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Hydrogen Gas Inhalation Attenuates Seawater Instillation-Induced Acute Lung Injury via the Nrf2 Pathway in Rabbits

Mengyuan Diao [1] [2], Sheng Zhang [1], Lifeng Wu [3], Le Huan [1], Fenglou Huang [2], Yunliang Cui [1], Zhaofen Lin [4]

Affiliations

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Abstract

Seawater instillation-induced acute lung injury involves oxidative stress and apoptosis. Although hydrogen gas inhalation is reportedly protective in multiple types of lung injury, the effect of hydrogen gas inhalation on seawater instillation-induced acute lung injury remains unknown. This study investigated the effect of hydrogen gas on seawater instillation-induced acute lung injury and explored the mechanisms involved. Rabbits were randomly assigned to control, hydrogen (2 % hydrogen gas inhalation), seawater (3 mL/kg seawater instillation), and seawater + hydrogen (3 mL/kg seawater instillation + 2 % hydrogen gas inhalation) groups. Arterial partial oxygen pressure and lung wet/dry weight ratio were detected. Protein content in bronchoalveolar lavage fluid (BALF) and serum as well as tumor necrosis factor (TNF)-α, interleukin (IL)-1β, and IL-6 levels were determined. Hematoxylin-eosin staining was used to monitor changes in lung specimens, and malondialdehyde (MDA) content and myeloperoxidase (MPO) activity were assayed. In addition, NF-E2-related factor (Nrf) 2 and heme oxygenase (HO)-1 mRNA and protein expression were measured, and apoptosis was assessed by measuring caspase-3 expression and using terminal deoxy-nucleotidyl transferase dUTP nick end-labeling (TUNEL) staining. Hydrogen gas inhalation markedly improved lung endothelial permeability and decreased both MDA content and MPO activity in lung tissue; these changes were associated with decreases in TNF-α, IL-1β, and IL-6 in BALF. Hydrogen gas also alleviated histopathological changes and cell apoptosis. Moreover, Nrf2 and HO-1 expressions were significantly activated and caspase-3 expression was inhibited. These results demonstrate that hydrogen gas inhalation attenuates seawater instillation-induced acute lung injury in rabbits and that the protective effects observed may be related to the activation of the Nrf2 pathway.

Keywords: NF-E2-related factor 2; acute lung injury; heme oxygenase-1; hydrogen; seawater instillation.

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