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Hydrogen-rich saline attenuates anxiety-like behaviors in morphine-withdrawn mice

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Abstract

Hydrogen therapy is a new medical approach for a wide range of diseases. The effects of hydrogen on central nervous system-related diseases have recently become increasingly appreciated, but little is known about whether hydrogen affects the morphine withdrawal process. This study aims to investigate the potential effects of hydrogen-rich saline (HRS) administration on naloxone-precipitated withdrawal symptoms and morphine withdrawal-induced anxiety-like behaviors. Mice received gradually increasing doses (25-100 mg/kg, i.p.) of morphine over 3 days. In the naloxone-precipitated withdrawal procedure, the mice were treated with three HRS (20 µg/kg, i.p.) injections, and naloxone (1 mg/kg, i.p.) was given 30 min after HRS administration. Body weight, jumping behavior and wet-dog shakes were immediately assessed. In the spontaneous withdrawal procedure, the mice were treated with HRS (20 µg/kg, i.p.) every 8-h. Mice underwent naloxone-precipitated or spontaneous withdrawal were tested for anxiety-like behaviors in the elevated plus-maze (EPM) and light/dark box (L/D box) paradigm, respectively. In addition, the levels of plasma corticosterone were measured. We found that HRS administration significantly reduced body weight loss, jumping behavior and wet-dog shakes in mice underwent naloxone-precipitated withdrawal, and attenuated anxiety-like behaviors in the EPM and L/D box tests after naloxone-precipitated withdrawal or a 2-day spontaneous withdrawal period. Hypo-activity or motor impairment after HRS administration was not observed in the locomotion tests. Furthermore, HRS administration significantly decreased the levels of corticosterone in morphine-withdrawn mice. These are the first findings to indicate that hydrogen might ameliorate withdrawal symptoms and exert an anxiolytic-like effect in morphine-withdrawal mice.

Keywords: Anxiety-like behavior; Hydrogen-rich saline; Hypothalamic-pituitary-adrenal axis; Molecular hydrogen; Morphine withdrawal.

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