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Research Report

Hyperbaric oxygen preconditioning attenuates neuroinflammation after intracerebral hemorrhage in rats by regulating microglia characteristics

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ABSTRACT

Intracerebral Hemorrhage (ICH) results in a detrimental neurologic disorder with complicated secondary brain injury. Hyperbaric oxygen preconditioning (HBOP) may be a safe and effective therapeutic method for ICH victims. Our previous studies have demonstrated that HBOP induces neuroprotection in cerebral ischemia and traumatic brain injury. This study aimed to investigate whether HBOP could alleviate neuroinflammation by regulating changes in microglia characteristics in a rat model of ICH. ICH was induced by autologous arterial blood injection, and animals were sacrificed at 12, 24, and 72 h post injury. We measured motor function and brain water content to evaluate the extent of inflammation. Fluoro-Jade C and TNF-α staining was used to characterize neuronal degeneration and neuroinflammatory cytokines, and immunofluorescence staining was performed for CD11b to show activated microglia and Iba-1 to show microglia. Our results indicate that motor dysfunction and brain water content are alleviated by HBOP, and Fluoro-Jade C staining demonstrates that neuron degeneration decreased in the HBOP group. The growth of Iba-1-positive microglia decreased in the HBOP group. Moreover, TNF-α was dynamically reduced in the HBOP group compared with the ICH group. CD11b-Iba-1 double staining demonstrated that the ratio of CD11b and Iba-1 was significantly decreased in the HBOP group. Overall, the data demonstrated that HBOP could significantly alleviate the ICH-induced neuroinflammation by regulating microglia characteristics changing. The phenomenon may propel the progress of the relation between microglia and HBOP and represent a novel target for ICH treatment.

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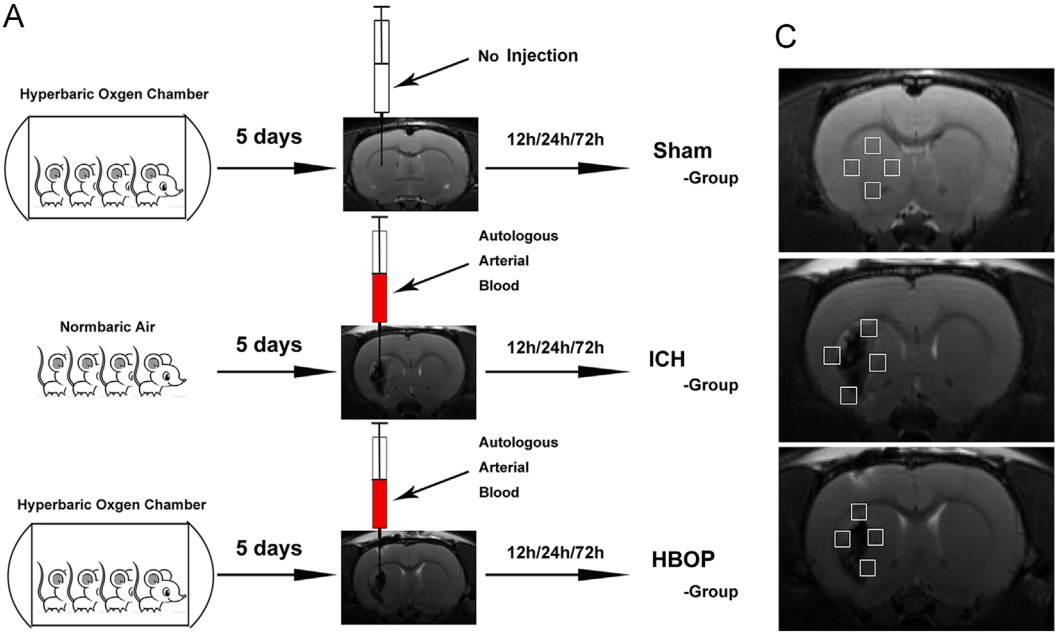
1. Introduction

Intracerebral hemorrhage (ICH) is a neurologic disorder with increasing prevalence in adults that occurs after brain surgery. ICH poses a significant financial burden on society and physical and emotional burden on victims and caregivers. This condition may result in brain damage because of different factors including edema, incisions, and trauma, which may lead to postoperative neurological deficits (Matula and Schoeggl, 2000; Jadhav and Zhang, 2008). Therefore, a safe and effective cerebral protection method is needed before surgery in clinical medical practice. Hyperbaric oxygen preconditioning (HBOP) may be beneficial for such people. In fact, previous evidence has demonstrated that repeated hyperbaric oxygenation before surgery could induce protection against artery bypass grafts in patients (Alex et al., 2005; Yogaratnam et al., 2010). Increasing studies show that HBOP can induce neuroprotection against ischemia/hypoxia, trauma, hemorrhage, and surgical injury in different organs including the spinal cord and brain (Harch et al., 2007; Qin et al., 2008a, 2008b; Yogaratnam et al., 2010; Yan et al., 2011). However, the exact mechanism underlying HBOP is not well understood.

The impact of ICH on brain tissue has been studied for many decades, and these studies have shown that complications after ICH involve more than the initial tissue damage induced directly by hematomas. Delayed secondary events, such as ischemia, lipid degradation, free radical formation, and protease release can be equally devastating (Qu et al., 2007; Yang et al., 2014). For example, secondary events can lead to brain edema, neuron degeneration, neuronal death, cavitation, and glial scarring around the area of initial damage (Masuda et al., 2010; Tang et al., 2015). The activation of resident microglial cells is integral to subsequent inflammatory responses. An increasing number of studies now agree that microglia are highly plastic cells that can assume diverse phenotypes and engage different functional programs in response to specific microenvironment signals (Miron et al., 2013; Tang and Le, 2015). The dual roles of microglia have been reported in several CNS disorders, including traumatic brain injury (TBI), ischemia, multiple sclerosis (MS), and spinal cord injury (SCI) (Wang et al., 2013; Shin et al.,



B

Experimental Design

Group		Experiment Form					
		Behavior	Brain Edema(72h)	Flouro-Jade C	Iba-1+DAPI	TNF-α+Iba-1	Iba-1+CD11b
Sham	12h	Sham (n=6)	Sham (n=6)	Sham (n=4)	Sham (n=4)	Sham (n=4)	Sham (n=4)
ICH	24h	ICH (n=6)	ICH (n=6)	ICH (n=4)	ICH (n=4)	ICH (n=4)	ICH (n=4)
HBOP	72h	HBOP (n=6)	HBOP (n=6)	HBOP (n=4)	HBOP (n=4)	HBOP (n=4)	HBOP (n=4)

Fig. 1 – (A) A model of the different groups is shown. (B) Table listing the overall experimental procedures. (C) Magnetic resonance imaging showing the tissue parts chosen for western blotting and immunofluorescence.