Effect of Shuxinyin (舒心饮) on In-Stent Restenosis after Coronary Artery Stenting*

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ABSTRACT  Objective: To evaluate the effect of anti-platelet regimens and its combination with Shuxinyin (SXY, 舒心饮, ) on in-stent restenosis after stent implantation. Methods: Forty-four patients with successful stent implantation in a coronary artery were randomly assigned to the treated group (n = 20) and the control group (n = 24). The treated group received SXY and anti-platelet therapy. The control group were treated with anti-platelet regimens only. Platelet activation was assessed before and immediately after the stenting by flow cytometry, the expression of P-selectin (CD62P) and glycoprotein(GP) IIb/III a receptor. It was reassessed on the 30th day after stenting. Plasma fibrinogen (Fg) and C-reaction protein (CRP) were measured by biuret and laser scattering turbidimetry respectively at the same time. Observation was made on the scoring of the symptoms of Qi deficiency syndrome, Qi-Yin deficiency syndrome and blood stasis syndrome in the two groups. Differences between groups were compared. Results: Compared with the control group, combination with SXY and anti-platelet therapy was remarkable in reducing plasma CRP (P < 0.05), and also with the tendency to decrease plasma Fg, GP II b/III a and CD62P. It could also evidently decrease the scoring of Qi-Yin deficiency syndrome, Qi deficiency syndrome and blood stasis syndrome after stenting (P < 0.05, 0.01, 0.01) respectively. Follow-up survey found 40% relapse of angina pectoris with 4 cases of in-stent restenosis proved by angiography in the treated group. But the relapse of angina pectoris in the control group was 67% with 2 cases of myocardial infarction (MI), 7 cases of in-stent restenosis proved by angiography and one death. Conclusions: Combination with SXY and anti-platelet regimens can prevent stent thrombosis and in-stent restenosis after stent implantation, and it seems superior to anti-platelet therapy only.

KEY WORDS  angioplasty, stenting, in-stent restenosis, platelets, glycoprotein, Shuxinyin

People had done a great deal of work to prevent coronary artery in-stent restenosis (ISR). Drug-coated and drug-eluted stent and β, γ ray brief radiation therapy within lumen of blood vessel are hotspot at present. The preventive function of platelet derived growth factor inhibitor, antioxidant, valsartan and promoting blood circulation to remove stasis herbs on ISR have showed efficacy to a certain extent. But there was no breakthrough on clinical progress. The purpose of this study was to evaluate the effect of the combination of Shuxinyin (SXY, 舒心饮, invigorating Qi and nourishing Heart-Yin, promoting blood circulation to remove stasis) with anti-platelet regimens on ISR after stent implantation.

METHODS

Diagnosis Standard

Indications and contraindications for stenting refer to literature¹-³; criteria for successful stent implantation and in-stent restenosis refer to literature³; criteria for increased risk for subacute stent thrombosis⁴; criteria for coronary heart disease (CHD) typing⁵; Scoring method and diagnosis criteria for Qi-Yin deficiency syndrome and Qi deficiency syndrome according to literatures⁵,⁶ and syndrome differentiation experience from Professor LIN Zhong-xiang, the scoring: none 0, mild 1, moderate 2, severe 3. Scoring method and diagnosis criteria for blood stasis syndrome according to literature⁷ and syndrome differentiation in CHD according to literatures⁶,⁷ and syndrome differentiation experience from Pro-

* Project supported by College Foundation of Shanghai Educational Committee (99C66)
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Professor LIN Zhong-xiang, it was performed.

