Evaluation of Buprenorphine in a Postoperative Pain Model in Rats

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Abstract
We evaluated the commonly prescribed analgesic buprenorphine in a postoperative pain model in rats, assessing acute postoperative pain relief, rebound hyperalgesia, and the long-term effects of postoperative opioid treatment on subsequent opioid exposure. Rats received surgery (paw incision under isoflurane anesthesia), sham surgery (anesthesia only), or neither and were treated postoperatively with 1 of several doses of subcutaneous buprenorphine. Pain sensitivity to noxious and nonnoxious mechanical stimuli at the site of injury (primary pain) was assessed at 1, 4, 24, and 72 h after surgery. Pain sensitivity at a site distal to the injury (secondary pain) was assessed at 24 and 72 h after surgery. Rats were tested for their sensitivity to the analgesic and locomotor effects of morphine 9 to 10 d after surgery. Buprenorphine at 0.05 mg/kg SC was determined to be the most effective; this dose induced isoalgesia during the acute postoperative period and the longest period of pain relief, and it did not induce long-term changes in opioid sensitivity in 2 functional measures of the opioid system. A lower dose of buprenorphine (0.01 mg/kg SC) did not meet the criterion for isoalgesia, and a higher dose (0.1 mg/kg SC) was less effective in pain relief at later recovery periods and induced a long-lasting opioid tolerance, indicating greater neural adaptations. These results support the use of 0.05 mg/kg SC buprenorphine as the upper dose limit for effective treatment of postoperative pain in rats and suggest that higher doses produce long-term effects on opioid sensitivity.