Evaluation of Analgesic Efficacy of Firocoxib in an Incisional Model of Pain in Mice
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**Introduction:** Providing effective treatment of pain is a cornerstone of laboratory animal medicine. Selection of the appropriate analgesic agent typically requires consideration of the type of pain, route of administration, adverse effects, species specific considerations, and controlled substance regulations. While opioids provide excellent pain relief, their use in laboratory animal medicine is limited by drug diversion precautions and the problems associated with high dosing frequencies (i.e., multiple daily injections and dosing outside of regular work hours).

NSAIDs are the primary alternative to opioids in the treatment of mild–moderate pain and typically have a longer duration of action than opioids. Currently, ketoprofen is one of the most widely used NSAIDs for treatment of pain in laboratory animals. However, since ketoprofen is a non-selective cyclooxygenase (COX) inhibitor, it has the potential to result in adverse gastrointestinal effects. As such, selection of a COX–2 inhibitor is preferable for treatment of mild–moderate pain.

**Methods:** We evaluated the analgesic effectiveness of firocoxib (a COX–2 selective NSAID) relative to buprenorphine in the mouse model of plantar incisional pain. Analgesic effectiveness was objectively assessed (T= -24, 4, 24, 48, and 72 hours post plantar incision) by paw withdrawal response to vonFrey filaments (alldynia) and applied heat (Hargreaves method). We used five experimental groups (n=10 mice/group): i) Firocoxib @10 mg/kg (F10) i.p. every 24 hours [q24h], ii) Firocoxib @20 mg/kg (F20) i.p. q24h, iii) Buprenorphine @0.2mg/kg (Bup) s.c. q8h (positive control), iv) Normal Saline i.p. q24h (negative control) and v) sham group (anesthesia, no incision) treated with firocoxib 20 mg/kg i.p. q 24 hours. All drugs were administered preemptively and continued for 72 hours post-surgery.

**Results:** Buprenorphine provided alleviation (p<0.05) from alldynia at all time points post–incision. F10 alleviated alldynia at 4, 24, and 48h post–incision while F20 alleviated alldynia at 24, 48, and 72h. For thermal hyperalgesia, none of the drug groups provided alleviation at 4h. With the exception of Bup and F10 at 24h (P=0.06 and 0.19, respectively), thermal hyperalgesia was alleviated for all drug groups at 24, 48, and 72h.

**Summary:** Our results indicate that once daily i.p. firocoxib alleviates mild–moderate pain resulting from soft tissue injury in mice. While there were some statistical differences between the buprenorphine and the two firocoxib doses, the response profiles were similar across all drug treatment groups. No adverse drug effects were observed clinically or upon gross examination of the GI tract, histopathologic analysis is pending.

Firocoxib is FDA approved for once daily dosing in other species, rat T1/2 =12–14 hours. Thus, we chose once daily dosing in this study. Further testing (e.g., mouse pharmacokinetics or assessment of analgesia throughout the post–dosing period) would be necessary to determine the most appropriate dosing in mice.

**References**