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ABSTRACT

Objective To investigate the protective effects of the combination of Xuesaitong (XST) and aspirin on cerebral ischemia and reperfusion injury (CIRI) in rats, and further explore the underlying mechanisms. **Methods** A total of 150 male Sprague-Dawley (SD) rats were randomly divided into five groups with 30 rats in each group: sham group, middle cerebral artery occlusion/reperfusion (MCAO/R) model group, XST group, aspirin group, and XST + aspirin group. Rats were pretreated with XST, aspirin, or XST + aspirin for 7 d. One hour after the last administration, a model of CIRI was induced by MCAO/R. Neurological deficits were assessed using Longa's five-point scale. Cerebral edema was detected by the measurement of brain water content. The volume of cerebral infarction was determined by 2,3,5-triphenyltetrazolium chloride (TTC) staining. The activities of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px), as well as levels of malonaldehyde (MDA) were detected by commercial kits. Enzyme-linked immunosorbent assay (ELISA) was used to determine the levels of interleukin-1 (IL-1β), interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-10 (IL-10), tumor necrosis factor-alpha (TNF-α), monocyte chemotactic protein 1 (MCP-1), and kynurenine in serum, cerebral cortex, and hippocampus of MCAO/R rats. The protein expression of nuclear factor erythroid 2-related factor (Nrf2), heme oxygenase-1 (HO-1), I-kappa B alpha (IκBα), and nuclear factor kappa B (NF-κB)/p65 in the cortex were analyzed by western blotting. **Results** Treatment of XST, aspirin, and XST + aspirin significantly alleviated the neurological deficits, cerebral edema, and cerebral infarct volume induced by MCAO/R. Treatment of XST, aspirin, and XST + aspirin also reduced MDA, IL-1β, IL-6,TNF-α, MCP-1, and kynurenine levels, and increased SOD, CAT, GSH-Px, IL-4, and IL-10 levels in serum, cerebral cortex, and hippocampus of MCAO/R rats. Furthermore, treatment of XST, aspirin, and XST + aspirin decreased the expression of nuclear NF-κB/p65 and increased the expression of IκBα, nuclear Nrf2, and HO-1. Importantly, the combination of XST and aspirin enhanced the protective effects of XST or aspirin treatment alone on CIRI in rats. **Conclusion** The combination of XST and aspirin significantly inhibited oxidative stress and inflammation in serum, cerebral cortex, and hippocampus of MCAO/R rats. The combination of XST and aspirin exerted more protective effects than XST or aspirin treatment alone. The combination of XST and aspirin might provide the synergistic therapeutic effects on CIRI, and deserve further clinical investigation.

Keywords aspirin; cerebral ischemia and reperfusion injury; inflammation; oxidative stress; Xuesaitong (XST)

1. Introduction

Stroke is one of the most common serious clinical diseases, characterized by high morbidity, mortality, disability, and recurrence rate (GBD 2016 Causes of Death Collaborators., 2017). In recent years, the prevalence of stroke in China has increased the trend and now presents a serious threat to health (Wang et al., 2017). Stroke is generally ischemic or hemorrhagic types; ischemic stroke account for about