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Original article

Effects of Scrambling trumpet Creeper flavone on transient cerebral ischemia model (TIA) in rats

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ABSTRACT

To investigate the effects of Scrambling Trumpet Creeper flavone on neurological function score, brain tissue lesion and related biochemical indexes in rat TIA model. Methods: TIA model was induced by tail vein injection of t-butanol (t-BHP). The rats in each administration group were given large, medium and low dose of Scrambling Trumpet Creeper flavone 0.1% CMC suspension, nimodipine and Yangxueqingnao particles group 0.1% CMC suspension, model group and blank group fed the same volume 0.1% CMC. Once a day, continuous administration of 7d. On the 3rd and 6th day after administration, t-BHP was injected into the tail vein, and then placed in a sealed 1 L jar. After 10 min of hypoxia, the neurological function score (NDS) was performed. After the first 2 days of TIA administration, the hem rheology was measured immediately after 1 h of administration, and blood rheology was measured immediately after the administration of blood, blood clotting, hematocrit, hematocrit and whole blood viscosity. After HE is staining to observe the pathological changes of hippocampus and cortex in the left-brain tissue. (LDH) and adenosine triphosphate (ATP) were measured. The right brain tissue of the cerebral cortex was observed. The expression of lactate (LD), lactate dehydrogenase (LDH) Fibroblast growth factor (FGF) and insulin growth factor (IGF) were detected by immunohistochemistry.

Results: Compared with the blank group, the coagulation time of the model rats was significantly shortened. The red blood cell deformation index was significantly decreased. Erythrocyte sedimentation rate, hematocrit, plasma viscosity, whole blood viscosity, erythrocyte rigidity index and blood sedimentation equation K value were significantly increased; LD content increased significantly, and LDH, ATP enzyme activity decreased significantly. The positive expression of FGF and IGF in the cortical area had a trend of increasing.

Conclusion: The Scrambling Trumpet Creeper flavone significantly improved the indexes of whole blood rheology; the energy metabolism of cerebral ischemia was increased, and the positive expression of neurotrophic factor in cortex was significantly increased.

1. Introduction

TIA occurs several hours or days before the onset of stroke. Signs before the onset including signs of sudden speech loss, blurred speech, physical paralysis, limb weakness, recurrent episodes, etc (Chen, 2016). TIA is a precursor of cerebral infarction (Jia et al., 2015). Early diagnosis and treatment of TIA is important to prevent ischemic stroke. Current clinical use drugs and other chemical drugs to protect cell function and structural, but the mechanism of action is single, and Combination of drugs affected by many factors (Zhang, 2016; Muhammad et al., 2017). Traditional Chinese medicine treatment of TIA has a long history. Enhance blood circulation, heat detoxification in the prevention and treatment of cerebral ischemia is an important rule (Wang et al., 2017; Sarfaz et al., 2017). Modern studies have shown that Campsis grandiflora can enhance blood circulation (Yang and Zhu, 2014; El-Meligy et al., 2017), anti-inflammatory and other pharmacological effects. There is no report on the Scrambling

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Trumpet Creeper flavone in the treatment of TIA. In this paper, we observed the effects of Scrambling Trumpet Creeper flavone on the neurological function score and brain histopathological changes of TIA rats, as well as the changes of blood rheology and the energy metabolism, and discussed the protective effect on the brain. The clinical application of the Scrambling Trumpet Creeper Flavone Prevention and treatment of transient ischemic attack to provide experimental basis.

2. Experimental material

2.1. Drugs and reagents

Scrambling trumpet Creeper flavone were supplied by the Analytical Chemistry Laboratory of Henan College of Traditional Chinese Medicine with a content of 66%, batch number 20101016; Nimodipine, Shandong Xinhua Pharmaceutical Company Limited, batch number 1107091; *tert*-butyl hydroperoxide (t-BHP), China Pharmaceutical Group Chemical Reagent Company Limited, batch number T20110303; CMC (sodium carboxymethyl cellulose), Tianjin Fu Chen Chemical Reagent Factory, batch number 20090826; Yangxue Qingnao Granule, Tianjin Tianshi Li Pharmaceutical Co., Ltd., batch number 110725; LD assay kit, Nanjing Bioengineering Research Institute, batch number 20111107; ATPase assay kit, Nanjing Institute of Biotechnology, batch number 20111206; Coomassie Brilliant Blue Protein Assay Kit, Nanjing Institute of Bioengineering, batch number 20111202.

2.2. Animals

Wistar rats, male, clean grade, 260–280 g, 105, by the Hebei Experimental Animal Center, Certificate No. 1110122. Laboratory certificate number: SYXK (Yu) 2010-001. Feeding environment is 22 ± 2 °C, 55 ± 5% relative humidity, 12 h light/dark cycle. Free drinking water.

