

## Application of Shuangshen Tongmai granule in restenosis after percutaneous coronary intervention (PCI)

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### Abstract

**Objective:** To investigate the application of Shuangshen Tongmai granule in restenosis after percutaneous coronary intervention (PCI). **method:** 100 patients diagnosed as acute coronary syndrome and undergoing PCI in the emergency department of Weifang Hospital of traditional Chinese medicine were collected. 50 cases in the case-control group and 50 cases in the treatment group were established according to the treatment methods. The treatment group was treated with Shuangshen Tongmai granule + routine treatment after PCI, and the control group was treated with routine treatment after PCI. The clinical effect was observed 6 months after operation, the incidence of restenosis was determined by coronary angiography, and IL - 6 , TNF-  $\alpha$  and MMP-9 were detected by ELISA. And observe whether there are adverse reactions. **Results:** compared with the control group, the treatment group had good clinical efficacy, low incidence of restenosis, IL - 6 and TNF-  $\alpha$ , MMP-9 and other inflammatory factors decreased without obvious adverse reactions. **Conclusion:** Shuangshen Tongmai granule can effectively prevent and treat restenosis after PCI and adjust inflammatory factors. Reduce the recurrence rate of angina pectoris after PCI without increasing various adverse events.

### Keywords

Shuangshen Tongmai granule, Restenosis after PC, IL - 6, TNF-  $\alpha$ , MMP-9.

### 1. Introduction

Restenosis after coronary intervention is the main factor affecting the prognosis of patients. PCI can save the lives of patients with acute myocardial infarction after coronary intervention, but in stent restenosis (ISR; the incidence is about 20 ~ 30%) is the main factor affecting the prognosis of patients, and reducing the restenosis rate is a hot issue in the medical field [1].

ISR is caused by vascular elastic retraction, negative remodeling, thrombosis at the damaged site, proliferation and migration of smooth muscle cells and excessive proliferation of extracellular matrix. It involves immune inflammatory response, intimal proliferation and extracellular matrix remodeling [2]. At present, the effect of conventional western medicine on patients with restenosis after PCI is difficult to say and ideal. Traditional Chinese medicine and its preparations have unique advantages in the prevention and treatment of this disease, and have received strong attention. Shuangshen Tongmai granule is composed of ginseng, *Ophiopogon japonicus*, *Angelica sinensis*, *Astragalus membranaceus*, *Salvia miltiorrhiza* and *Ligusticum chuanxiong*. This experiment was to evaluate the efficacy and safety of shuangshentongmai granule after six months after PCI, which provided clinical case support and experimental data support for the prevention and treatment of restenosis after PCI, provided evidence for the clinical application of the combined treatment of traditional Chinese and Western medicine, and reduced the rate of restenosis after PCI and improved the quality of life of patients, Reducing the burden on families and society has broad application prospects.

## 2. Materials and methods

### 2.1. Case selection.

Collect 100 patients diagnosed as acute coronary syndrome with PCI in the emergency department of Weifang Hospital of traditional Chinese medicine from September 1, 2020 to August 30, 2021, and formulate strict inclusion and exclusion criteria. Inclusion criteria: coronary heart disease patients aged 30-79 years who underwent PCI and successful intracoronary stent implantation (interventional vessel lumen stenosis less than 20%, TIMI blood flow grade III), the number of stents was 1-3, and there was angina pectoris and / or ECG ST-T change ischemic basis (new or transient ST segment depression  $\geq 0.1$  MV, T wave inversion  $\geq 0.2$  MV. Or ST segment was significantly elevated, or even arched upward). Exclusion criteria: Patients with vascular disease after ISR or CABG after PCI, more than 3 stents, EF < 35%, uncontrolled severe hypertension (> 180/110 mm Hg), severe left main artery disease, severe valvular heart disease, diabetes, patients with severe primary diseases such as liver, kidney, hematopoietic system, nervous system, psychosis and malignant tumor, who refuse to sign informed consent and participate in other clinical trials.

### 2.2. Implementation plan.

According to the treatment methods, 50 cases in the case-control group and 50 cases in the treatment group were established. The treatment group was treated with Shuangshen Tongmai granule + routine treatment after PCI, and the control group was treated with routine treatment after PCI. Shuangshen Tongmai Granules (ginseng 20g, Salvia miltiorrhiza 20g, Astragalus 15g, Ophiopogon japonicus 10g, Ligusticum chuanxiong 10g, angelica 10g) were made into granules by Weifang Hospital of traditional Chinese medicine in Shandong Province, 1 dose / D, washed with warm water for 6 months. The patients' eating habits and lifestyle remained basically unchanged during the medication period.

