

Mitragynine attenuates morphine withdrawal effects in rats—a comparison with methadone and buprenorphine

ABSTRACT

Background: Opiate addiction is a major health problem in many countries. A crucial component of the medical treatment is the management of highly aversive opiate withdrawal signs, which may otherwise lead to resumption of drug taking. In a medication-assisted treatment (MAT), methadone and buprenorphine have been implemented as substitution drugs. Despite MAT effectiveness, there are still limitations and side effects of using methadone and buprenorphine. Thus, other alternative therapies with less side effects, overdosing, and co-morbidities are desired. One of the potential pharmacotherapies may involve kratom's major indole alkaloid, mitragynine, since kratom (*Mitragyna speciosa* Korth.) preparations have been reported to alleviate opiate withdrawal signs in self-treatment in Malaysian opiate addicts. **Methods:** Based on the morphine withdrawal model, rats were morphine treated with increasing doses from 10 to 50 mg/kg twice daily over a period of 6 days. The treatment was discontinued on day 7 in order to induce a spontaneous morphine abstinence. The withdrawal signs were measured daily after 24 h of the last morphine administration over a period of 28 abstinence days. In rats that developed withdrawal signs, a drug replacement treatment was given using mitragynine, methadone, or buprenorphine and the global withdrawal score was evaluated. **Results:** The morphine withdrawal model induced profound withdrawal signs for 16 days. Mitragynine (5–30 mg/kg; i.p.) was able to attenuate acute withdrawal signs in morphine dependent rats. On the other hand, smaller doses of methadone (0.5–2 mg/kg; i.p.) and buprenorphine (0.4–1.6 mg/kg; i.p.) were necessary to mitigate these effects. **Conclusions:** These data suggest that mitragynine may be a potential drug candidate for opiate withdrawal treatment.

Keyword: Mitragynine; Kratom; Morphine; Withdrawal; Substitution; Methadone; Buprenorphine