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Intrathecal infusion of hydrogen-rich normal saline attenuates neuropathic pain via inhibition of activation of spinal astrocytes and microglia in rats

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Abstract

Background: Reactive oxygen and nitrogen species are key molecules that mediate neuropathic pain. Although hydrogen is an established antioxidant, its effect on chronic pain has not been characterized. This study was to investigate the efficacy and mechanisms of hydrogen-rich normal saline induced analgesia.

Methodology/principal findings: In a rat model of neuropathic pain induced by L5 spinal nerve ligation (L5 SNL), intrathecal injection of hydrogen-rich normal saline relieved L5 SNL-induced mechanical allodynia and thermal hyperalgesia. Importantly, repeated administration of hydrogen-rich normal saline did not lead to tolerance. Preemptive treatment with hydrogen-rich normal saline prevented development of neuropathic pain behavior. Immunofluorochrome analysis revealed that hydrogen-rich normal saline treatment significantly attenuated L5 SNL-induced increase of 8-hydroxyguanosine immunoreactive cells in the ipsilateral spinal dorsal horn. Western blot analysis of SDS/PAGE-fractionated tyrosine-nitrated proteins showed that L5 SNL led to increased expression of tyrosine-nitrated Mn-containing superoxide dismutase (MnSOD) in the spinal cord, and hydrogen-rich normal saline administration reversed the tyrosine-nitrated MnSOD overexpression. We also showed that the analgesic effect of hydrogen-rich normal saline was associated with decreased activation of astrocytes and microglia, attenuated expression of interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) in the spinal cord.

Conclusion/significance: Intrathecal injection of hydrogen-rich normal saline produced analgesic effect in neuropathic rat. Hydrogen-rich normal saline-induced analgesia in neuropathic rats is mediated by reducing the activation of spinal astrocytes and microglia, which is induced by overproduction of hydroxyl and peroxynitrite.

Figures

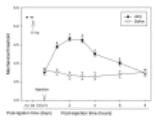

Figure 1. Effects of intrathecal injection of...

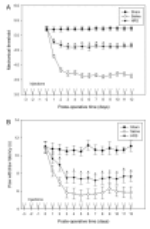

Figure 2. Effects of repeated injection of...

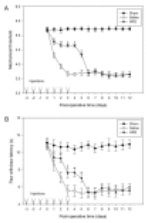

Figure 3. Effects of HRS pretreatment on...

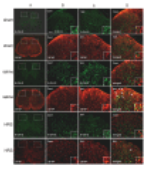

Figure 4. Immunostaining for 8-OH-G and GFAP...

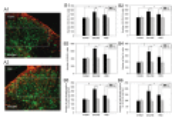

Figure 5. Numbers of cells expressing 8-OH-G,...

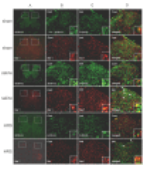

Figure 6. Immunostaining for 8-OH-G and Iba1...

All figures (9)

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