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Combination therapy of molecular hydrogen and hyperoxia improves survival rate and organ damage in a zymosan-induced generalized inflammation model

Yunchuan Hong [1], L I Sun [2], Ruiqiang Sun [3], Hongguang Chen [4], Yonghao Yu [4], Keliang Xie [5]

Affiliations

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Abstract

Multiple organ dysfunction syndrome (MODS) is a leading cause of mortality in critically ill patients. Hyperoxia treatment may be beneficial to critically ill patients. However, the clinical use of hyperoxia is hindered as it may exacerbate organ injury by increasing reactive oxygen species (ROS). Hydrogen gas (H_2) exerts a therapeutic antioxidative effect by selectively reducing ROS. Combination therapy of H_2 and hyperoxia has previously been shown to significantly improve survival rate and organ damage extent in mice with polymicrobial sepsis. The aim of the present study was to investigate whether combination therapy with H_2 and hyperoxia could improve survival rate and organ damage in a zymosan (ZY)-induced generalized inflammation model. The results showed that the inhalation of H_2 (2%) or hyperoxia (98%) alone improved the 14-day survival rate of ZY-challenged mice from 20 to 70 or 60%, respectively. However, combination therapy with H_2 and hyperoxia could increase the 14-day survival rate of ZY-challenged mice to 100%. Furthermore, ZY-challenged mice showed significant multiple organ damage characterized by increased serum levels of aspartate transaminase, alanine transaminase, blood urea nitrogen and creatinine, as well as lung, liver and kidney histopathological scores at 24 h after ZY injection. These symptoms where attenuated by H_2 or hyperoxia alone; however, combination therapy with H_2 and hyperoxia had a more marked beneficial effect against lung, liver and kidney damage in ZY-challenged mice. In addition, the beneficial effects of this combination therapy on ZY-induced organ damage were associated with decreased serum levels of the oxidative product 8-iso-prostaglandin F2α, increased activity of superoxide dismutase and reduced levels of the proinflammatory cytokines high-mobility group box 1 and tumor necrosis factor-α. In conclusion, combination therapy with H_2 and hyperoxia provides enhanced therapeutic efficacy against multiple organ damage in a ZY-induced generalized inflammation model, suggesting the potential applicability of H_2 and hyperoxia in the therapy of conditions associated with inflammation-related MODS.

Keywords: hydrogen gas; hyperoxia; inflammatory cytokines; multiple organ dysfunction syndrome/failure; reactive oxygen species.

Figures

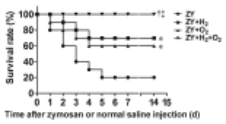

Figure 1. Effects of H_2 and/or...

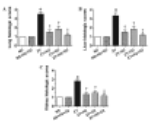

Figure 2. Effects of H_2 and/or...

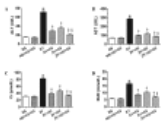

Figure 3. Effects of H_2 and/or...

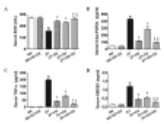

Figure 4. Effects of H_2 and/or...

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