

Effect of paroxetine on tolerance to analgesic effect of morphine in male rats

Aims: Several studies have indicated the important role of serotonergic system in tolerance to analgesic effects of morphine. The aim of the present study, is to investigate the effect of paroxetine, a specific serotonin reuptake inhibitor, on morphine tolerance in rat.

Methods: Male Wistar rats (weight 250-300g, n=10) were used in two studies: In the first study, the preventive effect of paroxetine was investigated on naïve rats during induction of tolerance to morphine. In the Second study, the effect of paroxetine was determined on previously established tolerance to morphine in animals.

In order to induce tolerance, one group of rats received daily intraperitoneal injection of morphine (7mg/kg). After 5days of injection tolerance to morphine was observed. Thereafter, the animals received intraperitoneal injection of 7mg/kg paroxetine before morphine administration for 6 next days. In the other group, in order to investigate the preventive effect of paroxetine, animals received 7mg/kg paroxetine 30 min before morphine injection until the tolerance was observed. In each group, the tail-flick test was done before drug administration (time 0) and after drug injection.

Result: Results showed that paroxetine can significantly attenuate tolerance to morphine in tolerated rats ($P<0.001$). However, in preventive study, with paroxetine pretreatment, tolerance was observed on the 5th day and the analgesic effect of morphine was not significantly increased by pretreatment of paroxetine compared to control group.

Conclusions: Our data indicate that, paroxetine showed an effective treatment effect in established tolerance, but it cannot prevent tolerance to morphine

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