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Effect of Salvia miltiorrhiza on cytokines in patients with unstable angina pectoris

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ABSTRACT

Objective: To investigate the effect of Salvia miltiorrhiza (SM) on cytokines in patients with unstable angina pectoris (UAP). **Methods:** A total of 50 cases of UAP patients from October 2014 to October 2015 as the research object, randomly divided into treatment group and control group, two groups were treated with conventional bed rest, oxygen inhalation, ECG, nitroglycerin intravenous infusion, beta blockers, aspirin, statins, antiplatelet drug therapy, the treatment group on the basis of salvianolate 200 mg+5% glucose 250 mL (neutralization amount of 0.9% sodium chloride was used in patients with diabetes or glucose insulin) intravenous drip, 1 times/d, two groups were treated for 2 weeks; detected before and after treatment of plasma pregnancy associated plasma protein A (PAPP-A), soluble cell differentiation antigen ligand (sCD40L) and the level of serum interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) level. **Results:** after the end of treatment, the treatment of PAPP-A and sCD40L levels decreased than the control group, which had statistical significance; treatment group IL-1, IL-6, TNF-α level lower than control group, which had statistical significance. **Conclusion:** On the basis of conventional treatment combined with salvianolate in treatment of UAP, can inhibit platelet aggregation, control inflammatory reaction, stabilize atherosclerotic plaque, reduce risk of cardiovascular events in therapeutic effect, it is worth clinical promotion.

1. Introduction

Unstable angina pectoris (UAP) is a common clinical disease, good hair in the elderly and serious state of coronary heart disease, the disease between stable angina and acute myocardial infarction, its pathological basis for impaired endothelial function of coronary artery and atherosclerotic plaque formation and rupture, thrombosis and vascular obstruction, clinical manifestations of acute myocardial ischemia in clinical syndrome, onset is sudden, extremely easy to progress for acute myocardial infarction (AMI), resulting in sudden death in patients[1,2]. Research shows that serum cell factor in atherosclerotic plaques in expression and predict coronary heart disease risk events are important, so treatment should reduce inflammation and improve endothelial function, in order to reduce the incidence of cardiovascular events[3]. The study confirmed that the effect of Salvia miltiorrhiza on vascular endothelial function, expression of inflammatory factors and blood rheology in patients with UAP was significantly improved[4,5]. To this end, the author selected from October 2014 to October 2015 treated UAP patients, the use of Salvia miltiorrhiza to treat the treatment of acid salt, in order to observe its impact on the related cytokines.

2. Clinical data

2.1. General information

A total of 50 cases of patients with UAP were selected as the object of study, all patients are in line with the UAP diagnosis and treatment recommendations[6]; before admission angina within 48 h of onset > 1 times above, attack wave inverted T electrocardiogram associated with two or more adjacent precordial

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ST segment depression >0.1 mV, down; And the removal of severe heart, lung, liver, renal insufficiency, excluding patients with severe hypertension, infection, autoimmune, malignant tumor and other diseases, and were randomly divided into treatment group and control group. Treatment group of 25 cases, male 14 cases, female 11 cases; age 45-69 years old, average (61.5±5.7) years old; primary labor type angina 8 cases, deterioration of labor type angina 10 cases, 7 cases of angina pectoris. The control group of 25 cases, male 15, female 10; age 46 to 70 years old, average (62.3±6.0) years old; primary labor type angina 9 cases, deterioration of labor type angina 10 cases, 6 cases of angina pectoris. There was no statistical significance (P>0.05) in the two groups.

2.2. Method

Two groups were routine bed rest, oxygen inhalation, ECG, nitroglycerin intravenous continuous pumping, beta blockers, aspirin, antiplatelet agents, statins treatment, treatment group on the basis of salvianolic acid salt (Shanghai Lvgu pharmaceutical, Chinese medicine quasi word Z20050249) 200 mg+5% glucose solution 250 mL (diabetic patients with 0.9% sodium chloride solution or glucose plus and the amount of insulin) intravenous drip, 1 times/D. The course of treatment was 2 weeks in two groups.

2.3. Observation index

Before and after treatment collected fasting venous blood 5 mL, after centrifugation using ELISA method for the determination of plasma levels of PAPP-A and sCD40L levels; using ELISA to detect serum IL-1, IL-6, TNF- α level; kits were provided by Wuhan boster company, strict according to kit instructions.

2.4. statistical processing

To represent the measurement data by (Mean ± SD), Using t test, Count data by using the χ^2 test, the analysis of SPSS 18 software, P<0.05 was statistically significant.

3. Results

3.1. Comparison of plasma PAPP-A and sCD40L levels before and after treatment

Before treatment, plasma levels of PAPP-A and sCD40L were not statistically significant (P>0.05). After treatment, the levels of sCD40L and PAPP-A in the treatment group were lower than those in the control group, and there was statistical significance (P<0.05). See Table 1

3.2. The levels of IL-1, IL-6 and TNF- α were compared before and after treatment

Before treatment, the serum levels of IL-1, IL-6 and TNF- α were not statistically significant (P>0.05). After treatment, the levels of IL-1, IL-6 and TNF- α in treatment group were lower than those in control group, and there was statistical significance (P<0.05). See table 2.

Table 1.
The plasma levels of PAPP-A and sCD40L were compared between the two groups before and after treatment (Mean±SD).

