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Pain in rabbits: a review for veterinary nurses part 2: management of pain in hospital

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ABSTRACT: Pain management involves considering pain, recognising pain, and managing pain. Part 1 looked at assessment and recognition of pain. This discussed the physiological and behavioural signs that can indicate pain in rabbits. Part 2 (this article) will look at managing pain in the hospitalised rabbit. Analgesic options are discussed to cover all aspects of the pain pathway. Dose ranges for constant rate infusions are available. Local anaesthesia and analgesia techniques are discussed. Part 3 (next article) will look at managing the chronic pain rabbit at home.

Keywords: Rabbit pain; rabbit pain management; rabbit analgesia

Introduction

There is still a lot of progression required for pain management and anaesthesia in exotics, to achieve a level comparable to cat and dog standards. However, knowledge is always moving forward: there is new information coming through all the time.

This article aims to review the information available and provide some tips and techniques.

Managing pain

Pain is the fourth vital sign in any animal. A patient evaluation that includes a pain assessment should occur on admission, post-temperature/pulse/respiration (TPR) and/or pre- and post-analgesia administration. Changes in the analgesia plan should be made accordingly.

In surgery, we should no longer 'turn up the gas' on a painful anaesthetised rabbit. Increasing inhalants only mask pain and cause hypotension (Nugent-Deal, 2016), therefore compromising patient safety. Injectable analgesia should be administered incrementally based on assessment. If pain is a recurrent problem during certain procedures, the whole analgesia and anaesthesia protocol should be re-evaluated. For more information regarding good standards of rabbit and small mammal anaesthesia see Nugent-Deal (2016).

No single analgesia is suitable for all situations: multi-modal analgesia is generally gold-standard. An example of a multi-modal protocol is found in **Figure 1**.

Use more effective opioids (see Appendix 1 in supplementary files)

For moderate to severe pain, morphine at 0.5–2 mg/kg every 2–4 hours is advised (Hedley, 2020). Morphine has been widely studied in laboratory rabbits but often not from an analgesia

Premedication
Morphine 1mg/kg Midazolam 0.5mg/kg
Induction
Ketamine 5–10mg/kg diluted, given slowly IV and to effect, to enable intubation
Maintenance
Minimal levels of isoflurane or sevoflurane, and oxygen Ketamine CRI or fentanyl/ ketamine CRI on standby/ peri-operatively if required
Epidural
Lidocaine 1mg/kg Bupivacaine 1mg/kg
Post – operatively
Morphine 1–2mg/kg Q4–6h or buprenorphine 0.03–0.06mg/kg Q6–8h (based on assessment/ success of epidural)
Meloxicam 0.6mg/kg Q12h given pre–or post–operatively, dependent on clinical status.
Ketamine CRI or fentanyl/ ketamine CRI post-operatively if required.

Figure 1. Example of analgesia plan for a hindlimb fracture repair in a healthy rabbit (author's own). Additionally: pro-kinetics, antibiotics, fluid therapy, post-operative thermotherapy. With thanks to Matthew Johnston.

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perspective useful to veterinary medicine. However, this research helps us establish initial safety protocols. Lesser researched full μ -agonists, such as methadone and fentanyl, are also successful.

Methadone has suggested doses in clinical practice of up to 0.7 mg/kg (Hedley, 2020). Pignon (2018) describes doses of 1–2 mg/kg every four hours. A 2015 study compared methadone and morphine in healthy pain-free rabbits, administered at 2 mg/kg. Analgesia was superior in methadone compared to morphine during a 20-min period in the six hours study, using a pressure algometer on the lumbosacral junction (Touzot-Jourde et al., 2015).

Otherwise, morphine and methadone have similar effects in rabbits (Pignon, 2018). One advantage of methadone is that it can be used slowly intravenously (IV), whereas IV morphine may cause histamine release.

Fentanyl patches can achieve plasma levels equivalent to analgesia in humans. However, several factors affect absorption rate, and patches have not been studied in relation to nociception and pain behaviours following a painful stimulus (Foley et al., 2001). Using a fentanyl constant rate infusion (CRI) offers more control over pain levels than patches, as the dose or rate can be altered, based on assessment. Extreme care needs to be taken to ensure the rabbit cannot access the patch to chew it, and the companion rabbit is separate from them.

