

CLINICAL STUDY

Role of Dongchongxiacao (*Cordyceps*) in prevention of contrast-induced nephropathy in patients with stable angina pectoris

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Abstract

OBJECTIVE: To study the preventative effects of Dongchongxiacao (*Cordyceps*) on contrast-induced nephropathy (CIN) in patients with stable angina pectoris (SAP).

METHODS: One-hundred and three SAP inpatients were divided randomly into two groups: basic treatment ($n=51$) and Dongchongxiacao (*Cordyceps*) treatment ($n=52$); corbrin capsules (3 g; t.d.s.) were used 3 days before angioplasty and 3 days after angioplasty. Serum creatinine (Scr) was assessed at the time of hospital admission and 1, 2, and 3 days after angioplasty. Values of kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL) and interleukin (IL) 18 in the kidney were detected before angioplasty and 1 day after angioplasty in the patients of both groups. The prevalence of CIN between the two groups was then compared.

RESULTS: CIN occurred in 9 of 103 patients (8.74%). The prevalence of CIN in the Dongchongxiacao (*Cordyceps*) treatment group was lower than that of the basic treatment group (5.77% vs 11.76%) but the difference was not significant ($P>0.05$). The post-procedure mean peak of Scr, post-procedure increase in Scr levels from baseline, and urine levels

of KIM-1, NGAL and IL18 after the procedure in the Dongchongxiacao (*Cordyceps*) treatment group were significantly lower than those in the basic treatment group ($P<0.05$).

CONCLUSION: Prophylactic treatment with Dongchongxiacao (*Cordyceps*) in SAP patients who undergo coronary angiography or coronary intervention could prevent contrast-induced renal impairment.

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Key words: *Cordyceps sinensis*; Angina pectoris; Creatinine; Contrast-induced nephropathy

INTRODUCTION

The incidence of contrast-induced nephropathy (CIN) is increasing owing to the increasing use of contrast media in percutaneous coronary intervention (PCI). CIN is an adverse event that results in an increased risk of morbidity and mortality during hospitalization, prolongs hospital stay, increases the incidence of chronic end-stage renal disease and increases the cost of healthcare.¹ No adjunctive medical or mechanical treatment has been proved to be efficacious in reducing the risk of CIN.² There have been few clinical trials to evaluate the role of Traditional Chinese Medicine (TCM) in the prevention of CIN.

The objective of the present study was to evaluate the role of the mushroom Dongchongxiacao (*Cordyceps*) for the prophylaxis of CIN in patients with stable angina pectoris (SAP) who underwent coronary angiography or coronary intervention.

METHODS

Ethical approval of the study protocol

The study protocol was approved by the Ethics Com-

mittee of Tianjin Nankai Hospital (Tianjin, China). All patients provided written informed consent to be included in this study.

Study population

The present study was conducted at the Department of Cardiology at Tianjin Nankai Hospital from October 2011 to September 2012. Samples were selected by using a Random Number Table. One hundred and three eligible patients with SAP were divided randomly into two groups: basic treatment ($n=51$) and Dongchongxiacao (*Cordyceps*) (DCXC) treatment ($n=52$). Subjects had to be >18 years and <80 years of age, and SAP had to conform to guidelines set by the relevant organization in China in 2007.³ The exclusion criteria were patients that were hyperpyrexemic or allergic to iodine or who had: tumors; severe heart failure; severe liver or kidney failure; disorders of the immune system; blood diseases.

Intervention

Subjects in the basic treatment group received hydration, anti-platelet agents, statins, and anticoagulant therapy. Patients in the DCXC group received corbrin capsules (Hangzhou Zhongmei Huadong Pharmaceuticals, Hangzhou, China; 3 g; p.o.; t.d.s.) for 3 days before and after angioplasty. All patients received physiological (0.9%) saline (i.v.) at $1 \text{ mL/kg}^{-1} \cdot \text{h}^{-1}$ for 6 h before, and 12 h after, contrast exposure. An interventional team carried out PCI according to standard practice using conventional guide catheters, guidewires, balloon catheters and stents via femoral or radial approaches. Decisions regarding the procedure were left to the discretion of the interventional cardiologist. All procedures were undertaken with low-osmolarity non-ionic contrast media (iopamidol, i.v.). The volume of contrast media used was recorded for all patients during catheterization.

Outcome measures

Serum levels of triglycerides (TG), total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), uric acid, and fibrinogen were assessed at the time of hospital admission. Serum creatinine (Scr) was assessed at the time of hospital admission and 1, 2, and 3 days after the procedure. Values of kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL) and interleukin (IL) 18 in urine were recorded before and 1 day after the procedure in patients of both groups.

