Mol Neurobiol. 2016 Jul;53(5):3462-3476. doi: 10.1007/s12035-015-9242-y. Epub 2015 Jun 20.

Hydrogen-Rich Saline Attenuated Subarachnoid Hemorrhage-Induced Early Brain Injury in Rats by Suppressing Inflammatory Response: Possible Involvement of NF-κB Pathway and NLRP3 Inflammasome

Anwen Shao [1], Haijian Wu [1], Yuan Hong [1], Sheng Tu [2], Xuejun Sun [3], Qun Wu [1], Qiong Zhao [4], Jianmin Zhang [5 6], Jifang Sheng [7 8]

Affiliations
PMID: 26091790 DOI: 10.1007/s12035-015-9242-y

Abstract

Early brain injury (EBI), highlighted with inflammation and apoptosis, occurring within 72 h after subarachnoid hemorrhage (SAH), is associated with the prognosis of SAH. Recent studies have revealed that hydrogen-rich saline (HS) exerted multiple neuroprotective properties in many neurological diseases including SAH, involved to anti-oxidative and anti-apoptotic effect. We have previously reported that HS could attenuate neuronal apoptosis as well as vasospasm. However, the underlying mechanism of HS on inflammation in SAH-induced EBI remains unclear. In this study, we explored the influence of HS on nuclear factor-κB (NF-κB) pathway and nucleotide binding and oligomerization domain-like receptor family pyrin domain-containing 3 (NLRP3) inflammasome at early stage after SAH, by injecting HS intraperitoneally to SAH rats. One hundred and twenty-nine SD rats were randomly divided into four groups: sham group, SAH group, SAH+vehicle group, and SAH+HS group. SAH model was conducted using endovascular perforation method; all rats were sacrificed at 24 h after SAH. Protein level of pIκBα, cytosolic and nuclear p65, NLRP3, apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC), caspase-1, interleukin-1β (IL-1β), and cleaved caspase-3 were measured by western blot. mRNA level of IL-1β, interleukin-6 (IL-6), tumor necrosis factor-c (TNF-α) were evaluated by RT-PCR. Cellular injury and death was detected by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) and Nissl staining, respectively. Our results showed that pIκBα, nuclear p65, NLRP3, ASC, caspase-1, IL-1β, cleaved caspase-3 proteins, as well as the mRNA of IL-1β, IL-6, and TNF-α increased at 24 h after SAH, while cytosolic p65 decreased. TUNEL and Nissl staining presented severe cellular injury at 24 h post-SAH. However, after HS administration, the changes mentioned above were reversed. In conclusion, HS may inhibit inflammation in EBI and improve neurobehavioral outcome after SAH, partially via inactivation of NF-κB pathway and NLRP3 inflammasome. Graphical Abstract Schematic representation of the mechanism of HS-mediated anti-inflammatory effect in EBI after SAH. The NF-κB inflammatory pathway and NLRP3 inflammasome are involved in the anti-neuroinflammatory effect of HS post-SAH. SAH-induced oxidative stress enhances the activation of NF-κB, thus promoting the translocation of p65 subunit into nucleus and increasing the mRNA level of its downstream proinflammatory cytokines (IL-1β, IN-6, TNF-α) and NLRP3. Elevated expression of NLRP3 mRNA increases the assembly of NLRP3 inflammasome. In addition, oxidative stress after SAH stimulates the activation of NLRP3 inflammasome, therefore, promoting caspase-1 activation and the cleavage of pro-IL-1β into mature IL-1β. Finally, activation of NF-κB pathway and NLRP3 inflammasome contribute to the inflammation response and cellular injury in EBI after SAH. HS

treatment reversed the detrimental effect mentioned above via inactivation of NF-κB pathway and NLRP3 inflammasome. NF-κB nuclear factor-κB, IκB inhibitor of NF-κB, IKK Iκ kinase, NLRP3 nucleotide binding and oligomerization domain-like receptor family pyrin domain-containing 3, ASC apoptosis-associated speck-like protein containing a caspase recruitment domain.

Keywords: Early brain injury; Hydrogen; Inflammation; NLRP3 inflammasome; Nuclear factor κB; Subarachnoid hemorrhage.

Related information

MedGen
PubChem Compound (MeSH Keyword)

LinkOut – more resources

Full Text Sources
Springer

Research Materials
NCI CPTC Antibody Characterization Program

Miscellaneous
NCI CPTAC Assay Portal