

Evaluation of the effects of piracetam on morphine tolerance and dependence

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Background and Aims: Piracetam increases the intracellular cAMP in nervous system. Therefore, piracetam effects on morphine acute and chronic effects were evaluated. The antinociceptive effects of piracetam were examined using tail flick test. At all doses, the acute administration of piracetam did not show analgesic effects. Tolerance to morphine was induced by twice daily injection of morphine 20 mg/kg, S.C. for four days. The antinociceptive response to morphine 10 mg/kg S.C. was determined on day 1 and 6 using tail flick test. In order to evaluate the chronic effect of piracetam on morphine tolerance piracetam 50, 100 and 200 mg/kg i.p. was injected simultaneously with morphine and in order to evaluate the acute effect of piracetam on morphine tolerance, on day 6, piracetam 50, 100 and 200 mg/kg i.p. was administered. Dependence was induced by injection of morphine three times daily 50, 50 and 75 mg/kg s.c. On day 4, a single dose of morphine 50 mg/kg was injected 2h prior naloxane treatment (5 mg/kg i.p.). 30 min prior to naloxane treatment, piracetam (50, 100 and 200 mg/kg i.p.) or clonidine (0.1 mg/kg i.p.) was injected. Following naloxane administration, number of jumping during 30 min was considered as the intensity of withdrawal syndrome. The results showed that acute administration of piracetam 50, 100 and 200 mg/kg decreased the jumping in dependent mice in comparison with control group. Also, chronic administration piracetam 50, 100 and 200 mg/kg decrease the locomotor activity in comparison with control group. Acute and chronic administration of piracetam at all doses did not attenuate the development of tolerance to antinociceptive effects of morphine in mice. It is concluded that piracetam can reduce withdrawal syndrome in single dose administration this effect is not mediated via opioid receptors. Piracetam does not have significant effect on morphine tolerance.

Keywords: Piracetam; Morphine; Morphine dependence