Resveratrol reverses morphine-induced neuroinflammation in morphine-tolerant rats by reversal HDAC1 expression.

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ABSTRACT

Background/purpose: We previously showed that subsequent intrathecal (i.t.) injection of resveratrol (30 mg) significantly reverses morphine-evoked neuroinflammation in morphine-tolerant rats. The present study examined the underlying mechanism.

Methods: Male Wistar rats were implanted with two i.t. catheters, one of which was connected to a miniosmotic pump and used for morphine (15 mg/h) or saline infusion for 120 hours. To examine the effects on spinal cord expression of histone deacetylase 1 (HDAC1), the inflammatory cytokine tumor necrosis factor-α (TNF-α), and TNF receptor (TNFR) 1 and TNFR2 during tolerance induction, a tail-flick test was performed prior to infusion and after 24 hours, 48 hours, 72 hours, 96 hours, and 120 hours of infusion.

Results: Resveratrol treatment prior to morphine challenge restored the antinociceptive effect of morphine in morphine-tolerant rats and reversed the morphine infusion-induced increase in HDAC1, TNF-α, and TNFR1 expression. Moreover, chronic morphine infusion increased TNFR1-specific expression in neuron in morphine-tolerant rat spinal cords, and this effect was almost completely inhibited by resveratrol treatment prior to morphine challenge.

Conclusion: Resveratrol restores the antinociceptive effect of morphine by reversing morphine infusion-induced spinal cord neuroinflammation and increase in TNFR1 expression. The reversal of the morphine-induced increase in TNFR1 expression by resveratrol is partially due to reversal of the morphine infusion-induced increase in HDAC1 expression. Resveratrol pretreatment can be used as an adjuvant in clinical pain management for patients who need long-term morphine treatment or with neuropathic pain.

Keywords: epigenetic; intrathecal; opioid; spinal

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