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Protection of Shuxuetong combined with aspirin against cerebral ischemia/reperfusion injury through ameliorating coagulation and fibrinolysis system

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ABSTRACT Objective To explore the influence of the combination of Shuxuetong (SXT) and aspirin on coagulation and fibrinolysis system of rats.

Methods Suture method was applied to establish focal cerebral ischemia-reperfusion injury models in rats. A total of 50 SD rats were randomly divided into sham group, middle cerebral artery occlusion/reperfusion (MCAO/R) group, aspirin (10 mg/kg) group, SXT (0.6 mL/kg) group, and SXT (0.6 mg/kg) + aspirin (10 mg/kg) group. The neurological deficits were assessed according to Longa's grade 5 scoring method. The cerebral edema was determined by measuring the content of water in brain tissue. The volume of cerebral infarction was observed by 2,3,5-Triphenyltetrazolium chloride (TTC) staining. Blood plasma was collected by abdominal aortic method to test maximum platelet aggregation rate and four blood coagulation. Cerebral blood flow velocity (CBFV) was measured by transcranial Doppler sonography. Blood SXT concentration was measured by radioimmunoassay.

Results The results showed that the combination of SXT and aspirin had a better effect on improving neurological deficits, alleviating cerebral edema, and decreasing cerebral infarct size. Compared with the sham group, the model group showed a significant increase in neurological deficits, cerebral edema, and cerebral infarct size. The combined treatment significantly decreased these indices. The results of coagulation function tests showed that compared with the model group, the combined treatment significantly decreased platelet aggregation and the content of coagulation factors. The combination treatment significantly increased the blood flow velocity in the middle cerebral artery. The blood SXT concentration in the combined group was significantly higher than that in the aspirin-treated group.

Conclusion SXT combined with aspirin can effectively improve cerebral ischemia-reperfusion injury by improving coagulation and fibrinolysis system, and the maximum concentration of platelets and fibrin concentration, and improve coagulation function and fibrinolysis system.

Keywords: aspirin; blood coagulation; fibrinolysis system; Shuxuetong

1. Introduction

Stroke is a growing epidemic around the world, and ranks to second leading cause of death over past 60 years. The risk factors of stroke are the same as those of atherosclerosis, but the relative incidences of the various risk factors keep changing with time, cultural and environmental factors. Ischemic stroke accounts for about 80% of the stroke, and shows an increasing trend year by year. As a common and frequently-occurring disease, the mechanism study of cerebrovascular disease and clinical research is of great significance. The current treatments of ischemic stroke include thrombolytic therapy (Lansberg et al., 2012), recommended t-PA or urokinase, has a sharp treatment time window (Muchada et al., 2014), and only a small number of patients could gain the benefits. The clinical commonly used drugs in thrombolytic therapy (Diedler et al., 2005; Qu et al., 2014). Moreover, lumbrukinase, a natural thrombin inhibitors, which is the main components are lumbrukinase and hirudin, which is the strongest natural thrombin inhibitors (Yang ZC, et al., 2006; Li Z, 2008). SXT displays multiple pharmacological effects on cerebral disease, including antithrombotic activity, anticoagulant activity, fibrinolytic activity, anti-inflammatory effect, and neuroprotective activity, and can attenuate myocardial ischemia-reperfusion injury by improving coagulation and fibrinolysis system. Several attempts have shown that the combination of aspirin and TCMs improved the treatment effects for ischemic stroke (Huang et al., 2016; Chang et al., 2015; Hassan et al., 2015). Combination therapy may provide greater protections against subsequent stroke than single drug alone. In the present study, the effects and possible mechanisms were investigated following posttreatment of SXT, aspirin and their combination (S&A) in middle cerebral artery occlusion and reperfusion (MCAO/R) model in rats.

2. Materials and methods

2.1 Animals

Healthy male Sprague–Dawley rats (280-300 g) of SPF class were provided by Beijing Vital River Laboratory Animal Technology Co., Ltd. (Beijing, China), and the license number is SCXK (Beijing) 2012-0001. All animal experiment was approved by the Institutional Animal Experiment Committee of Peking Union Medical University (approval ID SYXX (Beijing) 2007-0023) and conducted in accordance with the National Institutes of Health Guidelines on the Use and Care of Animals. Animals were raised in the Institute of
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