (106.97)	188.70 (92.79)	0.250	171.52 (93.00)	149.20 (103.81)	0.000	0.263	0.106
eGFR [*n* (%)]	43.12 (15.66)	41.26 (14.34)	0.713	41.80 (25.38)	52.58 (20.99)	0.000	0.598	0.046
Rate of GFR decrease	− 0.26		-	2.37		0.000	-	-
Albuminuria [*n* (%)]	678.01 (820.49)	605.61 (909.01)	0.715	680.43 (838.32)	264.60 (425.13)	0.050	0.991	0.089
Hb_{A1C} [*n* (%)]	7.23 (1.50)	6.75 (0.77)	0.320	7.26 (1.38)	6.68 (1.31)	0.050	0.964	0.874
TC [*n* (%)]	6.62 (1.93)	5.83 (1.41)	0.199	5.89 (1.89)	5.99 (1.41)	0.815	0.232	0.740
SBP [*n* (%)]	149.76 (24.03)	140.47 (14.55)	0.078	145.33 (23.05)	136.90 (15.97)	0.020	0.501	0.421

Notes: all patients took a modified Shenzhuo formula (200 mL, b.d.). Shenzhuo formula was taken 30 min before or after breakfast and supper. Worsened: patients whose kidney function worsened; improved/non-worsened: patients whose kidney function improved/did not worsen; DKD: diabetic kidney disease; DM: diabetes mellitus; Scr: serum creatinine; eGFR: estimated glomerular filtration rate; Hb_{A1C}: glycosylated hemoglobin; TC: total cholesterol; SBP: systolic blood pressure.

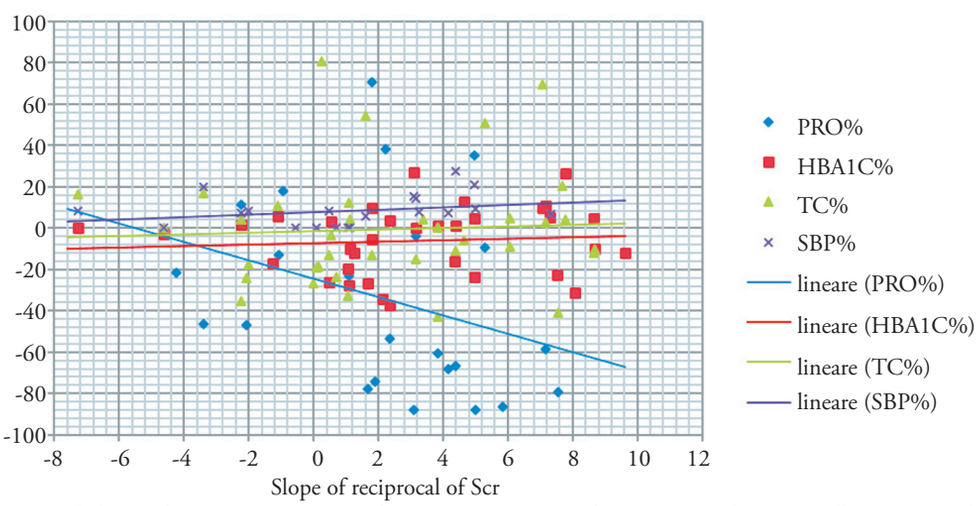

Figure 3 Relationships among reciprocal serum creatinine and percentage change in albuminuria, glycemia, BP, and lipid profile
SBP: systolic blood pressure; Hb_{A1C}: glycosylated hemoglobin; TC: total cholesterol.

Table 6 Control of glycosylated hemoglobin, blood pressure, and lipid profile in patients with DKD with worsened and improved/non-worsened kidney function after intervention [*n* (%)]

Treatment outcome	Worsen	Improved/not worsened	*P* value
Uncontrolled Hb_{A1C}	8 (60.0)	39 (51.9)	0.563
Uncontrolled blood pressure	4 (28.6)	10 (27.8)	0.607
Uncontrolled blood cholesterol	10 (44.4)	30 (46.1)	0.619

Notes: all patients took a modified Shenzhuo formula (200 mL, b.d.). Shenzhuo formula was taken 30 min before or after breakfast and supper. Worsened: patients whose kidney function worsened; improved/not worsened: patients whose kidney function improved/did not worsen; uncontrolled Hb_{A1C}: prevalence of uncontrolled glycosylated hemoglobin; uncontrolled blood pressure: prevalence of uncontrolled blood glucose; uncontrolled blood cholesterol: prevalence of uncontrolled blood cholesterol; DKD: diabetic kidney disease; Hb_{A1C}: glycosylated hemoglobin.

related to worsening kidney function. rScr and percentage change in urinary protein have been reported to affect the progression of kidney damage.[20] Well-controlled levels of glucose and lipids in the blood, as well

as BP, would benefit kidney function. Our results were limited by the small study cohort and short follow-up period, but outcomes similar to ours have been reported.[5-7,16-19] Thus, our preliminary findings suggest that Shenzhuo formula is effective against DKD.

Generation of free radicals is increased, and levels of free radical-scavenging antioxidant enzymes (e.g., superoxide dismutase) are reduced with the development of DM. Along with increases in the products of lipid peroxidation (e.g., malondialdehyde), this results in kidney tissue damage. Research has shown that Rheum palmatum can "mop up" various reactive oxygen species.[21] Huangqi (*Radix Astragali Mongolici*) and Danshen (*Radix Salviae Miltiorrhizae*) can increase the activity of superoxide dismutase, reduce the level of malondialdehyde, inhibit lipid peroxidation, and improve peroxide-induced injury in vascular endothelial cells.[22,23] A combination of these two herbs could correct the imbalance in oxidative stress and eliminate the pathologic abnormalities of DKD. Shuizhi (*Hirudo*) can protect the kidney by lowering the expression of endothelin-1.[24] Rhein can reverse the hypertrophy of proximal tubular epithelial cells induced by transforming growth factor (TGF)-β1, inhibit the synthesis of the extracellular matrix stimulated by TGF-β1,[25] and postpone PKD progression. Conversely, abnormalities in the expression of lipid metabolites participate in PKD progression.[26] Oxidized low-density lipoprotein plays an important part in this process. Research has shown that tanshinone can lower expression of the low-density lipoprotein receptor by inhibiting the signaling pathway of nuclear factor-kappa B, which can decrease the generation of macrophage foam cells.[27] Dahuang (*Radix et Rhizoma Rhei Palmati*) can also improve lipid metabolism disorders.[28]

In another retrospective study, Shenzhuo formula was used to treat 63 DKD patients with micro-albuminuria.[29] Results showed that after intervention for 3 months and 6 months, micro-albuminuria was decreased in 92.1% and 90.5% of patients, respectively. Simultaneously, levels of Hb_{A1C}, SBP, and TC were reduced significantly.

The present retrospective study showed that Shenzhuo formula can slow DKD progression and, to a certain extent, control blood levels of glucose and lipids as well as BP. Large-scale randomized clinical trials should be launched to assess the efficacy of Shenzhuo formula against DKD.

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