

ASSESSING AND MANAGING PAIN IN EXOTIC COMPANION MAMMALS

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Introduction

Small mammals in this document refers to exotic animal species commonly kept as pets such as rodents (rats, mice, chinchillas, guinea pigs), rabbits, and ferrets. A part of managing pain in an animal also includes managing stress in that patient, including making sure they are well hydrated, have normal GI sounds, are at a comfortable temperature and humidity, they have familiar and favorite foods available, any concurrent diseases are being treated, non-stressful sounds and smells, appropriate hiding place, appropriate dry and clean substrate is available, handling is kept to a minimum, and the patient is weighed daily.

Research

Because of the advanced field of laboratory animal medicine, there is more scientific information available regarding analgesia in small mammals than what is known about birds and reptiles combined. Remember that there is no generic small mammal. Some differences in drug metabolism that are known include: after tramadol IV or PO rabbits make over 5 different metabolites and levels of the active drug drops precipitously after just a few minutes, rabbits can seizure and die after being given fipronyl (Frontline®), and rabbits' GI flora is disrupted by certain antibiotics including oral penicillins, macrolides and cephalosporins. There are probably some unknown differences in metabolism within each species and, as some researchers are finding out, there are even subtle differences between strains.

The most is known about the rat, including published studies of pharmacokinetics, pharmacodynamics (using the tail flick test) and established, standard methods of assessing pain.⁶ Remember that laboratory animals are usually young, healthy, and all one strain when tested, and these doses may be too high for a sick patient in your hospital, especially if used in combination with other drugs. A study was performed determining the magnitude and duration of analgesia using the standard hot plate test and the tail flick test, showing (n=61 ea. spp.). In this study, butorphanol SC (2.0 mg/kg for rat; 5.0 mg/kg for mouse) provided mild pain relief for the shortest amount of time (1-2 hours) compared to morphine SC (10 mg/kg in either rat or mouse) that provided intermediate pain relief for the longest amount of time (6-8 hours for rat; 3-5 hours for mouse) and buprenorphine SC (0.5 mg/kg rat; 2.0 mg/kg mouse) provided the highest degree of pain relief for an intermediate amount of time (2-3 hours).

Assessing Pain

It is very difficult to assess pain in small mammals. They seem very stoic and do not cry out in pain unless they are in extreme pain. Small mammals are prey animals, so they do not want to be conspicuous if they are in pain or injured. So, try to observe your patient before they are aware you are observing them. Dr. Flecknell has available a training video with an objective scoring system to evaluate pain in rats. By counting the number of times a rat "flinches" the skin on its back, stretches like a cat or falters in its gait during a set period of time, a numerical score is assigned as to how much pain that rat is experiencing. It is my opinion that all practitioners should learn how to assess pain in their rat patients from this video. There is much laboratory animal medicine information available in the literature and from colleagues. Small mammal practitioners would do well to consult and use this large body of information. Less is known about objectively assessing pain in the mouse and rabbit, but recently a facial grimace scale has been developed for both these species (and the rat) and practitioners should familiarize themselves with these signs of pain: half closed eyes (orbital tightening), pointed or bunched up nose, and whiskers pulled back.

Opioids

Opioids include full agonists such as morphine, oxymorphone, hydromorphone, fentanyl, and alfentanil, and partial agonists such as buprenorphine, and agonist/antagonists such as butorphanol. Tramadol is a weak μ opioid agonist, but can have significant analgesic efficacy due to its inhibition of the reuptake norepinephrine and serotonin.

Advantages of opioids are potent pain relief, well studied in rats, and choices available of varying levels or types of pain relief. Disadvantages of opioids are respiratory depression, nausea, GI Stasis, sedation, and pica with buprenorphine in rats. In rabbits, it is difficult to evaluate if the pain or the analgesic being given is causing the GI stasis. Care should be taken to not give too much opioid and cause too much sedation, or induce too much respiratory depression, because of the possible inability to quickly intubate small mammals.

