Journal of Traditional Chinese Medical Sciences (2017) 4, 82–91

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Effect of acupuncture on the genetic expression of myocardial endothelin-1 and atrial natriuretic peptide in rats with stress-induced prehypertension

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Received 30 September 2016; received in revised form 20 November 2016; accepted 30 November 2016
Available online 14 January 2017

KEYWORDS
Acupuncture;
Myocardial damage;
Endothelin-1;
Atrial natriuretic peptide

Abstract *Objective:* To explore the protective effect of acupuncture against myocardial injury in rats with stress-induced prehypertension (SIPH) by observing the genetic expression of myocardial endothelin-1 (ET-1) and atrial natriuretic peptide (ANP).
Methods: Thirty-six Wistar rats were randomized into three groups: the control group, model group, and model + acupuncture (AP) group (n = 12 rats per group). During the 11-day modeling period, the model group and the model + AP group experienced plantar electric stimulation in combination with noise exposure, and daily acupuncture intervention was applied simultaneously in the model + AP group; the control group did not experience modeling or acupuncture. Systolic pressure (SP) was measured the day before modeling began, and on the 3rd, 5th, 7th, 9th, and 11th day after modeling initiation. On the 12th day, histopathological observation of the left ventricle was made with hematoxylin-eosin staining and quantitative genetic expression of myocardial ET-1, and ANP was tested by quantitative real-time polymerase chain reaction (PCR).
Results: SP was higher in the model group than the control group on the 3rd, 5th, 7th, 9th, and 11th days (all $P < .01$). SP in the model + AP group was lower than that in the control group on the 5th and 7th days (respectively, $P = .008$, $P = .002$) and on the 9th and 11th days ($P = .029$, $P = .039$). Hematoxylin-eosin staining showed normal myocardial cellular structure in the

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Peer review under responsibility of Beijing University of Chinese Medicine.
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http://dx.doi.org/10.1016/j.jtcms.2017.08.004

control group. The model group showed disordered arrangement of cardiac cells with morphological changes in some nuclei, including enlargement or dissolution; there was also infiltration of inflammatory cells and proliferation of collagen fibers. In the model + AP group, most of the myocardial cells were normally structured, and only part of the cells had morphological changes with enlarged nuclei or dissolution. Real-time PCR showed that expression of ET-1 and ANP mRNA in the model group was greater than the control group (respectively, $P = .024$, $P = .000101$). The model + AP group had lower expression of ET-1 and ANP mRNA compared with the model group (respectively, $P = .033$, $P = .043$).

Conclusion: Acupuncture may lower blood pressure and downregulate the genetic expression of myocardial ET-1 and ANP in SIPH rats, suggesting a protective effect of acupuncture against myocardial damage.

Introduction

Research suggests that there is a close correlation between prolonged stressful stimulus and the onset/progression of hypertension.[1] Cardiovascular hyperfunction such as tachycardia and a rise in blood pressure might occur in animals exposed to prolonged stress, which tends to progress gradually into stress-induced hypertension (SIH). Along with the increasing pressure in modern society, the prevalence of SIH has been increasing markedly in those engaged in prolonged mentally stressful work. The pathogenesis of SIH involves a prehypertensive phase in the development from a physiological state to a pathological one.[2]

The concept of prehypertension was first proposed in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure in 2003.[3] Prehypertension refers to the stage where the systolic pressure (SP) is 120—139 mmHg and/or the diastolic pressure is 80—89 mmHg.[3] A large amount of epidemiological evidence has suggested that the prevalence of prehypertension was 30%—50% in some countries,[4,5] and that prehypertension is closely correlated with morbidity in cardiovascular diseases.[6—9] In the prehypertensive stage, there can be potential subclinical damage to target organs and alterations of the expression of corresponding genes and proteins.[8,10]

The heart is the target organ most vulnerable to hypertension, with the most common morbidity being hypertensive myocardial hypertrophy.[11] Previous research has found that abnormal vascular endothelial function already exists in rats with stress-induced prehypertension (SIPH), with impaired cardiac function and pathological changes such as myocardial injury.[10] Therefore, prompt prevention of SIPH will effectively suppress the occurrence of hypertension, alleviate injury to the vascular endothelium and myocardium, and protect target organs such as the heart.

Acupuncture is an alternative therapy to drugs, with the prominent advantages of convenience, security, and less incidence of adverse reactions; it has been used to treat numerous cardiovascular diseases, including hypertension.[12] Prophase studies conducted by our group have found that acupuncture may effectively lower the blood pressure of SIPH rats,[9] but its potential effect on alleviating myocardial injury in SIPH rats remains unclear. Therefore, we have designed the present study to observe the genetic expression of endothelin-1 (ET-1) and atrial natriuretic peptide (ANP) in SIPH rats using real-time PCR, and to assess whether acupuncture exerts a cardioprotective effect in SIPH rats.

Materials and methods

Animals and grouping

Thirty-six SPF 9-week-old, male Wistar rats each weighing (220 ± 30) g were purchased from Beijing Weitong Lihua Experimental Animal Technology (Beijing, China). During the experiment, the ambient temperature and humidity were controlled at (24 ± 1)°C and 50%, respectively, with a cycle of 12-hour light and 12-hour darkness. All rats were fed ad libitum. All animal-related procedures were approved by the Ethics Committee of Experimental Animals of Beijing University of Chinese Medicine (BUCM-3-2016040201-2003). The 36 rats were divided into the control group, the model group and the model + acupuncture (model + AP) group (n = 12 rats per group) by a random number table.

Model preparation

The model of SIPH rats was made by the combination of plantar electric stimulation and exposure to noise. Rats from the model group and the model + AP group were kept in a cage (22 × 22 × 26 cm) of a maze (type MG-2; Huaibei Zhenghua Biological Instrument, Anhui, China) from 8 am to 10 am and from 2 pm to 4 pm every day. The plantar electric stimulus was created by a copper gate located at the bottom of the cage that was charged with an intermittent alternating current. The electrical discharge occurred randomly once every 2—25 seconds and persisted for 5 seconds each time with a voltage of 30 V (controlled by a computer). A buzzer was used to produce noise (80—100 db). Rats in the control group were kept in an identical cage during the same two periods of model preparation each day; however, they did not receive