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Hydrogen-rich saline mediates neuroprotection through the regulation of endoplasmic reticulum stress and autophagy under hypoxia-ischemia neonatal brain injury in mice

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Abstract

Hydrogen as a new medical gas exerts organ-protective effects through regulating oxidative stress, inflammation and apoptosis. Multiple lines of evidence reveal the protective effects of hydrogen in various models of brain injury. However, the exact mechanism underlying this protective effect of hydrogen against hypoxic-ischemic brain damage (HIBD) is not fully understood. The present study was designed to investigate whether hydrogen-rich saline (HS) attenuates HIBD in neonatal mice and whether the observed protection is associated with reduced endoplasmic reticulum (ER) stress and regulated autophagy. The results showed that HS treatment significantly improved brain edema and decreased infarct volume. Furthermore, HS significantly attenuated HIBD-induced ER stress responses, including the decreased expression of glucose-regulated protein 78, C/EBP homologous protein, and down-regulated transcription factor. Additionally, we demonstrated that HS induced autophagy, including increased LC3B and Beclin-1 expression and decreased phosphorylation of mTOR and Stat3, as well as phosphorylation of ERK. Taken together, HS exerts neuroprotection against HIBD in neonatal mouse, mediated in part by reducing ER stress and increasing autophagy machinery.

Keywords: Autophagy; Endoplasmic reticulum stress; Hydrogen-rich saline; Hypoxia-ischemia.

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