Evaluation the effect of intraperitoneally administration of Atomoxetine in preventing of morphine dependence in male rat

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Abstract: Long-term exposure to opiates induces physical dependence, however Several mechanisms associated with morphine tolerance have been identified. Previous studies have shown the role of norepinephrine on reducing the total withdrawal scores. Atomoxetine hydrochloride is a selective norepinephrine reuptake inhibitor used in this study. The goal of this investigation was to evaluate the co-administration of Atomoxetine & Morphine on the morphine withdrawal syndrome in rats. Male Wistar rats (220-250 g) were studied. The animals were divided into 5 groups each with six rats, including: one saline treated group (non-dependent group) and 4 morphine dependent groups. Atomoxetine (10, 20, 40mg/kg) was dissolved in normal-saline and injected intraperitoneally. On the way to provoke the dependency, increasing daily doses of morphine were injected subcutaneously for nine days. On the 10th day, 12 hours after the last dose of morphine, naloxone (4mg/kg) was injected intraperitoneally. Some withdrawal behaviors (jumping, rearing, writhing, teeth chattering, wet dog shake, hand tremor, head tremor) were counted for 45 min. Our findings indicated that Atomoxetine (20,40mg/kg) evidently reduced all morphine-induced withdrawal signs. In this study we showed for the first time that chronic administration of Atomoxetine as a norepinephrine reuptake inhibitor, prevented naloxone-precipitated withdrawal symptoms.

Keyword: Morphine, Atomoxetine, Withdrawal symptoms, Dependence, Tolerance