Clinical Study of Xiongshao Capsule (芎芍胶囊) in Preventing Restenosis after Coronary Intervenational Treatment

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ABSTRACT  
Objective: To evaluate the effect of Xiongshao Capsule (XS, 芎芍胶囊) in preventing clinical and angiographic restenosis after coronary angioplasty or/and stenting. 
Methods: The total of 108 coronary heart disease patients with successful coronary angioplasty or/and stenting were randomly divided into the control group (55 cases, routine treatment) and the XS group (53 cases, routine treatment combined with XS). The recurrence of angina, clinical end-point events, changing of blood-stasis syndrome score (BSSS) and coronary angiography within 6 month after coronary angioplasty or/and stenting were observed. 
Results: Follow-up angiography was performed in 42 patients including 18 cases in the XS group (restenosis was observed in 7 patients) and 24 cases in the control group (restenosis was observed in 17 patients), there was significant difference between the occurrence of restenosis in XS and that in control group \((P<0.05)\). The occurrence of clinical end-point events (death, nonfatal target lesion myocardial infarction, coronary artery bypass graft surgery, or repeat target-vessel angioplasty) in the XS group (18.8\%) was significantly lower than that in the control group (40\%) \((P<0.05)\). The recurrent angina was observed in 13 cases in the XS group, there was significant difference as compared with 27 cases in the control group \((P<0.05)\). There was also remarkable significance for the difference of base-line and follow-up BSSS between groups \((P<0.01)\). Logistic multivariate stepwise regress analysis and multivariate regress analysis of the related factors with restenosis confirmed by coronary angiography showed that, the base-line BSSS and the difference of base-line and follow-up BSSS were important influencing factors on the occurrence of restenosis after interventional treatment \((P<0.05)\). 
Conclusion: XS could markedly reduce the occurrence of angiographic restenosis, clinical end-point events and recurrent angina, improve condition of blood-stasis after coronary angioplasty or/and stenting. The severity of blood-stasis syndrome was an important influencing factor on the occurrence of restenosis. It still needs to be further demonstrated by large-scale, double-blinded, randomized and controlled study.

KEY WORDS  
Xiongshao Capsule, angioplasty, stent, restenosis

Since percutaneous transluminal coronary angioplasty (PTCA) and/or coronary stenting can reconstruct coronary blood circulation without thoracotomy, it has become one of the main effective treatments for coronary heart disease. However, restenosis is the major limitation of the long-term success of this procedure. Despite numerous trials of pharmacological interventions, including antiplatelet agents, heparin, coronary vasodilators, angiotensin-converting enzyme inhibitor, and fish oils, the frequency of restenosis has not diminished since the inception of PTCA. Coronary stents are the only devices that have shown a reduction in the incidence of restenosis, although it is still about 22\% to 29\%\(^{(1)}\). How to prevent restenosis after coronary interventional treatment has become one of the major problems in area of cardiology.

The pathogenesis of restenosis is complex and not fully understood. According to theory of traditional Chinese medicine (TCM), restenosis is a syndrome of blood stasis. Treatment with XS is a direct method to eliminate blood stasis. Many randomized controlled trials of XS have been conducted in China to treat restenosis after PTCA and coronary stenting, with encouraging results.
Enosis falls into the category of blood-stasis syndrome. Our previous study (one of the Eighth Five-Year Projects) have shown that Concentrated Xuefu Zhuyu Pill (a classic formula of promoting blood circulation to remove stasis) had certain effect in preventing restenosis after PTCA. Xiongshao Capsule consists of the main active position of Ligusticum chuanxiong Hort. and Paeonia lactiflora Pall (both are the main ingredients in Concentrated Xuefu Zhuyu Pill). In previous study, we have demonstrated that XS could inhibit intimal hyperplasia and pathological vascular remodeling after balloon dilation in a porcine coronary injury model, as well as proliferation of smooth muscle cells induced by endothelin in vitro. Based on this, we further observe its clinical effect in preventing restenosis after coronary angioplasty and/or stenting in patients with coronary heart disease.

METHODS

Diagnostic Criteria

The diagnostic criteria of coronary heart disease refers to related criteria on ischemic heart disease of WHO. The diagnostic criteria of blood-stasis syndrome consults the criteria formulated by Speciality Committee of Promoting Blood Circulation to Remove Stasis in Chinese Association of Integrated Chinese and Western Medicine. The symptoms and signs of blood stasis including angina, purple and dark tongue or with ecchymosis, purple and dark lip and gingiva, sublingual varices, uneven pulse or slow pulse with regular or irregular intervals were scored according to methods introduced by literature. Since some patients in this study was acute myocardial infarction, the item of symptom (angina) replenished “acute myocardial infarction” and the score was 15.

Patient Selection and Inclusion and Exclusion Criteria

Patients were eligible for inclusion if they were 35 to 75 years old, had angina, and/or objective evidence of myocardial ischemia, or acute myocardial infarction, and there was at least one significant (> 50%) stenosis that was documented on a recent coronary angiogram, and with successful PTCA and/or coronary stenting. Patients were excluded if they met any of the following criteria: insulin-dependent diabetes, severe uncontrolled hypertension, severe renal or hepatic function impairment, participation in another study.

The total of 108 patients were enrolled between January 1999 and February 2000 in The Third Hospital Affiliated to Peking University, Health Science Center and Anzhen Hospital Affiliated to Capital University of Medical Sciences, they were randomized into routine western medicine treatment group (control group) and routine treatment plus Xiongshao capsule group (XS group). The 53 patients in the XS group comprised 41 males and 12 females, aged 38 – 73 years, 55.3 ± 9.0 years on average, 22 cases diagnosed unstable angina (UA), 8 cases stable angina (SA), 22 cases acute myocardial infarction (AMI). The 55 patients in the control group comprised 46 males and 9 females, aged 36 – 75 years, 58.7 ± 9.1 years on average, 28 cases diagnosed UA, 5 cases SA, 21 cases AMI. The baseline characteristics of the patients between the two groups showed insignificant statistic difference (P > 0.05), therefore, they were comparable.

Treatment Methods

Standard balloon angioplasty was performed through the transfemoral approach according to standard techniques. After written informed consent was obtained, patients were randomized to receive routine western medicine treatment or routine treatment combined with XS (consisting of Chuanxingol and paeoniflorin and produced by Chinese Medicine Institute of Suzhou Medical College. Each capsule contains 0.25 g medicinal powder which corresponds to 7.5 g crude herbs. Three times a day and 0.5 g each time. Batch No. 980501), which begins from the day of inter-