Statistical analyses

Continuous variables and categorical variables are the mean \pm standard deviation (*SD*) and percentages, respectively. All samples were tested to ascertain if they followed a normal distribution. Comparisons between groups were undertaken using the Student's *t*-test for independent groups. Categorical variables were com-

pared using the χ^2 test or the Fisher exact test (if appropriate). $P < 0.05$ (two-tailed) were considered significant. Statistical analyses were done using SPSS ver 13.0 (SPSS, Chicago, IL, USA).

RESULTS

Baseline clinical and procedural characteristics are listed in Table 1. There was no significant difference between the two groups with regard to the general condition for CIN ($P > 0.05$). Overall, CIN occurred in 9 of 103 patients (8.74%). The prevalence of CIN in the DCXC treatment group was lower than that in the basic treatment group (5.77% vs 11.76%) but this difference was not significant ($P > 0.05$). The mean peak value of Scr and the increase in Scr level from baseline (Δ Scr) after the procedure in patients in the DCXC treatment group were significantly lower than those in the basic treatment group ($P < 0.05$). Within 3 days after the procedure, all Scr levels were lower in patients in the DCXC treatment group than those in the basic treatment group, but only on day 2 was the difference significant ($P < 0.05$) (Table 2). Within 1 day after the procedure, all urine levels of KIM-1, NGAL, and IL18 in patients in the DCXC treatment group were lower than in those in the basic treatment group ($P < 0.05$) (Table 3).

DISCUSSION

CIN is defined as a relative increase in Scr level from a baseline value of $\geq 25\%$ or an absolute increase of $\geq 0.5 \text{ mg/dL}$ within 3 days after intravascular administration of contrast medium without an alternative etiology.^{4,6} However, the change in Scr level precedes kidney damage and does not demonstrate losses in renal function in a timely manner. Recent studies have suggested that urine levels of KIM-1, NGAL and IL18 can predict the development and progression of CIN.^{7,8}

It is widely recognized that the renal ischemia induced by hemodynamic change and renal vascular constriction have major roles in the pathogenesis of CIN.⁹ However, recent studies have shown that oxidative stress plays an important part in the development and progression of CIN.^{10,11} In accordance with these observations, antioxidants such as N-acetylcysteine and ascorbic acid have been used in experimental and clinical trials to protect against CIN.^{12,13} Additional evidence of the effectiveness of an antioxidant strategy comes from a recent observation with probucol. Probuco-
col was shown to attenuate renal damage in patients who underwent coronary angiography or coronary intervention.¹⁴

The renal impairment caused by CIN belongs to the categories of Bilong, Guange, and Nidu. Contrast medium can be classified into the TCM category of "medicine poison, hot and humid, blood stasis". CIN involves the lung, spleen, kidney and other viscera. Triple

Table 1 Baseline clinical and procedural characteristics of study patients

Characteristic	Dongchongxiacao (<i>Cordyceps</i>) group (n=52)	Basic treatment group (n=51)	P value
Age (years)	62.58±3.71	63.9±4.3	0.47
Men/women	27/25	28/23	0.45
BMI	25.6±4.4	25.0±5.8	0.68
SBP (mm Hg)	138.5±17.8	141.3±18.2	0.36
DBP (mm Hg)	70.0±12.3	72.1±10.1	0.49
HR (beats per minute)	73.5±10.0	75.3±11.2	0.41
Hypertension [n (%)]	32 (61.54)	28 (54.90)	0.56
Diabetes mellitus [n (%)]	22 (42.31)	19 (37.25)	0.62
Stroke [n (%)]	12 (23.08)	10 (19.61)	0.73
Smoking [n (%)]	35 (67.31)	32 (62.74)	0.55
DOTP (mL)	246.8±49.7	248.9±48.7	0.69
VOCM (min)	70.8±8.5	65.9±10.6	0.71
Cholesterol (mmol/L)	4.8±1.1	4.9±1.10	0.28
Triglycerides (mmol/L)	1.9±1.4	2.0±1.2	0.91
LDL-C (mmol/L)	3.0±0.9	3.0±1.0	0.41
HDL-C (mmol/L)	1.2±0.3	1.2±0.2	0.85
Uric acid (μmol/L)	340.0±65.7	332.0±70.6	0.56
Fibrinogen (g/L)	3.1±0.8	3.0±1.0	0.41
LVEF (%)	59.3±11.6	61.4±12.0	0.37

Notes: BMI: body mass index; DBP: diastolic pressure; DOTP: duration of the procedure; HR: heart rate; LVEF: left ventricular ejection fraction; SBP: systolic pressure; VOCM: volume of contrast medium; LDL-C: low-density lipoprotein-cholesterol; HDL-C: high-density lipoprotein-cholesterol.

