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## Prevention of morphine discontinuation phenomenon in mice by ondansetron, a selective 5-HT3 antagonist.

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### Abstract

The effects of ondansetron, a highly potent and selective 5-HT3 receptor antagonist, in the prevention of tolerance to and dependence on morphine were studied in mice using a 9-day schedule. Chronic administration of morphine (10 mg/kg i.p. twice daily for 9 days) produced tolerance to the analgesic effects and animals showed withdrawal jumps on day 10 when challenged with naloxone (2 mg/kg). Chronic treatment with ondansetron (0.01 and 0.1 mg/kg) followed by saline on days 1-9 failed to produce any significant change in tail-flick latency in the saline-pretreated group. Repeated administration of ondansetron (0.01 and 0.1 mg/kg) for 9 days, however, attenuated the development of tolerance to the analgesic effect of morphine (10 mg/kg). The higher dose of ondansetron (0.1 mg/kg) also suppressed the development of morphine dependence as assessed by naloxone (2 mg/kg)-precipitated withdrawal on day 10 of testing.

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