Cerebral ischemic postconditioning

Experimental studies have demonstrated the neuroprotection of ischemic postconditioning (IPostC) in acute ischemic stroke by attenuating cerebral ischemia-reperfusion injury. A study aimed to investigate the safety and tolerability of direct IPostC in both a dog model and patients with acute ischemic stroke treated with thrombectomy.

The study involved 2 parts. First, IPostC was induced by repeated balloon inflation and deflation in dogs, where a low-pressure balloon was navigated to the anterior spinal artery, and 4 cycles of 5-minute ischemia followed by 5-minute reperfusion were performed. Vascular injuries were assessed using angiography and vascular tissue specimens. Then, a 3+3 dose-escalation trial was conducted in patients with acute ischemic stroke following successful thrombectomy recanalization. Patients received direct IPostC with ischemia and reperfusion durations in progressive increments of 0, 1, 2, 3, 4, and 5 minutes ×4 cycles. Major adverse responses were defined as vessel perforation, rupture, dissection, reocclusion, severe vasospasm, thrombotic events, and rupture of the balloon.

Results: IPostC was investigated in 4 dogs. No vessel perforation or rupture, dissection, or vasospasm was observed under the angiography. Only 1 vessel experienced mild injury between the intima and the internal elastic membrane detected on a histopathologic slide. Then, 18 patients were recruited. The duration of IPostC was progressively escalated with no major response happened. No patient experienced agitation, discomfort, or other tolerability issues. Five patients (27.8%) experienced any intracranial hemorrhage after thrombectomy, and 1 (5.6%) was symptomatic. At 3-month follow-up, no patient died, and 9 patients (50%) achieved functional independence.

Conclusions: Direct IPostC inducing by 4 cycles of 5-minute ischemia followed by 5-minute reperfusion is safe, feasible, and tolerable in patients with acute ischemic stroke treated with thrombectomy. Further investigations are needed to determine the safety and preliminary efficacy of direct IPostC [1)].

Cerebral ischemic postconditioning (PostC) refers to a series of brief ischemia and reperfusion (I/R) cycles applied at the onset of reperfusion following an ischemic event. PostC has been shown to have neuroprotective effects, and represents a promising clinical strategy against cerebral ischemia-reperfusion injury. Many studies have indicated that cerebral PostC can effectively reduce neural cell death, cerebral edema and infarct size, improve cerebral circulation, and relieve inflammation, apoptosis and oxidative stress. In addition, several protective molecular pathways such as Akt, mTOR and MAPK have been shown to play a role in PostC-induced neuroprotection. PostC represents an attractive therapeutic option because of its ability to be induced rapidly or in a delayed fashion, as well as being inducible by pharmacological agents. As a potential clinical treatment, PostC is therapeutically translatable as it can be induced remotely. The underlying mechanisms of PostC have been systematically investigated, but still need to be comprehensively analyzed. As most PostC studies to date were conducted preclinically using animal models, future studies are needed to optimize protocols in order to accelerate the clinical translation of PostC [2)].

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Wu L, Wei M, Zhang B, Zhang B, Chen J, Wang S, Luo L, Liu S, Li S, Ren C, Hess DC, Song H, Zhao W, Ji X. Safety and Tolerability of Direct Ischemic Postconditioning Following Thrombectomy for Acute Ischemic Stroke. Stroke. 2023 Jul 27. doi: 10.1161/STROKEAHA.123.044060. Epub ahead of print. PMID: 37497674.
2)

Xie R, Li J, Zhao H. The underlying mechanisms involved in the protective effects of ischemic postconditioning. Cond Med. 2018;1(2):73-79. PubMed PMID: 29782624.