Table 2 Scr levels at baseline and after the procedure in patients from the two groups

Characteristic	Dongchongxiacao (<i>Cordyceps</i>) group (n=52)	Basic treatment group (n=51)	P value
Baseline Scr (mg/dL)	0.98±0.39	1.06±0.61	0.278
Day 1 after procedure (mg/dL)	1.05±0.38	1.16±0.65	0.192
Day 2 after procedure (mg/dL)	1.07±0.45	1.25±0.77	0.035
Day 3 after procedure (mg/dL)	1.06±0.41	1.15±0.63	0.120
Peak Scr after procedure (mg/dL)	1.15±0.47	1.32±0.75	0.044
^Δ Scr (mg/dL)	0.16±0.01	0.27±0.19	0.001
Prevalence of CIN [n (%)]	3 (5.77)	6 (11.76)	0.126

Notes: CIN: contrast-induced nephropathy; Scr: serum creatinine. warmer gasification suffocate is the key to pathogenesis of CIN. The essence of CIN belongs to the scope of deficiency syndrome. The pathogenesis specialty of CIN is deficiency origin and excess in superficiality.¹⁵ Dongchongxiacao (*Cordyceps*) comprises many amino acids and inorganic elements. It can increase the tolerance of the body to anoxia, promote proliferation of tubular epithelial cells *in vitro*, and accelerate the repair

of damaged cells.¹⁶ Dongchongxiacao (*Cordyceps*) can reduce renal vascular resistance, increase renal blood flow, and elevate the rate of clearance of insulin.¹⁷ Dongchongxiacao (*Cordyceps*) may ameliorate nephrotoxicity-induced renal dysfunction in rats via antioxidant, anti-apoptotic, and anti-autophagic mechanisms.¹⁸ Dongchongxiacao (*Cordyceps*) can also alleviate oxidative stress to delay formation of atherosclerotic le-

Table 3 Urine levels of KIM-1, NGAL and IL18 at baseline and after the procedure in patients from the two groups

Characteristic	Dongchongxiacao (<i>Cordyceps</i>) group (n=52)	Basic treatment group (n=51)	P value
Baseline KIM-1 (ng/mL)	0.72±0.06	0.69±0.05	0.365
Day 1 after procedure (ng/mL)	2.21±0.29	5.81±0.32	0.019
Baseline NGAL (ng/mL)	7.98±4.02	7.62±3.76	0.523
Day 1 after procedure NGAL (ng/mL)	39.65±8.42	67.36±11.85	0.001
Baseline IL18 (ng/L)	41.98±4.81	40.62±5.85	0.412
Day 1 after procedure IL-18((ng/L)	48.10±3.52	61.79±4.85	0.008

Notes: IL18: interleukin-18; KIM-1: kidney injury molecule-1; NGAL: neutrophil gelatinase-associated lipocalin.

sions in rats.¹⁹

We used Dongchongxiacao (*Cordyceps*) to prevent CIN. CIN occurred in 9 of 103 patients. The prevalence of CIN in the DCXC treatment group was lower compared with that in the basic treatment group. We selected ⁵¹Scr, peak Scr, and urine levels of KIM-1, NGAL and IL18 after the procedure as an index of renal function. Treatment with Dongchongxiacao (*Cordyceps*) markedly suppressed the increase in peak values of Scr and ⁵¹Scr. After the procedure, all urine levels of KIM-1, NGAL and IL18 in patients in the DCXC group were lower than those in the basic treatment group. These results strongly suggest the preventative effect of Dongchongxiacao (*Cordyceps*) on CIN in SAP patients exposed to contrast media. Dongchongxiacao (*Cordyceps*) can reinforce the kidney, replenish *Qi*, and strengthen essence. It can also correct obvious primary deficiency syndrome.

The present study had a limitation. The study cohort was small, which would have weakened the statistical power of the results. The randomized small-scale study described here showed that prophylactic treatment with Dongchongxiacao (*Cordyceps*) in SAP patients who undergo coronary angiography or coronary intervention could prevent CIN. Further studies are warranted to clarify the preventative effects of Dongchongxiacao (*Cordyceps*) on CIN.

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