For mild to moderate pain: buprenorphine at 0.03–0.06 mg/kg Q6–8 hours based on assessment is successful. Analgesic efficacy under 0.03 mg/kg is questionable. Administration by the subcutaneous route (SQ) causes a large variation in plasma levels (Freijis, 2016), therefore IV or IM is recommended, although IM administration of the multi-dose preparation has anecdotally been described as painful (Hedley, 2020). Sustained release buprenorphine and hydrogel transdermal buprenorphine patches may become available soon (Hawkins, 2015).

Butorphanol is often advised for mild pain. However, it is important to remember that by the time we are able to observe rabbit pain, and rabbits are displaying pain behaviours, the pain is no longer mild, and the patient would likely benefit from a more effective analgesic.

Butorphanol is useful as part of a sedation in a non-painful animal, for a non-painful procedure. Similarly to midazolam, it may

be useful to manage stress in some cases of dyspnoea.

It is also important to remember that these opioids are not licenced for the use in rabbits, and are therefore used according to the cascade system, under veterinary direction.

Managing veterinary myths about opioids in rabbits

An unfortunate and still prevalent myth is using no or 'low' doses of opioids in gastrointestinal stasis management for fear of 'slowing down motility' further. This is considered no longer clinically relevant (Benato et al., 2019; Deflers et al., 2018; Nugent-Deal, 2016).

Pain is usually responsible for gut stasis (Hollwarth, 2020; Pignon, 2018). Based on assessment, a full μ -agonist such as methadone or morphine, or a high dose buprenorphine is recommended initially, to break the pain cycle (Nugent-Deal, 2016; Pignon, 2018). Analgesia can be then continued based on assessment.

Gastrointestinal stasis patients then require working up: stasis is a symptom, not a cause.

Occasionally gut stasis may be caused by stress rather than pain. In these cases, pain management does not need to be as aggressive, but is still essential, because gut stasis *in itself* will cause discomfort (due to gastrointestinal/ visceral distension).

Use more local analgesia (see Appendix 2)

Local analgesia *blocks* pain perception: it is the most effective method of prevent



Figure 2. Intra-testicular block. The aim is to reach the spermatic cord, which receives direct clamp stimulation during castration. The remainder is used as an incisional block.

sensitisation of the central nervous system (Lafferty et al., 2015). For routine procedures it is easy to do incisional line blocks, splash blocks and intra-testicular blocks on castrations (Figure 2). Ovarian pedicle blocks are described in dogs and cats, but the author does not know whether this is easily achievable in rabbits.

Epidurals, placing a wound soaker catheter (Figures 3 and 4) or specific nerve blocks may require practice (for instance, practicing on cadavers or attending workshops). For advanced procedures such as ear canal ablations, mandibular and auriculopalpebral blocks have shown successful pain management (D'Urso et al., 2018).

In the US, Lichtenberger and Lennox (2008) described a marked improvement in post-operative recovery in small mammal patients receiving epidurals. The rabbit is a common laboratory model for

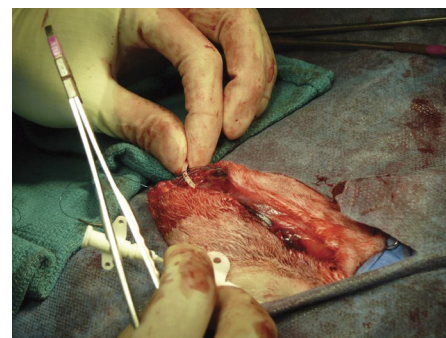


Figure 3. Placing a wound soaker catheter on an hindlimb amputation site. The catheter can be injected with bupivacaine, which will infiltrate the surgical site and block pain sensation for six to eight hours. With kind permission from Matthew Johnston.



Figure 4. Wound soaker catheter in-situ. With kind permission from Matthew Johnston.

epidurals (Pollock, 2002), but epidurals are still under-utilised in UK veterinary practice. Using morphine (or an alpha 2 adrenergic agonist in a healthy patient) significantly prolongs analgesic duration (Figures 5 and 6).

