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Effects of different classes of drugs on morphine-induced antinociception and hyperthermia in rats

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Aim of investigation It is well known that the opioids exert complex action on the body temperature in rodents and mammals. This study aimed to investigate the effects of different classes of drugs (naloxone hydrochloride - nonselective opioid receptors antagonist, ondansetron - 5-HT3 receptor antagonist, ketamine - NMDA receptor antagonist, diclofenac - non-steroid anti-inflammatory drug), on the morphine-induced antinociception and hyperthermia in rats.

Methods Analgesic activity was assessed by tail-immersion test in male Wistar rats (200-250 g). Body temperature was determined by insertion of a thermometer probe 5 cm into the colon of unrestrained rats. Experiments were done at ambient temperature of 21±0.5°C. The animals were tested in groups of 6-8 rats per dose. Control animals received saline. Data were statistically interpreted with Student’s t test and One-Way ANOVA followed by Bonferroni test. ED50 values were calculated according to Tallarida and Murray (1).

Results Morphine (1.1-3.2 mg/kg; i.p.) produced dose-dependent antinociception (ED50=2.59 mg/kg; 95%CL 1.89-3.55) and hyperthermia (ED50=1.27; 95%CL 0.67-2.39). Diclofenac (3 mg/kg, i.p.) and ketamine (5-30 mg/kg; i.p.) given alone did not produce antinociception, but potentiated morphine-induced analgesia (p<0.05 for both drugs). Ondansetron failed to evoke antinociception on its own, and did not affect morphine analgesia (p>0.05). Naloxone hydrochloride (0.1-1 mg/kg; s.c.) reduced both the analgesic and hypothermic effects of morphine in a dose-dependent manner (p<0.01 for both effects), but given alone did not change neither basal body temperature, nor tail-withdrawal response. Diclofenac (3 mg/kg, i.p.) or ondansetron (4 mg/kg i.p.) did not have influence on morphine hyperthermia. Diclofenac given alone decreased baseline body temperature by 0.4±0.1°C (p>0.05). Ondansetron given alone significantly decreased the baseline body temperature by 0.5±0.1°C (p<0.05). Ketamine at doses of 20 and 30 mg/kg significantly decreased baseline body temperature in a dose-dependent manner (p<0.05). Also, ketamine at dose of 30 mg/kg significantly reduced the hyperthermic effect of morphine by 0.9±0.2 (p<0.01).

Conclusions The present results suggest that opioid and NMDA receptors, but not 5-HT3 receptors and prostaglandins, are involved in the morphine-induced hyperthermia. Morphine analgesia is mediated via opioid receptors. Block of the NMDA receptor and inhibition of the synthesis of prostaglandins enhance analgesic response to morphine while 5-HT3 receptors are not implicated in morphine analgesia.