### 2.3. Index monitoring

#### 2.3.1 Clinical efficacy judgment

A significant effect: the main symptoms such as chest pain and chest tightness disappear or significantly reduce, and the ECG returns to normal. B effective: the main symptoms such as chest pain and chest tightness are alleviated or reach relevant standards, and the ECG is generally normal. C ineffective: the main symptoms such as chest pain and chest tightness have not improved, and the ECG is the same as that before treatment. D aggravation: the main symptoms such as chest pain and chest tightness and the changes of ECG ST-T were more serious than those before the experiment. In the judgment of comprehensive curative effect, if the symptoms and ECG curative effect are inconsistent, the result with low curative effect shall prevail.

2.3.2 Determine the incidence of restenosis by coronary angiography. ISR criteria for restenosis: restenosis is defined as restenosis within 5 mm adjacent to the stent and / or 50% or more of the diameter of the vascular lumen in the stent.

2.3.3 IL - 6 and TNF were detected by ELISA-  $\alpha$ , MMP-9。

2.3.4 Whether there are adverse reactions, such as bleeding, liver and kidney function examination.

### 2.4. Draw conclusions through statistical analysis.

To evaluate the efficacy and safety of Shuangshen Tongmai granule after PCI.

### 3. Results

#### 3.1. Comparison of efficacy criteria for recurrent angina pectoris

The main symptoms of angina pectoris such as chest pain and chest tightness disappeared after PCI in the treatment group and the control group, and the ST-T changes of the original ECG were significantly improved or normal. Clinical observation was conducted based on the main symptoms and ECG. There was significant difference in the recurrence of angina pectoris between the treatment group and the control group ( $P < 0.05$ ). The recurrence rate of angina pectoris after PCI in the observation group was significantly reduced. See Table 1.

Table 1 Comparison of symptom relief rate of angina pectoris between the two groups 6 months after operation

Group	n	Significant effect	Effective	Ineffective	Aggravation	Total effective rate (%)
Treatment group	50	45	2	3	0	94
Control group	50	35	1	13	1	72

#### 3.2. 2.2 Coronary angiography observation

Coronary angiography was performed in all cases within 6 months after PCI. In the observation group, individual cases were treated with PCI (such as LAD)

There was no ISR in the original site, but new stenosis occurred in other vessels and sites (such as RCA). The restenosis rate was 6%, which was significantly lower than 20% in the control group. There was significant difference between the groups ( $P < 0.05$ ). See Table 2

Table 2 Comparison of effects on in stent restenosis between the two groups

Troup	n	Restenosis	Percentage (%)
Treatment group	50	3	6
Control group	50	10	20

#### 3.3. Comparison of inflammatory factor levels between the two groups before and after treatment

Before treatment, there was no significant difference in the level of inflammatory factors between the two groups ( $P > 0.05$ ). After treatment, the levels of inflammatory factors in both groups decreased, and the levels of inflammatory factors in the study group were significantly lower than those in the control group ( $P < 0.05$ ), as shown in Table 3.

Table 3 Comparison of inflammatory factor levels between the two groups before and after treatment

Group	n	IL - 6		TNF- $\alpha$		MMP-9	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Treatment group	50	13.01 $\pm$ 5.26	6.68 $\pm$ 3.91	62.01 $\pm$ 17.37	33.98 $\pm$ 11.21	194.36 $\pm$ 31.71	174.42 $\pm$ 25.43
Control group	50	13.22 $\pm$ 4.28	9.22 $\pm$ 3.28	61.98 $\pm$ 17.45	22.65 $\pm$ 8.25	192.28 $\pm$ 31.72	57.93 $\pm$ 20.15

t	0.012	3.305	0.008	4.437	0.012	4.209
p	> 0.05	< 0.05	> 0.05	< 0.05	0.990	0.000

### 3.4. Adverse events

There was no significant difference in the incidence of adverse events between the two groups ( $P > 0.05$ ). Although 12 cases of bleeding occurred, they were all black stool, no obvious bleeding phenomena such as hematemesis, subcutaneous blood stasis and nasal bleeding. After omeprazole and other treatment, the upper symptoms disappeared and Shuangshen Tongmai Granules were not stopped. Three cases of non fatal myocardial infarction occurred in the control group and were discharged after conservative treatment in cardiology. See Table 4. There were no significant abnormalities in liver and kidney functions in the two groups.

