INFLUENCE OF KETAMINE ON THE ANALGESIC EFFICACY OF THE AGONIST-ANTAGONIST OPIOIDS

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It is known, that anaesthetics potentiate the analgesic effect of the opioid drugs with pure agonistic properties. This agonism is important from the clinical point of view since the combination of these classes of drugs minimize side effects and discomfort of the patient.

The aim of this study was to evaluate the analgesic effect of mixed agonist-antagonist opioids with the short acting general anaesthetic ketamine, which has also a potent analgesic properties.

Experimental procedure. Wistar, male rats weighting 180-220g were used. The animals were housed under natural light-dark cycle and had free access to water and food. 20 or 40 mg/kg of ketamine were administered ip. simultaneously with 1 or 10 mg/kg ip. of nalbuphine, 5 or 10 mg/kg ip. of pentazocine and a specific receptor kappa opioid agonist U-62066E intrathecally in a dose of 60 μg/10 μl [1]. Analgesia was assessed using the "tail immersion" test. The cut-off time was 10 sec. The data were expressed as a percent of analgesia. Statistical significance of the data was determined utilizing the Student's t-test and compared using the two-way analysis of variance (ANOVA).

Results. The analgesic effect of 1 mg/kg ip. of nalbuphine, 5 mg/kg ip. of pentazocine and 60 μg/10 μl it. of U-62066E were supressed by simultaneous administration of 40 mg/kg ip. ketamine (Fig.).
The analgesic effect of the highest doses of nalbuphine or pentazocine (10 mg/kg ip.) were not abolished by ketamine (40 mg/kg ip.). The smaller dose of ketamine (20 mg/kg ip.) did not alter the analgesic effect of nalbuphine.

Discussion. The dual properties of the mixed agonist-antagonist opioids are explained by their different actions on the μ, kappa or delta opioid receptors [2]. Nalbuphine and pentazocine exert their agonistic effects primarily at the kappa receptor and seem to act as competitive antagonist at μ opioid receptor [3]. Whereas ketamine exerts partial agonistic effect at μ opioid receptor [4]. The degree to which ketamine suppress the analgesia induced by mixed agonist-antagonist depend upon the dose of ketamine and opioid used. The time between the injection of ketamine and substances studied or the nociceptive stimulus used, may be also of great importance.

This study suggests, that ketamine acts as a partial antagonist of kappa opioid receptor because we found, that this anaesthetic suppress the analgesic effect induced not only by the mixed agonist-antagonist, but also by the specific receptor kappa agonist U-62066E.

References