Iron is a critical factor in focal cerebral ischemia-reperfusion injury

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Abstract

Background: Clinical studies have shown that disturbance of iron homeostasis in ischemic stroke influenced recovery and functional outcome following blood reperfusion of obstructed cerebral vessels, but the mechanism of iron-mediated toxicity in ischemic strokes has not been fully elucidated.

Methods: A middle cerebral artery occlusion (MCAO) mouse model was established by introducing an embolus into the middle cerebral artery, with or without intravenous injection of a potent iron chelator SIH and iron transport protein APPeC after MCAO/reperfusion. The neurological deficit was evaluated by a five-point scale. After 24 hours of reperfusion, mice were sacrificed and brains were separated. TTC staining and Nissl staining were performed respectively to detect the area of brain infarction and hippocampal CA1 neuronal survival rate. Mouse tissue metal content was measured by inductively coupled plasma mass spectrometry (ICP-MS) in the lesioned hemisphere 6 hours after reperfusion in mouse MCAO model.

Results: Iron level was significantly increased in the lesioned hemisphere 6 hours after reperfusion in mouse MCAO model of ischemic stroke. A potent iron chelator, SIH significantly prevented MCAO-induced behavioral deficits and brain infarct volumes at 24h post-reperfusion. APPeC showed protective effect on ischemia/reperfusion injury, and could prevent iron accumulation in the lesioned hemisphere after MCAO without altering the iron content in the unlesioned hemisphere.
Conclusions: This study indicates that iron overload is the main cause of neuronal injury after focal cerebral ischemia/reperfusion, and the accumulation of iron could due to insufficient iron export.

Keywords: iron, iron overload, MCAO, ischemia/reperfusion, stroke