Table 4 statistics of major adverse events

Group	n	Hemorrhage	Non-fatal myocardial infarction	death
Treatment group	50	4	0	0
Control group	50	8	3	0

## 4. Discussion

### 4.1. Discussion on the mechanism of restenosis after PCI for coronary heart disease

The mechanism of coronary stent restenosis is multifaceted: the target vessel injury response caused by coronary stent implantation is characterized by vascular endothelial cell exfoliation and rupture; Restenosis and elastic retraction; Vascular remodeling is related to intimal hyperplasia and smooth muscle cell proliferation.

### 4.2. Analysis of TCM Intervention ideas and methods for restenosis after PCI

There is no record of "restenosis after percutaneous coronary intervention" in the literature of traditional Chinese medicine, but according to its syndrome classification, clinical manifestations, treatment principles and methods, evolution and prognosis, it belongs to the category of "chest arthralgia and heartache" in traditional Chinese medicine. There are many descriptions of chest arthralgia in traditional Chinese medicine. "Su Wen · discussion on the method of storing Qi" has "self sick, chest pain, full hypochondriac branches, hypochondriac pain, pain between the back and shoulder, and pain in both arms". It is a description of the pain parts of chest arthralgia. The pain parts can be in the chest, hypochondriac, back and inner sides of both arms, which is consistent with the pain parts described in modern science; Wang Qingren of the Qing Dynasty treated the disease with Xuefu Zhuyu Decoction and clarified that its pathogenesis was qi stagnation and blood stasis [3].

The basic pathogenesis of restenosis after PCI is blood stasis. Multi-target intervention of traditional Chinese medicine is used to intervene in the treatment of restenosis after PCI.

### 4.3. Discussion on TCM theory of Shuangshen Tongmai granule

Shuangshen Tongmai granule is composed of ginseng, *Ophiopogon japonicus*, *Angelica sinensis*, *Astragalus membranaceus*, *Salvia miltiorrhiza* and *Ligusticum chuanxiong*. This prescription is based on the effects of ginseng tonifying heart qi and *Salvia miltiorrhiza* activating blood circulation and removing blood stasis. It is a king's medicine; The minister used *Astragalus membranaceus* to replenish qi and Yang, *Angelica sinensis* to activate blood and replenish blood; *Ligusticum chuanxiong* can promote blood circulation and Qi, *Ophiopogon japonicus* can nourish yin and generate fluid, which are adjuvants. The combination of six herbs plays the

effects of Supplementing Qi and nourishing Yin, activating blood circulation and dredging collaterals, which can improve the symptoms of chest arthralgia and heartache, especially the chest arthralgia and heartache with deficiency of Qi and Yin. Modern pharmacological experiments show that ginsenoside is an effective chemical component of ginseng. Ginsenoside can protect myocardium by increasing SOD activity in serum, reducing MDA content, improving anti lipid peroxidation ability and scavenging oxygen free radicals. The protective effect of *Ophiopogon japonicus* on myocardium may be related to increasing SOD activity in cardiomyocytes, inhibiting lipid peroxidation and improving fatty acid metabolism. *Astragalus* injection can regulate the immune state of the body. *Ligusticum chuanxiong* has the effects of dilating blood vessels, increasing blood flow, preventing abnormal relaxation and contraction of coronary arteries, anti platelet aggregation, inhibiting the release of oxygen free radicals and relieving vasospasm of vascular smooth muscle<sup>[4-5]</sup>.

This study systematically observed the patients after PCI from the aspects of coronary angiography and inflammatory factors. The results show that the observation group can not only reduce the restenosis rate after PCI, but also effectively improve the inflammatory factors. The recurrence rate of angina pectoris symptoms 6 months after operation is significantly reduced, safe and reliable without obvious adverse reactions. Statistics show that this effect is better than that of the western medicine control group, There was no significant difference in adverse events (death, nonfatal myocardial infarction, fatal massive bleeding, epistaxis, gingival bleeding, skin ecchymosis) between the two groups.

In conclusion, the ingredients of this prescription have long-term clinical application and no toxic and side effects. Referring to the previous scientific research results, it is supported by both clinical practice and laboratory scientific research conclusions, and conforms to the principle of traditional Chinese medicine theory. It has safety, effectiveness and reliability, and is worthy of clinical application.

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