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Effect of glial inhibition in attenuation of neuropathic pain and improvement of morphine analgesic effect in a rat model of neuropathy

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Abstract

Introduction: Pharmacological blockage of glial activity has been proved useful for treatment of neuropathic pain by lowering proinflammatory cytokines. The present study is to confirm the effect of post-injury administration of pentoxifylline on chronic constriction injury (CCI)-induced neuropathic pain symptoms_ and improved the efficacy of morphine anti-nociception.

Methods: Male Wistar rats (230-270 g) underwent surgery for induction of CCI model of neuropathy. In the sham group the nerve was exposed but not ligated. In 5 groups (n=8) morphine (2.5, 5, 7.5, 10, 15 mg/kg s.c.) was administered in post-operative days (POD) 0, 6 and 14. To evaluate the analgesic effect of different doses of morphine, Von Frey and Hargreaves tests were performed before and 30 minutes after morphine administration. In different groups, pentoxifylline (8, 15, 30 mg/kg i.p.) or normal saline (vehicle) were administered from POD6 to POD13. Behavioral tests were utilized after last dose of pentoxifylline and also on POD14 again after injection of a single dose of morphine (5 mg/kg, s.c.).

Results: The analgesic effect of morphine (5 mg/kg) on POD6 and morphine (5, 7.5, 10, 15 mg/kg) on POD14 was significantly decreased in comparison to POD0. Pentoxifylline effectively attenuated thermal hyperalgesia (at 15 and 30 mg/kg) and mechanical allodynia (at 30 mg/kg) on POD13. However, pentoxifylline (15, 30 mg/kg) improved the anti-hyperalgesic effect of morphine (5 mg/kg s.c.) on POD14.

Conclusion: Analgesic effect of morphine was reduced after nerve injury and it may be due to the activation of glia. Inhibition of glial activity is an effective way to attenuate CCI-induced neuropathic pain and also to improve the anti-hyperalgesic effect of morphine, without significant effect on its anti-allodynic effect.

Key words: Neuropathic pain, Glia, Morphine, Allodynia, Hyperalgesia

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