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CLINICAL STUDY

# Effect of Dongchongxiacao (*Cordyceps*) therapy on contrast-induced nephropathy in patients with type 2 diabetes and renal insufficiency undergoing coronary angiography

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## Abstract

**OBJECTIVE:** To study the protective effects of Dongchongxiacao (*Cordyceps*) (DCXC) on contrast-induced nephropathy (CIN) in patients with type 2 diabetes and renal insufficiency undergoing coronary angiography.

**METHODS:** A total of 120 patients with type 2 diabetes whose estimated glomerular filtration rate (eGFR) was ≤ 60 mL/min·1.73 $m^2$, were divided randomly into three groups, basic treatment group ($n$ = 41), standard DCXC therapy group ($n$ = 39, 2-g corbrin capsules, 3 times/d, 3 days before and after angiography), and intensive DCXC therapy group ($n$ = 40, 3-g corbrin capsules, 3 times/d, 3 days before and after angiography). Serum creatinine (Scr) and eGFR were assessed at the time of admission to hospital, and on days 1, 2 and 3 after angiography. Urine neutrophil-gelatinase-associated-lipocalin (NGAL), kidney injury molecule-1 (KIM-1) and interleukin-18 (IL-18) were measured before angiography and at day 1 after angiography for all patients. The primary end point was the prevalence of CIN. The secondary end point was a 25% or greater reduction in eGFR.

**RESULTS:** CIN occurred in 11 of 120 patients (9.17 %). The prevalence of CIN was lower in the DCXC treatment groups than in the basic treatment group ($P < 0.05$), with a more significant decrease in the prevalence of CIN in the intensive DCXC therapy group ($P < 0.01$). Compared with the basic treatment group, a lower proportion of patients in the DCXC treatment groups had an eGFR decrease of 25% or greater ($P < 0.05$); patients with an eGFR decrease of 25% or greater accounted for an even lower proportion in the intensive DCXC therapy group ($P < 0.01$). Within 1 day of the procedure, urine levels of KIM-1, NGAL and IL-18 in patients in the intensive DCXC therapy group were lower than those in the basic treatment group and standard therapy group ($P < 0.05$).

**CONCLUSION:** DCXC treatment may protect against CIN in patients with type 2 diabetes and renal insufficiency undergoing coronary angiography, with intensive DCXC therapy being more effective.



**Key words:** Cordyceps sinensis; Diabetes mellitus, Type 2; Coronary angiography; Contrast-induced nephropathy

## INTRODUCTION

The prevalence of contrast-induced nephropathy (CIN) is rising due to the increased use of contrast media in percutaneous coronary intervention. CIN is an adverse event that results in increased health resource usage, prolongs hospital stay, and increases short- and long-term mortality, even after adjustment for other

co-morbidities. CIN has become the third leading cause of hospital acquired acute renal failure.[1,2] The risk factors for CIN include chronic kidney disease, the volume of contrast agent, diabetes, advanced age, sex, gender, congestive heart failure, anemia, and dehydration.[3] The prevalence of CIN in patients with diabetes and preserved renal function is only moderately increased or even comparable with the healthy population; however patients with diabetes and renal insufficiency have a significantly increased risk of CIN.[4] Once CIN develops, hydration status optimization is the only proven strategy to treat it, and no other adjunctive medical or mechanical treatment specifically targets CIN. The main goal for clinicians is to find preventative measures.[5] There have been few clinical trials to evaluate the role of traditional Chinese medicine in preventing patients with diabetic nephropathy from developing CIN. The objective of the present study was to evaluate Dongchongxiacao (*Cordyceps*) (DCXC) as prophylaxis for the development of CIN in patients with type 2 diabetes and renal insufficiency undergoing coronary angiography.

## METHODS

### *Ethical approval of the study protocol*

The study protocol was approved by the Ethics Committee of Tianjin Nankai Hospital (Tianjin, China). All patients provided written informed consent prior to inclusion in the study.

### *Study population*

The present study was conducted at the Department of Cardiology at Tianjin Nankai Hospital from October 2012 to January 2014. Patients with type 2 diabetes, whose estimated glomerular filtration rate (eGFR) was ≤ 60 mL/min/1.73 $m^2$, were enrolled into the current study. Patients > 18 years and < 80 years of age met the inclusion criteria. Samples were selected using a random number table. A total of 120 eligible patients were divided randomly into three groups, basic treatment group ($n$ = 41), standard DCXC therapy group ($n$ = 39, 2-g corbrin capsules, 3 times/day, 3 days before and after angiography), and intensive DCXC therapy group ($n$ = 40, 3-g corbrin capsules, 3 times/d, 3 days before and after angiography). Type 2 diabetes was defined as any of the following: fasting plasma glucose level greater than 7.0 mmol/L or a random plasma glucose level of 11.1 mmol/L or greater. Repeated measurement of fasting or random plasma glucose levels on subsequent days was used to confirm the diagnosis of diabetes. The eGFR was calculated using the modification of diet in renal disease (MDRD) equation.[6] The exclusion criteria included patients who were hyperpyrexic or allergic to iodine or who had one of the following: tumors; severe heart failure; severe kidney failure; severe liver failure; disorders of the immune system; blood diseases.

### *Intervention*

All patients were given intravenous isotonic saline (0.9%) at a rate of approximately 1 mL/kg per hour for 6 h before, and 12 h after, contrast exposure. All patients received aspirin (100 mg/d was administered indefinitely), clopidogrel (600 mg loading dose, followed by 75 mg/d for at least 12 months), rosuvastatin (10 mg/d), metoprolol (23.75 mg/d), benazepril (10 mg/d), fondaparinux (2.5 mg/d for at least 5 days), furosemide (20 mg/d). Patients in the DCXC groups received corbrin capsules (Hangzhou Zhongmei Huadong Pharmaceuticals, Hangzhou, China). The use of aspirin (Bayer Pharmaceuticals, Beijing, China), clopidogrel (Sanofi Pharmaceuticals, Hangzhou, China), statins (Pfizer Pharmaceuticals, Shanghai, China), beta-blocker (Astrazeneca Pharmaceuticals, Wuxi, China), anticoagulation agents (Sanofi Pharmaceuticals, Hangzhou, China), angiotensin converting enzyme inhibitors (Novartis Pharmaceuticals, Beijing, China), and diuretics (Tianjin LiSheng Pharmaceuticals, Tianjin, China), was left to the discretion of the cardiologist according to clinical requirements or guideline recommendations. 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), blood glucose, and glycosylated hemoglobin, were measured at the time of hospital admission. Serum creatinine (Scr) and eGFR were measured at the time of hospital admission and 1, 2 and 3 days after the procedure. The concentration of urine neutrophil-gelatinase-associates-lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and interleukin-18 (IL-18) in urine were detected before and one day after the procedure for patients in three groups. The urine levels of NGAL, IL-18 and KIM-1 were determined by enzyme-linked immunosorbent assay (ELISA) in the clinical laboratory of Tianjin Nankai Hospital.

### *Statistical analyses*

Continuous variables and categorical variables are expressed as the mean ± standard deviation ($\bar{x} \pm s$) and percentages, respectively. All samples were tested to ascertain if they followed a normal distribution. Categorical variables were compared using the $\chi^2$ test or the Fishers exact test where appropriate. One-way analysis of variance was applied for the analysis of continuous variables among the three groups. Two-tailed $P$ values of $P < 0.05$ were considered statistically significant. Statistical analyses were performed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA).