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Rabbit Analgesia

The intent of this Standard Operating Procedure (SOP) is to describe commonly used analgesics provided to rabbits housed at Comparative Medicine (CM). This SOP is intended for use by those CM staff and investigators whose IACUC protocols are approved to use analgesics. This procedure is approved by the NUS Institutional Animal Care and Use Committee (IACUC). Any deviation must be approved by the IACUC prior to its implementation.

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1. INTRODUCTION

This SOP presents signs of pain and commonly used analgesics for managing pain in rabbits.

2. DEFINITIONS

Pain: Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, and should be expected in an animal subjected to any procedure or disease model that would be likely to cause pain in a human

Analgesia: absence of pain in response to stimulation which would normally be painful.

Preemptive analgesia: the administration of preoperative and intraoperative analgesia

Pain descriptors:

- *Momentary pain:* short-lasting, brief, transient (e.g., seconds) and usually of low intensity.
- *Postprocedural/postsurgical pain:* longer-lasting than momentary (hours to days to weeks), a consequence of tissue injury due to surgery or other procedures.
- *Persistent pain:* lasts for days to weeks such as encountered in studies that investigate pain (and caused by mechanisms other than post procedural pain).
- *Chronic pain:* pain of long duration (i.e., days to weeks to months) typically associated with degenerative diseases, without relief, difficult to manage clinically.

3. MATERIALS

i. Analgesics
ii. Support materials:
    a. Species appropriate scale
    b. 0.9% sterile saline
    c. Needles and syringes

4. PROCEDURES

a. Pain recognition and assessment
    i. Adapt an observation frequency and duration relevant to the protocol (minimum of once during the first 24 hours post-procedure).
    ii. Observe the animal from a distance and then more closely for changes in behavior and signs of pain. Refer to **Table 1**. The number and severity of clinical signs will vary among individual animals.
    iii. Look for changes in behavior and other signs of pain. Report animals in pain to the CM veterinary staff. Please refer to SOP #507 on reporting sick animals.
    iv. **Table 2** outlines procedures with varying pain potential.
    v. Tables 3a & 3b outlines pain potential and suggested non-pharmacologic and pharmacologic interventions given singly or in combination.

Table 1: Clinical signs of post procedural pain in rabbits

Clinical signs
reduced activity
failure to groom
reduced food and/or water intake
squint-eyed
pale eyes (if albino)
changed posture, tucking of abdomen, tensing of muscles
guarding, attempt to hide, or aggressiveness
grinding of teeth

Table 2: Pain potential

Minimal to Mild Pain	**Mild to Moderate Pain**	**Moderate to Severe Pain**
Catheter implantation Superficial tumor implantation Superficial lymphadenectomy Ocular procedures Multiple ID antigen injections Vasectomy Vascular access port implantation	Minor laparotomy incisions Thyroidectomy Orchidectomy C-section Embryo transfer Hypophysectomy Thymectomy	Major laparotomy/ organ incision Thoracotomy Heterotopic organ transplantation Vertebral procedures Burn procedures Trauma models Orthopedic procedures

Table 3a & 3b: Pain potential and suggested non-pharmacologic and pharmacologic interventions given singly or in combination

Table 3a: Pain potential and suggested non-pharmacologic interventions

Minimal to Mild	Mild to Moderate	Moderate to Severe
Wound care	Wound care	Wound care
Soft absorbent bedding	Soft absorbent bedding	Soft absorbent bedding
	Carprofen	Modified food and water access
		Increased food palatibility
		Hydration SC or IP
		Supplemental heat

Table 3b: Pain potential and suggested pharmacologic interventions

Minimal to Mild	Mild to Moderate	Moderate to Severe
Local anesthetic Lidocaine/bupivacaine	Local anesthetic Lidocaine/bupivacaine (adjunct to systemic analgesics) AND	Local anesthetic Lidocaine/bupivacaine (adjunct to systemic analgesics) AND
	Buprenorphine 0.01-0.05 mg/kg SC, IM, IV 6-12h OR	Buprenorphine 0.05 mg/kg SC, IM, IV 6-12h OR
Butorphanol 0.1-0.5 mg/kg IM, IV q 4h OR	Butorphanol 0.1-0.5 mg/kg IM, IV q 4h OR	Fentanyl patch 25 microgram/h, transdermal, q 72 h
Caprofen 4 mg/kg SC, 1.5 mg/kg PO once OR	Caprofen 4 mg/kg SC, q 24h, 1.5 mg/kg PO q 12h OR	
Meloxicam 0.2-0.3 mg/kg SC, PO once	Meloxicam 0.3-1.5 mg/kg SC, PO q 24h	

b. Provide preemptive analgesia unless otherwise approved by the IACUC. Preemptive techniques include parenteral administration of systemic analgesics and infiltration of a suture line with local anesthetics. E.g. Parenteral analgesia with an opioid or nonsteroidal anti-inflammatory drug (NSAID) should be administered prior to making a surgical incision.
c. When possible a combination of analgesics should be used. For example, an opioid may be given by injection as preemptive analgesia, and a post-procedural NSAID may be given orally. Consult a CM veterinarian regarding the usage of drug combinations prior to selection
d. Provide analgesics for a minimum period of 48 hours post-operation for surgical procedures, unless specifies otherwise and approved by the IACUC.

e. Infiltrate local analgesia to areas where a painful stimulus may be induced. Repeat infiltration, as necessary, at specified intervals to maintain analgesia.
f. Refer to **Table 4** for local analgesics and dose. A diffuse catheter can be used if repeat infiltrations are necessary.
g. Refer to **Table 5** for systemic analgesics and dosage regimes.
h. Ensure all drugs are within the expiration date, stored appropriately and usage logged.

Table 4 Local analgesics

Analgesic	Dose	Duration of action	comment
Lidocaine	Injectable or topical; dose for local effect varies with the area requiring anaesthesia. Do not exceed 10 mg/kg	30-60 minutes	Because this drug is acidic, a 0.5-2% lidocaine is diluted 1:10 with 8.4% sodium bicarbonate solution. The toxic dose varies widely across species; ascertain the toxic level prior to administration. Are metabolized by the liver and excreted by the kidneys. Local anesthetics block the action potential of axons by preventing the influx of sodium ions
Bupivacaine	Injectable or topical; dose for local effect varies with the area requiring anaesthesia. Do not exceed 2 mg/kg	3-4 hours	0.25% lidocaine is diluted 1:30 with 8.4% sodium bicarbonate solution. The toxic dose varies widely across species; ascertain the toxic level prior to administration. Are metabolized by the liver and excreted by the kidneys. Local anesthetics block the action potential of axons by preventing the influx of sodium ions
EMLA cream	Thick spread	30-60 minutes	

Table 5: Systemic analgesics

Drug	Dose	Route	Comment
Carprofen	4 mg/kg	SC q 24h	Non-steroidal anti-inflammatory (NSAID). Block peripheral nociception. Effective post surgical pain relief. Metabolised by the liver and excreted by the kidneys
	1.5 mg/kg	PO once or q 12h	
Buprenorphine	0.01-0.05 mg/kg	SC, IM, IV q 6-12h	Partial agonist opioid drug which has potent partial mu agonist activity. Block dorsal lamina neurons. Effective for moderate to severe acute pain. Bound to plasma proteins and excreted via bile in feaces.
Meloxicam	0.2-0.3 mg/kg	SC, PO SID q 24h	NSAID. Minimal to mild pain
	0.3-1.5 mg/kg	PO q 24h	Mild to moderate pain
Butorphanol	0.1-0.5 mg/kg	IM, IV q 4 h	Agonist-antagonist opioid with marked mu antagonist and kappa agonist properties. Effective for moderate to severe acute pain

5. PERSONNEL SAFETY

When working with animals wear appropriate PPE, observe proper hygiene, and be aware of allergy, zoonosis, and injury risks.

6. ANIMAL RELATED CONTINGENCIES

Please call the Emergency veterinary phone 90013073 for veterinary related contingencies out of hours or the duty veterinarian during office hours

7. REFERENCES

- Fish, R.E., Brown, M.J., Danneman, P.J. and Karas, A.Z., Eds. *Anesthesia and Analgesia in Laboratory Animals*, 2nd Edition, Academic Press: New York, 2008. p. 300-327
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- Kohn D. F., Foley P. L., Morris T. H., Swindle M. M., Vogler G. A., and Wixson S. K. *Guidelines for the Assessment and Management of Pain in Rodents and Rabbits*. 2007. JAALAS 46(2) p97-108