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Title: Hydrogen gas inhalation ameliorates direct lung injury and indirect contralateral lung injury in a murine aspiration pneumonia model

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Body: [Aim] Accumulated leukocytes in the lungs produce several inflammatory cytokines and reactive oxygen and nitrogen species (ROS and RNS), which will induce ALI/ARDS. It has been reported that hydrogen (H₂) gas has potential as eliminating highly reactive ROS and RNS. The aim of the present study was to clarify the effect of H₂ gas inhalation on direct lung injury and indirect contralateral lung injury. [Methods] Anesthetized C57BL/6J male mice were intubated, and 5 µl of 0.1N HCl was administered to the left lung. Mice were randomly grouped to saline treatment instead of HCI (Sham), HCI-treatment (HCI), and 2% H₂ gas inhalation with the HCl-treatment (HCl-H₂) groups. Extra-vascular wet to dry ratio, myeloperoxidase (MPO) activity in the treated left lung and untreated right lung, and serum IL-6 level were evaluated 4 hrs after the treatment. [Results] This aspiration pneumonia model induced direct lung injury and contralateral lung injury. The extra-vascular wet to dry ratios of the left and right lungs were significantly larger in the HCl group compared to the Sham and the HCl-H₂ group (n=10, P<0.01), suggesting that H₂ gas was effective not only in the direct injured lung but also in contralateral lung. MPO activity of the left lung was also significantly larger in the HCl group compared to those in the Sham and HCl- H_2 groups (n=3, P<0.05). IL-6 was increased in the HCl group, but it did not statistically differ to the level in the HCl-H₂ group, suggesting H₂ gas did not interfere in the cytokine production. [Conclusion] H₂ gas inhalation ameliorated direct lung injury and indirect contralateral lung injury in a murine aspiration pneumonia model.