2.3. Laboratory apparatus

UV-2000 UV Visible Spectrophotometer, Unocal (Shanghai) Instrument Co., Ltd., LBY-N6K automatic hemorheological, Beijing Puli Health Instrument Co., Ltd.

3. Experimental methods

3.1. Administration and modeling (Seema et al., 2016)

105 waster rats weighing 280–300 g were randomly divided into 7 groups: blank group, model group, positive control group (Yangxueqingnao particles group and nimodipine group), large, medium and small dose of Scrambling Trumpet Creeper flavone group, each group of 15. In addition to the blank group, the other six groups were rat TIA model, and 6 model groups were fed large, medium and small doses of Scrambling trumpet Creeper flavone suspension (200 $mg{\cdot}kg^{-1}$, 100 $mg{\cdot}kg^{-1}$, 50 $mg{\cdot}kg^{-1}$, using 0.1% CMC to make a concentration of 20 $mg{\cdot}ml^{-1}$, 10 $mg{\cdot}ml^{-1}$, 5 $mg{\cdot}ml^{-1}$, 1 ml/100 g), a Yangxueqingnao particles suspension (1000 $mg{\cdot}kg^{-1}$, using 0.1% CMC to make a concentration of 2 $mg{\cdot}ml^{-1}$, 1 ml/100 g), nimodipine (20 $mg{\cdot}kg^{-1}$, using 0.1% CMC to make a concentration of 2 $mg{\cdot}ml^{-1}$, 1 ml/100 g). Model group and blank group were fed with the same volume of 0.1% CMC.

Modeling methods: When the rats were first induced, the tail vein injection concentration of 0.11 $mol{\cdot}L^{-1}$ *tert*-butyl hydroperoxide 5.2 $ml{\cdot}kg^{-1}$, after 10 min, placed in 1 L wide mouth bottle, the mouth of bottle was sealed with vaseline and the rats were anoxic for 10 min. Then taking out the rats, proceeding the behavioral scores and using a stopwatch to measure the attack latencies of the rats. When the rats were second induced, injected with 0.154 $mol{\cdot}L^{-1}$ t-butylperoxide 5.2 $ml{\cdot}kg^{-1}$ from the tail vein, after 10 min, then placed in 1 L wide-mouth jar to be sealed, and the rats were anoxic for 10 min. Then taking out the rats, proceeding the behavioral scores and using a stopwatch to measure the attack latencies, during 1 h the number and cumulative time of attack. Each wide mouth bottle was equipped with 25 g sodium lime and sodium lime was wrapped with gauze to avoid direct contact with the rats. Sodium lime can absorb CO_2 from rats. In the experiment, each rat used new sodium lime, and was to ensure adequate, no recycling. TIA induction was performed on the 3rd and 6th day after rats were continuous intragastrical administered for 1 h. During the experiment, the animals condition was observed at any time and the dead animals were removed and the mortality rate was calculated.

Detection of indicators: the second time in the second day after TIA administration of 1 h, immediately after the eye blood, measured blood clotting time. Heparin anticoagulation, used to measure the whole blood viscosity, hematocrit, erythrocyte sedimentation rate, plasma viscosity and other blood rheology indicators.

The brain was separated in the ice tray. The left side was quickly fixed in 10% formalin solution for HE is staining and immunohistochemistry. 10% of the right brain homogenate, used to determine the LD content, LDH, ATP enzyme content.

3.2. Statistical analysis

The data were analyzed by SPSS 17.0 for windows statistical package. The data were analyzed by means of variance analysis, and the mean ± standard deviation (± s) was used. The rank data were analyzed by rank sum test.

4. Results

4.1. On NDS in TIA rats

Compared with the sham-operated group, the scores of the model group, the number of attacks, the cumulative time and the onset latency of the model group were significantly shortened ($P < 0.01$). It indicated that the TIA model was successful. Compared with the model group, ($P < 0.05$). The first episode latency was significantly prolonged. The first episode and seizure cumulative time decreased ($P < 0.01$); the number of the first episode and the cumulative time of seizure in the middle and low dose group were significantly lower than those in the control group ($P < 0.01$). The time of the second episode of the large and middle dose groups was significantly decreased ($P < 0.01$); the second score of the large, middle and small dose groups decreased significantly, the latent period of the attack was prolonged and the frequency of seizures decreased ($P < 0.01$). The cumulative time of the second episode in low dose group was significantly decreased ($P < 0.05$). The death rate of the model rats in each administration group decreased to different degrees, and the effect of high dose was the most obvious.

4.2. On the TIA model of rat brain tissue changes in the rate of nerve cells

The neurons in cerebral cortex and hippocampus of rats in sham operation group were normal. The nerve cells in cerebral cortex of rats in model group showed severe edema with eosinophilic pathological changes, and the neurons in hippocampus area showed atrophy obviously. The brain of nimodipine group Most of the

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