Cerebral Ischemia Pathogenesis

Cerebral ischemia-reperfusion injury enhances brain injury and increases its morbidity and mortality.

The purpose of a study was to further explore the specific cerebral ischemia pathogenesis by studying the role of p53 in cerebral ischemia-reperfusion injury and its mechanism to provide a new target for the cerebral ischemia treatment.

Middle cerebral artery occlusion (MCAo) was established in rats. The changes in p53 and apoptotic proteins in the rat model were detected by quantitative real-time polymerase chain reaction (qRT-PCR) and Western blot. The effects of p53 inhibition on cerebral ischemia-reperfusion injury in rats were evaluated by modified neurological severity score (mNSS) and infarct area. Subsequently, neural stem cells (NSCs) were isolated and cultured in vitro, and oxygen and glucose deprivation (OGD) was induced to establish an in vitro ischemia-reperfusion injury model. Cell viability and migration were detected by CCK-8 and transwell assays. Apoptosis of NSCs was detected by flow cytometry. Finally, protein expression in the Wnt pathway activated by p53 was detected by Western blotting.

Compared with the sham group, p53 levels, mNSS, cerebral infarction area, and apoptosis were significantly increased in the MCAo group ($p < 0.05$). When the p53 inhibitor PFT-α was injected, the increase in these levels was reversed. Also, the viability and migration of cells decreased and apoptosis increased in the in vitro OGD model, whereas the viability, migration, and apoptosis were significantly reversed after the addition of p53 inhibitors ($p < 0.05$). Finally, p53 induced Wnt signaling pathway proteins β-catenin and cyclin D1 decrease in the MCAo group, while p53 inhibitors reversed their inhibitory effect on the Wnt signaling pathway.

They confirmed in vivo and in vitro that inhibition of p53 has a protective effect on the cerebral ischemia-reperfusion injury, which may be related to the activation of the Wnt signaling pathway [1].

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Liu Y, Wu X, Du D, Liu J, Zhang W, Gao Y, Zhang H. p53 Inhibition Provides a Pivotal Protective Effect against Cerebral Ischemia-Reperfusion Injury via the Wnt Signaling Pathway. Cerebrovasc Dis. 2021 Aug 2:1-9. doi: 10.1159/000516889. Epub ahead of print. PMID: 34340236.