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Reversal of Opioid Overdose Syndrome in Morphine-Dependant Rats Using Buprenorphine

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Abstract

Objective: Currently, the method of choice for reversal of opioid toxicity is administration of naloxone. This routine treatment is given in both addicted and non-addicted patients while it can potentially be accompanied by complications including acute lung injury, myocardial infarction, or withdrawal syndrome (the latter in addicted patients) and be even life-threatening. We aimed to evaluate the efficacy of an opioid receptor agonist-antagonist (buprenorphine) in reversal of opioid overdose syndrome in addicted rats.

Methods: We designed a prospective case-control study in which a total of 28 rats were put on addiction protocol with 10mg/kg of intra-peritoneal morphine twice daily for 10 days. After completion of the addicting protocol and confirmation of dependency/addiction by naloxone administration, the rats were overdosed by giving 16mg/kg of intra-peritoneal methadone. They were then divided into four 7-rat groups receiving naloxone (2mg/kg) and buprenorphine (3mg/kg, 6 mg/kg, and 10 mg/kg), respectively. These four groups were compared regarding reversal of opioid signs/symptoms and development of withdrawal syndrome.

Results: Weight of the rats was 180-200 mg. The dose of 16mg/kg of methadone showed signs/symptoms of toxicity (apnea, cyanosis at the plantar surface of rats' feet, becoming motionless or irritable). Rats in the first group showed signs/symptoms of opioid withdrawal (ptosis, wet shake dog, jumping, and diarrhea) severely. In the groups 2-4, all doses recovered the intoxicated rats without inducing signs/symptoms of withdrawal; however, the 3mg/kg dose reversed toxicity slower. None of the rats in none of the groups died. But, signs and symptoms of withdrawal were severe in the naloxone group.

Conclusions: Buprenorphine recovers the opioid overdose in morphine-dependant rats and bypasses the withdrawal syndrome due to administration of naloxone.