

## INFLUENCE OF DOXEPIN USED IN PREEMPTIVE ANALGESIA ON THE NOCICEPTION IN THE PERIOPERATIVE PERIOD. EXPERIMENTAL AND CLINICAL STUDY

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The aim of the present research was to assess in experimental and clinical study the influence of doxepin administered intraperitoneally (*ip*) as preemptive analgesia on the nociception in the perioperative period. The pain thresholds for mechanical stimuli were measured in rats. The objective of clinical investigation was to assess the influence of preemptive administration of doxepin on postoperative pain intensity, analgesic requirement in the early postoperative period as well as an assessment of the quality of postoperative analgesia by the patient.

Doxepin injected *ip* (3–30 mg/kg) dose-dependently increased the pain threshold for mechanical stimuli measured in paw pressure test in rats. Doxepin injected 30 min before formalin significantly increased the nociceptive threshold in the paw pressure test. In contrast, doxepin injected 240 min before formalin or 10 min after formalin did not change the nociceptive threshold. Morphine administered subcutaneously (*sc*) at a dose of 1 mg/kg increased the pain threshold measured in the paw pressure test 55 min after formalin treatment. Injection of 10 mg/kg of doxepin 30 min before formalin further enhanced the response after morphine administration. The results of the clinical study demonstrated that the patients who were administered doxepin preemptively showed significantly lower pethidine requirement in order to achieve a similar level of postoperative analgesia.

The results of the research under discussion confirm the theoretical assumptions that there is a possibility to modify the nociception process in the perioperative period through preemptive analgesia using a drug that modifies the activity of the descending antinociceptive system.

**Key words:** *doxepin, nociceptive threshold, formalin test, rat, pethidine requirement, VAS, PCA system, patients*

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