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MEETING ABSTRACT

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**Efficacy of the morphine–ketamine–magnesium sulphate combination in the tail-immersion test in rats**

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**Background:** *N*-methyl-D-aspartate (NMDA), ketamine and magnesium enhance the antinociceptive effects of opioid analgesics in different animal models of pain, as well as in humans. This study aimed at evaluating whether magnesium sulphate added to a morphine–ketamine combination produces a higher level of analgesia.

**Methods:** Analgesic activity was assessed by the tail-immersion test in male Wistar rats (200–250 g). The distal 5 cm of the tail was immersed in a warm water bath (55 ± 0.5 °C) and the time for tail withdrawal was measured as response latency.

**Results:** Magnesium sulphate (0.5–60 mg/kg, s.c.) and ketamine (5–30 mg/kg, i.p.) administered alone did not produce any effect. Magnesium sulphate (5 and 60 mg/kg) and ketamine (5 and 30 mg/kg) increased the antinociceptive effect of morphine (2.6 mg/kg, i.p.). Magnesium sulphate (5 mg/kg) increased the antinociceptive effect of the morphine (2.6 mg/kg)–ketamine (2.5 or 5 mg/kg) combination when magnesium sulphate was added to morphine after, but not before, ketamine. Magnesium sulphate also prolonged the duration of the antinociceptive effect of the morphine–ketamine combination. Low doses of morphine (2.6 mg/kg), ketamine (5 mg/kg) and magnesium sulfate (5 mg/kg) given together did not cause motor impairment, which was verified by the rotarod test. The antinociceptive effect of the triple combination was readily antagonized by naloxone (3 mg/kg, s.c.), a nonselective antagonist of opioid receptors, indicating that the effect is mediated via opioid receptors.

**Discussion:** These data suggest that the combined administration of low doses of ketamine and magnesium sulphate provides more profound effects without exceeding safe doses. This information may be useful for preventing or treating acute pain in several settings. However, interaction may also occur when magnesium sulphate is used as an electrolyte replenisher after morphine–ketamine analgesia. An additional bonus are the neuroprotective effects of ketamine and possibly magnesium. This study revealed that in the tail-immersion test in rats the efficacy of the morphine–ketamine–magnesium sulphate combination is influenced by the order of medication administration; a higher level of activity is demonstrated only when ketamine is added to morphine before magnesium sulphate.

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