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## Role of gabapentin in preventing fentanyl- and morphine-withdrawal-induced hyperalgesia in rats.

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### Abstract

**PURPOSE:** This study was undertaken to examine the effect of gabapentin for preventing hyperalgesia induced by morphine and fentanyl withdrawal in rats.

**METHODS:** To induce hyperalgesia, Sprague Dawley (SD) rats were subcutaneously injected with fentanyl four times at 15-min intervals (60 µg/kg per injection), resulting in total dose of 240 µg/kg over 1 h, and morphine 10 mg/kg twice daily for 7 days. The effect of gabapentin was detected with behavioral tail-flick and paw-withdrawal tests.

**RESULTS:** Drug termination produced significant decrease in antinociception thresholds ( $P < 0.05$  vs. saline group), indicating that the rats became sensitive to thermal stimuli. In rats that received combined treatment with fentanyl/morphine and gabapentin (25/50 mg/kg), results demonstrated that there were no significant decreases in antinociception thresholds (vs. saline group) after opioid withdrawal. Gabapentin (50 mg/kg) could also prevent morphine tolerance. The 50% effective dose (ED<sub>50</sub>) value was 12.5 mg/kg in tail-flick and 13.6 mg/kg in paw-withdrawal tests.

**CONCLUSIONS:** The study showed that gabapentin can significantly prevented opioid-induced hyperalgesia (OIH) induced caused by fentanyl and morphine, suggesting a role for the addition of gabapentin in the perioperative period and during chronic pain treatment as an effective drug to prevent OIH.

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