Abstract

Postoperative analgesia is a vital aspect of laboratory animal medicine. Novel analgesic formulations of opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) have recently been introduced to the laboratory animal market. The aim of this study is to investigate whether postoperative analgesia of sustained-release buprenorphine (Bup-SR), sustained-release meloxicam (Melox-SR), or carprofen gel (CG) is effective to control mechanical and thermal hypersensitivity in a model of incisional pain in rats.

Introduction

Many surgical procedures performed in rats cause postoperative pain for at least 48 hr, requiring personnel to handle the animals frequently. Bup-HCl, a partial μ-opioid receptor agonist, is considered the “gold standard” and has been widely used for postoperative analgesia for many surgical procedures in laboratory rats due to its long plasma half-life and effective postoperative analgesia. Due to its duration of action, it should be administered q 6-12 hrs; repeated dosing results in handling-associated stress which can significantly alter animal physiology and research data. Numerous novel formulations of opioid (sustained-release buprenorphine) and NSAID (sustained-release meloxicam or carprofen gel) analgesics have been recently brought to the laboratory animal market; many without published efficacy studies. Due to their longer duration of action and formulations, they may offer significant refinements to laboratory animal care.

AIM: To investigate whether postoperative analgesia of sustained-release buprenorphine (Bup-SR), sustained-release meloxicam (Melox-SR), or carprofen gel (CG) is effective to control mechanical and thermal hypersensitivity in a model of incisional pain in rats.

Methods

Animals: Thirty-three adult male Sprague Dawley rats weighing 350-400 gm.

Surgical incision: Rats were anesthetized with isoflurane (day 0). The incisional pain model was performed on the plantar surface of the left hindpaw (ipsilateral) of each rat based on a previously established model [1]. Rats recovered from surgery for 1 day prior to behavioral testing.

Drug administration and experimental groups: Rats were assigned to 1 of 5 treatment groups: Bup-SR (1.2 mg/kg SC once before an incision); Melox-SR (4 mg/kg SC once before an incision); CG (1 cup daily from days 0 to 2); Bup-HCl (0.05 mg/kg SC twice daily, days 0 to 3); control (0.9% NaCl, 1 ml/kg SC twice daily, days 0 to 3). Rats underwent mechanical and thermal hypersensitivity testing once daily on day 1-4.

Behavioral Testing

• Mechanical hypersensitivity (no. of foot raises): Rats were placed in a clear plastic chamber. Von Frey monofilaments with calibrated bending forces were used to deliver punctate mechanical stimuli (10 g force). No. of foot raises evoked by Von Frey monofilaments were obtained for 10 consecutive trials for each hindpaw. Mechanical hypersensitivity was defined as a significant increase in foot raise frequency evoked by Von Frey monofilaments. The right hindpaw (contralateral) served as a control.

• Thermal hypersensitivity (thermal latency): Rats were placed in a clear plastic chamber. A 50 W light bulb was focused on the middle of the plantar surface of each hindpaw for 4 consecutive trials. Thermal (paw withdrawal) latency (s) was measured as the mean of the last 3 trials. Thermal hypersensitivity was defined as a significant decrease in paw withdrawal latency evoked by thermal stimuli. The right hindpaw (contralateral) served as a control.

Statistical Analyses: Mean withdrawal responses were analyzed using repeated-measures ANOVA with Bonferroni correction for multiple comparisons to examine differences in withdrawal responses between groups and over time. Data were expressed as mean ± SEM. A P value of less than 0.05 was considered significant.

Results

Figure 1. Timeline of surgical procedure, behavioral testing, and drug administration.

Figure 2. Ipsilateral hindpaw: Mechanical hypersensitivity was attenuated in all treatment groups on days 1-4.

Figure 3. Ipsilateral hindpaw: Thermal hypersensitivity was attenuated in Bup-HCl and Bup-SR groups, but not in Melox-SR or CG, on days 1-4.

Conclusions

These findings suggest that postoperative analgesia of Bup-SR, but not Melox-SR or CG, is effective to attenuate both mechanical and thermal hypersensitivity in a model of incisional pain in rats.

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