Pharmacokinetics and Efficacy of Sustained-Release Buprenorphine in Guinea Pigs

LV Kendall, B Smith, D Wegenast, R Hansen, A Hess

Important Update:

In order to remain compliant with the most current regulatory guidelines, we have updated the labeling on our SR formulations from Buprenorphine and Meloxicam SR to Buprenorphine and Meloxicam in Polymer. **As of April 1, 2024, SR preparations mentioned in the attached study are now labeled as in Polymer**, with no changes to the formulation of the medication(s).

Table 2 Antinociceptive activities of μ-preferring opioid agonists in the mouse abdominal constriction test, rat paw pressure test and guinea-pig paw pressure test

	Antinociceptive activity ED_x (95% confidence limits) mg kg^{-1} s.c.		
Drug	*Mouse abdominal constriction test*	*Rat paw pressure test*	*Guinea-pig paw pressure test*
Morphine	0.47 (0.34–0.60)	0.44 (0.35–0.53)	0.54 (0.17–1.56)
Codeine	4.05 (2.24–7.74)	2.0 (1.5–2.7)	1.49 (0.50–3.16)
D-Propoxyphene	1.42 (0.87–2.12)	4.1 (2.6–6.0)	22.5 (6.2–131)
Fentanyl	0.004 (0.002–0.007)	0.003 (0.002–0.004)	0.004 (0.001–0.011)
Bromadoline	3.27 (2.32–4.62)	2.55 (1.86–3.38)	ND
Pentazocine	0.75 (0.17–2.34)	1.0 (0.1–10.8)	1.54 (0.49–4.68)
Nalbuphine	0.37 (0.18–0.76)	0.9 (0.4–1.7)	1.73 (0.09–3.22)
Buprenorphine	0.021 (0.010–0.033)	0.001* (0.0005–0.004)	0.003 (0.001–0.011)
Profadol	0.96 (0.068–1.35)	1.38 (0.90–1.99)	ND
Picenadol	0.38 (0.25–0.61)	0.98 (0.60–1.55)	ND

Doses are in mg kg^{-1} and were administered subcutaneously; the 95% confidence limits are in parentheses. ND: not determined. * Tyers, 1980.

Safety and handling: Normal precautions should be observed.

Contraindications: Combination with full OP3 agonists is not recommended for analgesia; therefore, do not use for premedication when administration of potent opioids during surgery is anticipated.

Adverse reactions: As a partial agonist, side effects are rare after clinical doses.

Drug interactions: In common with other opioids, buprenorphine will reduce the doses of other drugs required for induction and maintenance of anaesthesia.

DOSES

Dogs: 20 μg/kg i.v., i.m., s.c. q6h.

Cats: Doses as for dogs. Also well tolerated and effective when given sublingually.

Small mammals: Ferrets: 0.05 mg/kg s.c. q6-12h; Rabbits: 0.05-0.1 mg/kg i.m., s.c. q6-12h; Guinea pigs, Gerbils, Hamsters, Rats: 0.01-0.05 mg/kg i.m., s.c. q6-12h; Mice: 0.05-0.1 mg/kg i.m., s.c. q6-12h.

Birds: 0.01-0.05 mg/kg i.v., i.m q8-12h.

Reptiles: 0.01 mg/kg i.m. q24-48h.

Abstracts of Scientific Presentations
2015 AALAS National Meeting Phoenix, Arizona
by the American Association for Laboratory Animal Science

Pharmacokinetics and Efficacy of Sustained---Release Buprenorphine in Guinea Pigs

LV Kendall[*1], B Smith[1], D Wegenast[1], R Hansen[2], A Hess[3] [1]*Laboratory Animal Resources, Colorado State, Fort Collins, CO;* [2]*Clinical Sciences, Colorado State University, Fort Collins, CO;*

Guinea pigs are common animal models used for biomedical research due to similarities in symptoms and immune responses of human diseases, often requiring analgesic support. Buprenorphine hydrochloride (Bup---HCl) is one of the most common opioids given to laboratory animals and requires dosing every 6 to 12 hours, demanding repeated animal handling and increased animal stress. Sustained---release formulations of Buprenorphine (SR---Bup) have been shown to provide adequate analgesia for 48---72 hours in other rodent species, eliminating the need for repeated dosing and reducing animal stress. Fourteen guinea pigs separated into 2 groups were either given Bup---HCl (0.05 mg/kg) subcutaneously twice daily for 3 days or SR---Bup (0.3 mg/kg) subcutaneously once. Plasma collection and paw pressure pain analysis (PP) was conducted at 0, 1, 3, 6, 12, 26, 48, and 72 hours. The data shows SR---Bup and Bup---HCl PP coincided with the plasma concentrations averages over the 72 hours postinjection. Both groups PP were higher than base line for the 72---hour period. SR---Bup PP were significantly higher than Bup---HCl PP at 6--- and 12--- hour time points ($P < 0.075$). These results suggest that SR---Bup provides equal and consistent analgesia for a prolonged period of time compared to Bup---HCl and that SR---Bup may be an alternate method for analgesia in guinea pigs.