Int Immunopharmacol. 2015 Sep;28(1):643-54. doi: 10.1016/j.intimp.2015.07.034. Epub 2015 Aug 4.

Molecular hydrogen protects mice against polymicrobial sepsis by ameliorating endothelial dysfunction via an Nrf2/HO−1 signaling pathway

Hongguang Chen [1], Keliang Xie [2], Huanzhi Han [3], Yuan Li [1], Lingling Liu [1], Tao Yang [1], Yonghao Yu [4]

Affiliations

PMID: 26253656 DOI: 10.1016/j.intimp.2015.07.034

Abstract

Endothelial injury is a primary cause of sepsis and sepsis-induced organ damage. Heme oxygenase-1 (HO-1) plays an essential role in endothelial cellular defenses against inflammation by activating nuclear factor E2-related factor-2 (Nrf2). We found that molecular hydrogen (H2) exerts an anti-inflammatory effect. Here, we hypothesized that H2 attenuates endothelial injury and inflammation via an Nrf2-mediated HO-1 pathway during sepsis. First, we detected the effects of H2 on cell viability and cell apoptosis in human umbilical vein endothelial cells (HUVECs) stimulated by LPS. Then, we measured cell adhesion molecules and inflammatory factors in HUVECs stimulated by LPS and in a cecal ligation and puncture (CLP)-induced sepsis mouse model. Next, the role of Nrf2/HO-1 was investigated in activated HUVECs, as well as in wild-type and Nrf(-/-) mice with sepsis. We found that both 0.3 mmol/L and 0.6 mmol/L (i.e., saturated) H2-rich media improved cell viability and cell apoptosis in LPS-activated HUVECs and that 0.6mmol/L (i.e., saturated) H2-rich medium exerted an optimal effect. H2 could suppress the release of cell adhesion molecules, such as vascular cell adhesion molecule-1 (VCAM-1) and intercellular cell adhesion molecule-1 (ICAM-1), and pro-inflammatory cytokines, such as tumor necrosis factor (TNF)-α, interleukin (IL)-1β and high-mobility group box 1 protein (HMGB1). Furthermore, H2 could elevate anti-inflammatory cytokine IL-10 levels in LPS-stimulated HUVECs and in lung tissue from CLP mice. H2 enhanced HO-1 expression and activity in vitro and in vivo. HO-1 inhibition reversed the regulatory effects of H2 on cell adhesion molecules and inflammatory factors. H2 regulated endothelial injury and the inflammatory response via Nrf2-mediated HO-1 levels. These results suggest that H2 could suppress excessive inflammatory responses and endothelial injury via an Nrf2/HO-1 pathway.

Keywords: Endothelial dysfunction; H(2); HO-1; Nrf2; Sepsis.

Related information

MedGen
PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources
Elsevier Science

Medical

MedlinePlus Health Information

Miscellaneous

NCI CPTAC Assay Portal