Overall, butorphanol is recommended for mild pain of short duration, morphine for mild to moderate pain of increased duration, and buprenorphine for severe pain of short to medium duration. Remember to always reassess the patient to determine degree of pain, degree of sedation, and maintenance of normal GI motility. A survey of diplomats of the American College of Laboratory Animal Medicine showed opioids as the analgesic used most often for relief of pain in biomedical studies.

Unfortunately for rabbits, a PK study showed that after oral administration (11 mg/kg) tramadol and its major active metabolite, M1, decreased very quickly to what is considered non-therapeutic levels in a human. (Souza) In addition, an ISOMAC study (evaluating the isoflurane sparing effects of tramadol) using tramadol IV (4.4 mg/kg) there was a significant, but clinically unimportant, reduction of ISOMAC. Based in this PK study and the ISOMAC study, tramadol should not be used alone in rabbits for pain relief despite anecdotal reports to the contrary. Another note on rabbits and opioids: when using fentanyl patches watch for quick (24h) hair regrowth impeding absorption.

I use butorphanol at 0.2 – 0.3 mg/kg SC in most rabbits for mild pain of short duration and I use buprenorphine at 0.02-0.05 mg/kg SC in most rabbits for moderate to severe pain of longer duration. I use less if the animal is ill or is sensitive to the drug.

NSAIDS

Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase (COX) enzymes that help produce prostaglandins which induce inflammation. Two isoforms are of COX (COX-1 and COX-2) are generally targeted. NSAIDS include meloxicam, ketoprofen, carprofen and flunixin meglumine.

Pros – good for mild pain and provides anti-inflammatory action as well

Cons – gastric upset, renal, may lower blood pressure under anesthesia???

Recommendations – meloxicam currently seems to be the most commonly used of all the NSAIDs. I tend to use a dose of 0.2-0.3 mg/kg in most ECM's ; less if they are ill, and maybe not at all if they have renal disease. With any NSAID used long term (>5 days), I use a gastric protectant like omeprazole, famotidine, or sucralfate, and SQ or IV fluids, and check BUN and creatinine especially in geriatric animals (most rats get chronic progressive nephropathy starting at 6 months of age and progressing to significant loss by 1.5 years of age).

Local analgesics

Local analgesics include various routes such as topical, local infiltration, or nerve block (peripheral or as an epidural). The literature has many descriptions of how to place epidural catheters in various laboratory animals including guinea pigs, rabbits and ferrets, using a variety of analgesics. A study in pregnant guinea pigs described placing 27 gauge epidural catheter in the L3-4 intervertebral disc space and administering bupivacaine. Histopathological examination afterwards showed most catheters were properly placed, but some were inadvertently placed in the subdural space resulting in severe depression, and even penetrated the spinal cord. Several articles give detailed descriptions of anatomy and epidural catheter placement and use in ferrets. One study used morphine at 0.1 mg/kg via epidural for OHE and showed attenuation of pain compared to saline epidural. Epidural use in rabbits has been described using 0.1 mg/kg morphine, with care (Barter VCNA)

Note – The low therapeutic index of local analgesics is a good reason to calculate the dose every time prior to use. Dr. Darryl Heard in the Ferrets, Rabbits, and Rodents book states, "For example, if the toxic dose of lidocaine in a rabbit were 10 to 20 mg/kg, the equivalent volume of a 2% lidocaine solution would be 0.5 to 1.0 mL/kg." That is a very small volume! What we do in the clinic is calculate the dose, dilute 1:2 or 1:10 with saline and then administer no more than what we drew up in the syringe.

Pros –few side effects, preemptive, does not affect gut motility

Cons – narrow therapeutic index when consider comparably small size of animal
Recommendation – use more frequently

New methods of providing local pain relief are currently being studied. A recent study showed better pain relief in ferrets undergoing acute, experimentally induced hernia repair with bupivacaine impregnated SIS (small intestinal submucosa) incorporated for repair compared to those whose hernias were repaired with non-impregnated SIS. Also, there is bupivacaine impregnated foam infiltrated into acute hernia incisions in rabbits that showed no adverse effects at necropsy that may be used in the future.

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