Molecular hydrogen suppresses FcεRI-mediated signal transduction and prevents degranulation of mast cells

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Abstract

Molecular hydrogen ameliorates oxidative stress-associated diseases in animal models. We found that oral intake of hydrogen-rich water abolishes an immediate-type allergic reaction in mice. Using rat RBL-2H3 mast cells, we demonstrated that hydrogen attenuates phosphorylation of the FcεRI-associated Lyn and its downstream signal transduction, which subsequently inhibits the NADPH oxidase activity and reduces the generation of hydrogen peroxide. We also found that inhibition of NADPH oxidase attenuates phosphorylation of Lyn in mast cells, indicating the presence of a feed-forward loop that potentiates the allergic responses. Hydrogen accordingly inhibits all tested signaling molecule(s) in the loop. Hydrogen effects have been solely ascribed to exclusive removal of hydroxyl radical. In the immediate-type allergic reaction, hydrogen exerts its beneficial effect not by its radical scavenging activity but by modulating a specific signaling pathway. Effects of hydrogen in other diseases are possibly mediated by modulation of yet unidentified signaling pathways. Our studies also suggest that hydrogen is a gaseous signaling molecule like nitric oxide.

Consumption of water containing a high concentration of molecular hydrogen reduces oxidative stress and disease activity in patients with rheumatoid arthritis: an open-label pilot study

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Abstract

Background

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by the destruction of bone and cartilage. Although its etiology is unknown, the hydroxyl radical has been suggested to be involved in the pathogenesis of RA. Recently, molecular hydrogen (H_2) was demonstrated to be a selective scavenger for the hydroxyl radical. Also, the method to prepare water containing extremely high concentration of H_2 has been developed. We hypothesized that H_2 in the water could complement conventional therapy by reducing the oxidative stress in RA.

Methods

Twenty patients with rheumatoid arthritis (RA) drank 530 ml of water containing 4 to 5 ppm molecular hydrogen (high H_2 water) every day for 4 weeks. After a 4-week wash-out period, the patients drank the high H_2 water for another 4 weeks. Urinary 8-hydroxydeoxyguanine (8-OHdG) and disease activity (DAS28, using C-reactive protein [CRP] levels) was estimated at the end of each 4-week period.

Results

Drinking high H_2 water seems to raise the concentration of H_2 more than the H_2 saturated (1.6 ppm) water in vivo. Urinary 8-OHdG was significantly reduced by 14.3% ($p < 0.01$) on average. DAS28 also decreased from 3.83 to 3.02 ($p < 0.01$) during the same period. After the wash-out period, both the urinary 8-OHdG and the mean DAS28 decreased, compared to the end of the drinking period. During the second drinking period, the mean DAS28 was reduced from 2.83 to 2.26 ($p < 0.01$). Urinary 8-OHdG was not further reduced but remained below the baseline value. All the 5 patients with early RA (duration < 12 months) who did not show antibodies against cyclic citrullinated peptides (ACPAs) achieved remission, and 4 of them became symptom-free at the end of the study.

Conclusions

The results suggest that the hydroxyl radical scavenger H_2 effectively reduces oxidative stress in patients with this condition. The symptoms of RA were significantly improved with high H_2 water.