**Patients Data**

Forty-four patients with successful implantation of stent in their coronary artery from Zhongshan Hospital Affiliated to Fudan University from June 2000 to January 2001, were randomly by means of sealed envelopes assigned to the treated group \((n = 20)\) and the control group \((n = 24)\). Demographic data of the patients were: male 37 cases, female 7 cases, the mean age of treated group was 60.55 \(\pm\) 8.92 years \((58 - 72\) years\), control group 66.04 \(\pm\) 9.37 years \((59 - 75\) years\), the mean illness course of the treated group was 4.78 \(\pm\) 1.23 years \((0.5 - 8\) years\), the control group 4.96 \(\pm\) 1.45 years \((1 - 10\) years\). There were 28 cases with smoking, 36 cases hypertension, 33 cases hypercholesterolemia, 9 cases diabetes mellitus (DM), 9 cases stable angina, 16 cases unstable angina, 13 cases acute myocardial infarction (AMI), 11 cases old MI, 8 cases previous reconstruc-
tive vascular treatment (RVT). There was in-
significant difference in age, illness course and clinical feature of patients in both groups.

**Treatment Methods**

Coronary artery stent procedure and use of intravascular ultrasonography (IVUS) and rotablator during stenting refer literature \(^3\).

Drug therapy: All patients were pretreat-
ed with 100 mg aspirin \((50\) mg each tablet, made in Hunan Zhengya Company, batch No. 000210) once a day and 250 mg ticlopidine \((250\) mg, made in Tianjin Xinxin Pharmaceutical Company, batch No. 000103) twice daily for 3 days before stenting. Patients would chew 500 mg aspirin immediately before stenting. Heparin 10000 u \((12500\) u, Shanghai 1st Biochemical Pharmaceutical Factory, batch No. 000119) was used during stenting. Patients would receive additional 2000 u heparin if the operation time prolonged for 1 hour. According to the randomization schedule, patients were attributed to anti-platelet regimen and SXY, starting immediately after the procedure. Treated group: aspirin 100 mg once a day basically lifelong administered, ticlopidine 250 mg twice per day for 4 weeks and SXY 10 ml each time, 3 times a day, lasted for 6 months. Western medicines given to the control group were the same as in the treated group excepting SXY. SXY \((\) crude drug content: 1.8 g/ml, made in Shanghai Longhua Hospital, batch No. 001012) is composed of red sage, milkvetch, kudzuvine, rehmannia and prepared rehmannia, wolfberry, loranthulus mulberry mistletoe and lilyturf.

**Equipments**

Digit subtraction angiocardiography \((BH 2000)\), express injection meter \((ANGIOMAT 6000)\), IVUS meter \((GDM-17EOL)\) and rotablator \((RC5000)\) were provided by Shanghai Zhongshan Hospital Catheter Department.

**Observation Index**

Clinical index: It includes smoking, hyper-
tension, hypercholesterolemia, DM, stable angina, unstable angina, AMI, old MI, pre-
vious RVT.

Angiography index: Number and localiza-
tion of vessel stenosis, stent localization, stent number, stent title, maximal inflation pres-
sure, etc.

Laboratory index: glycoprotein \((\) GP \(\) II 
\(b/III a\) and P-selectin \(\) CD\(_{62}P\): Peripheral venous blood samples were taken from patients with a short venous catheter inserted into a forearm vein just before immediately following and on the 30th day after stenting. Platelet activation was assessed by flow cytometry \((FCM, \) Bec-
ton Dickinson, FACS Calibur\)) measurement of expression of \(\) GP \(\) II \(b/III a\) and \(\) CD\(_{62}P\) at the same time. Becton Dickinson antibody includ-
ed \(\) GP \(\) II \(b/III a\) a fluorescein isothiocyanate \((\) FITC, \) \(\) CD\(_{62}P\)-phycoerythrin \((\) PE, \) \(\) CD\(_{61}\)-peridinin chlorophyll protein \((\) PerCP\)) and Mouse \(\) IG\(_3\)-PE. We acquired 10000 activation-
independent platelet events by FCM every time and displayed activated platelets stained with \(\) CD\(_{61}\)PerCP with side scatter versus \(\) CD\(_{61}\) live gate selected as two-color dot plots, statis-