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Protective effects of Ginseng mixture on myocardial fibrosis in rats

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ABSTRACT

Objective: To explore the protective effects of ginseng mixture on myocardial fibrosis (MF) in rats. **Methods:** A total of 60 Wistar rats were randomly divided into control group without modeling operation, and another 4 groups using subcutaneous injections of isopropyl adrenaline for 10 d to set up the MF model: model group with saline lavage treatment after modeling, captopril group with captopril lavage, ginseng mixture group A and group B with low and high dose mixture treatment respectively. After treatment for 14 d, abdominal aorta and myocardial tissue were extracted to observe the pathological morphological changes and heart weight index in each group. **Results:** The left ventricular weight and heart heavy index of captopril group and group B were significantly lower than that of model group and group A (P<0.05); Model group and group A showed a higher hydroxyproline (Hyp) content in myocardial tissue than the control group and lower catalase (CAT) activity than control group (P<0.05); captopril group and group B showed a lower Hyp content and higher CAT activity compared with group A and model group (P<0.05), a significantly lower level of serum glutathione peroxidase (GSH-PX) and CAT and a higher level of serum creatine kinase, lactate dehydrogenase and H_2O_2 in model group and group A were observed compared with the control group (P<0.05). A higher level of GSH-PX and CAT and a lower level of creatine kinase, lactate dehydrogenase and H_2O_2 in captopril group and group B were observed compared with group A and model group (P<0.05); and histopathological examination showed that in captopril group and group B, secretion of collagen fiber was significantly inhibited and myocardial injury was significantly lighter than that of model group. **Conclusions:** Ginseng mixture plays a protective effect on myocardium by inhibiting antioxidant process of MF.

1. Introduction

Myocardial fibrosis (MF) often occur in the process of myocardial remodeling hypertensive heart disease, rheumatic heart disease and other diseases after myocardial infarction with a rising trend of fatality rate[1-3]. MF is a heart disease caused by collagen component change under increasing cardiac tissue collagen fibers due to all kinds of pathogenic factors[4]. Its occurrence and development accompanied by myocardial interstitial network reconfiguration and decreased cardiac function, can cause function decline of myocardial contraction and relaxation, seriously affecting the patients health[5]. The pathogenesis of MF is not entirely clear, its regulation also involves the renin-angiotensin aldosterone system, a variety of cytokines, cell apoptosis, and other systems. Studies have shown that[6], the oxidative stress plays an important role in the process of MF pathogenesis, therefore, reversal of MF by regulating oxidative stress is of great significance. Clinical treatment of anti myocardial fibrosis rely mainly on angiotensin-converting enzyme inhibitors (ACEI), AT1 receptor antagonist, endothelin receptor antagonist and β-blockers, of which the receptor antagonists of ACEI, AT1 are most commonly used yet with long-term side effects, and these antagonists can't completely reverse myocardial fibrosis process[7]. With the deepening of the motherland

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medicine research on MF pathogenesis, great progress has been made in the treatment of MF. On the theory basis of "cut the nut, conducting qi and blood in order to harmonize them" ("Plain question. To really theory"), ginseng mixture can promote blood circulation to remove the blood stasis, and activate the blood circulation. To observe the improvement of MF by ginseng mixture, the author selected Wistar rat to set up MF model treated with ginseng mixture lavage. The heart weight parameters, myocardial biochemical indexes and tissue morphology were observed to analyze the protection mechanism of ginseng mixture against MF in rats.

2. Materias and methods

2.1. Experimental animals

A total of 60 clean level Wistar rats aged 2 months, male and female unlimited, (216.1±12.3) g, were provided by the Animal Experiment Center, and bred with free food and water at room temperature (22±1) ℃, the experimental process handling of animals was strictly followed by the regulations of experimental animals administration.

2.2. Instrument and reagent

Automatic biochemical analyzer (Shanghai Schindler MedicalInstrument Company); Olympus BH- type 2 microcope (Japan); BI-2000 immunohistochemical analysis system; Isopropyl adrenaline hydrochloride injection (1 mg, batch number: H31021344), produced by Shanghai Hefeng Pharmaceutical Co., LTD.; Ginseng mixture provided by the traditional Chinese medicine center; Captopril (12.5 mg/tablet, batch number: H31022986) manufactured by Shanghai Squibb Co., LTD.; reagents including catalase (CAT), glutathione peroxidase (GSH-PX), hydroxyproline (Hyp), creatine kinase (CK), hydrogen peroxide (H_2O_2) and lactate dehydrogenase (LDH) were provided by Nanjing Institute of Biological Engineering.

2.3. Modeling

Isopropyl epinephrine injection was injected to set up the MF model as follows: subcutaneous injection 20.0 mg/kg for the first time, 10.0 mg/kg on the 2nd day, 5.0 mg/kg on the 3rd day, 3.0 mg/kg from 4th to 10th day. During the modeling period, rats were provided with free access to food and water. Modeling criteria: each 2 rats were randomly killed after modeling for 10 d, myocardial tissue was extracted for histological observation, once the microscopic result shows hyperplasia of a large number of collagen fibers between the endocardial myocardial fibers, the MF model was regarded as set up.

2.4. Grouping

A total of 60 Wistar rats were randomly divided into control group without modeling operation, and another 4 groups had subcutaneous injections of isopropyl adrenaline for 10 d to set up the MF model: model group with 2 mL saline lavage treatment after modeling for 2 d, captopril group with captopril lavage (0.45 mg/2 mL) after modeling for 2 d, ginseng mixture group A and group B with low (20 g/kg) and high dose (80 g/kg) mixture treatment respectively. After treatment for 14 d, abdominal aorta and myocardial tissue were extracted for observing the pathological morphological changes and heart weight index in each group. The lavage treatment were conducted for 14 consecutive d (1 time/d).

2.5. Observation indexes

At the end of the treatment, the rats were kept fasting for 24 h, anesthesed using intraperitoneal injection of 3% sodium pentobarbital, 5 mL blood was extracted from abdominal aorta for observing the changes of CAT, GSH-PX, Hyp, CK, H_2O_2, LDH and other indexes, operation process were strictly followed by the kit manual. After the extraction of blood, atrium, atrial, adipose tissue and valves were eliminated followed by PBS washing, ventricular weight/body weight index was calculated according to the heart weight and body weight. Then the left ventricular myocardium was fixed using 10% formalin followed by gradient ethanol dehydration, and embedding and sectioning using paraffin, dyeing, Masson collagen fiber was HE dyed for histopathological observation.

2.6. Statistical analysis

SPSS19.0 statistical software was used, measurement data were expressed with (mean ± sd), and analyzed by t test. $P<0.05$ was regarded as significant difference.

3. Results

3.1. Comparison between groups in the rat heart weight index

The left ventricular mass index and ventricular weight/body weight index of model group, captopril group and groups A and B were significantly higher than that of control group ($P<0.05$); left ventricular mass index and ventricular