Group	n	PAPP-A(pg/mL)		sCD40L(ng/L)	
		Before treatment	After treatment	Beforetreatment	After treatment
Treatment	25	23.35±2.32	11.12±1.34*	512.15±27.35	325.66±28.71*
Control	25	22.98±3.22	18.55±2.71	507.85±39.56	442.17±25.51

Note: compared with the control group,*P<0.05.

Table 2.
Comparison of the levels of IL-1, IL-6 and TNF- before and after treatment in two groups(ng/L, Mean±SD).

Group	n	IL-1		IL-6		TNF- α	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Treatment	25	107.22±30.41	78.42±15.65*	354.15±55.58	262.28±75.62*	515.41±132.55	359.71±102.31*
Control	25	106.58±31.71	95.47±22.15	353.55±54.40	313.07±55.65	514.75±128.63	451.25±98.77

Note: compared with the control group *P<0.05.

4. Discussion

UAP is one of the most critical patients with coronary atherosclerotic heart disease. It is more common and dangerous, and it is easy to progress to acute myocardial infarction. Coronary blood flow and myocardial need the contradiction between the blood is the root of the onset of the disease, coronary artery blood supply can not meet the myocardial metabolism, resulting in ischemia and hypoxia, the formation of anaerobic glycolysis and metabolism in the formation of pyruvic acid, performance, chest tightness, chest pain and other symptoms, therefore coronary artery spasm or narrow is lead to reduced myocardial blood supply contradictions[7]. UAP clinical changes fast, the instability of atherosclerotic plaque core lipid filled, interrupt coronary spasm, unstable rupture or thrombosis, activation of inflammatory factors, the coronary artery flow fall sharply in a short period of time, the collateral circulation to less than effective compensation, leading to myocardial ischemia or small necrotic foci, systemic or local cardiac inflammation reaction, and then evolved to acute myocardial infarction[3,8]. Studies have shown, aggravate the UAP and arterial wall immune inflammation and atherosclerosis plaque rupture and thrombus formation, synthesis of a variety of cytokines, therefore the clinical to modulate inflammatory process plays an important role in the inflammatory factor drugs became the focus of the study[9].

PAPP-A is metal protease of insulin like growth factor (IGF), by

cleaving IGF-4 enable IGF-1 biological function enhancement, promote vascular endothelial cells and smooth muscle cells apoptosis and extracellular matrix remodeling and release of inflammatory factors, promote the development of atherosclerosis[10]. The study showed that the expression of PAPP-A was increased in the serum and arterial plaque of atherosclerosis patients, which was most prominent in the most vulnerable plaque site, and it was considered that PAPP-A had significant correlation with plaque rupture[11]. SCD40L can promote the proliferation of endothelial cells and the formation of plaque neovascularization. It plays an important role in the formation of atherosclerotic plaque, which is more fragile and prone to rupture and thrombosis. In addition, sCD40L plays a decisive role in vascular inflammatory response, which can stimulate smooth muscle cells and vascular endothelial cells, promote plaque rupture, thrombosis and acute myocardial infarction[12].

IL-1 is atherosclerotic plaque in important proinflammatory cytokine, upregulation of vascular wall adhesion molecules and cytokines expression level, enhance the adhesion ability, the role in vascular smooth muscle cells and endothelial cells through mediated by IL-6, TNF alpha expression, promote cell proliferation, injury of endothelial function, inhibit the release of the vasodilator, intimal hyperplasia leading to the formation of atherosclerosis[13]. IL-6 by vascular endothelial cells and inflammatory cells secretion, is a multi effect of proinflammatory cytokines, through multiple pathways involved in atherosclerosis formation and the process of plaque rupture, induced macrophage produce interferon gamma and TNF-α cytokines and inflammatory reaction ring formation, cause the spot to block lipid core increases, the fibrous cap thinning, leading to plaque instability[14]. TNF-α can directly damage the vascular endothelial cells, enhance leukocyte adhesion and endothelial cell activation, promote platelet derived growth factor and the synthesis and secretion of IL-1, IL-6 and other cytokines[15].

Unstable angina pectoris (UAP) belongs to the category of traditional Chinese medicine chest, pathogenesis is blood stasis, and vascular wall integrity, blood related properties and hemodynamics[16]. Depside salt from Salvia miltiorrhiza is effective component extracted from Salvia miltiorrhiza, which magnesium lithospermate B content of more than 80%, with anti myocardial ischemia and protect the ischemic and reperfusion injury, anti platelet aggregation and adhesion, improve hemodynamics and regulate blood lipid metabolism and anti atherosclerotic plaque stability, promote angiogenesis and improve endothelial cell functions involved in inflammation[17]. Studies have shown that the effects of Salvia miltiorrhiza polyphenols on UAP, stable angina and so on are good[18]. This study shows that after the end of treatment, the treatment of PAPP-A and sCD40L levels decreased than the control group, which had statistical significance (P<0.05); treatment group IL-1, IL-6, TNF-α level lower than control group, which had statistical significance (P<0.05). The inhibition of the expression of, IL-1, IL-6, TNF-α, and the inhibition of the inflammatory response of atherosclerotic plaque of atherosclerosis plaque, stable plaque and decrease the incidence of cardiovascular events were showed by inhibiting the expression of PAPP-A, sCD40L and.

In on the basis of conventional treatment combined with salvianolate in treatment of UAP, can inhibit platelet aggregation, inflammatory reaction process control, stabilize atherosclerotic plaque, reduce risk of cardiovascular events in therapeutic effect, it is worth clinical promotion.

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