Use CRIs in rabbits (see Appendix 3)

Opioid CRIs combined with ketamine are widely advised by exotic animal practitioners (Biascochea, 2019; Hawkins, 2015; Huynh et al., 2016; Lennox, 2013; Lichtenberger & Lennox, 2008; Nugent-Deal, 2016, 2019). Effective doses are higher than those used in cats and dogs (Figure 7).



Figure 5. Rabbit epidural. With kind permission from Stephen Cital.

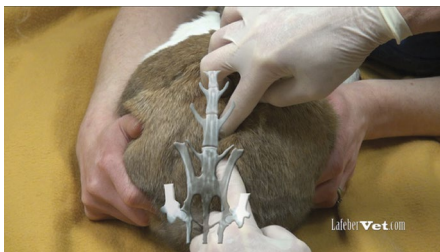


Figure 6. Rabbit epidural landmarks. With kind permission from LafeberVet.com.

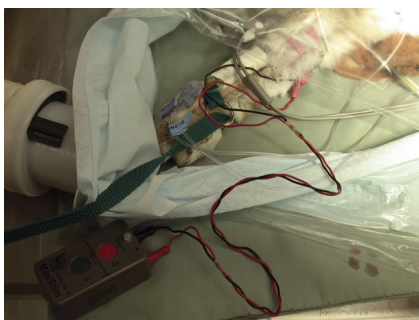


Figure 7. Photo showing cephalic vein catheterisation for an opioid CRI. The rabbit was having a targeted femoro-sciatic local block, hence the peripheral nerve stimulator. With kind permission from Matthew Johnston.

Fentanyl CRIs reduce the minimal alveolar concentration (MAC) of isoflurane in rabbits, therefore improving mean arterial pressure and cardiac output under anaesthesia (Tearney et al., 2015). Ensure intubation and ventilation if using peri-operatively, due to opioid-related respiratory depression under anaesthesia.

Lidocaine CRIs are recommended in gastrointestinal syndrome (Carpenter & Marion, 2018) and have been shown to reduce the inflammatory response, decrease volatile agent, increase gastrointestinal motility, and reduce pain in both human and veterinary medicine. In rabbits, lidocaine CRIs decrease the isoflurane MAC (Schnellbacher et al., 2013).

A study in rabbits comparing a lidocaine CRI group (at 100 µ/kg/min) and a buprenorphine group (at 0.06 mg/kg IV Q8h) following ovariohysterectomy showed that the lidocaine CRI group had significantly higher post-operative gastrointestinal motility, food intake, faecal output, lower glucose concentrations, lower overall heart rates, and a higher number of normal behaviours (sprawling, travelling and frolicking) compared to the buprenorphine group. This shows potentially better pain management than buprenorphine (Schnellbacher et al., 2017), although the pain score system utilised showed no difference in pain scores between the groups. Further studies would benefit looking at both agents together.

Use the effective non-steroidal anti-inflammatory (NSAID) dose (see Appendix 4)

Meloxicam is widely underdosed in rabbits. The effective rabbit dose is approximately 8× the dog dose, and this dose is then given twice daily (Varga, 2016), i.e. 0.6–0.8 mg/kg, every 12 hours; 1 mg/kg has also been quoted every 12 hours, in suitable patients (Pignon, 2018).

Giving an NSAID prior to surgery has greater efficacy (in dogs), but unless normotension can be guaranteed, it may be safer in some individuals to give post-operatively.

There are not the same concerns with oral NSAIDs and anorexia with rabbits as there are with dogs and cats, as they should be support fed, so their stomach is never empty (Varga, 2015). However, similarly, hydration and normal renal parameters are

recommended prior administration, especially if clinical signs indicate.

Because rabbits are a food-producing species in the EU, the licencing process for meloxicam use in rabbits is a lengthier process compared to other pet species.

More information about meloxicam dosing in rabbits can be found in Part 3.

Use adjunctive analgesia (see Appendix 5)

Adjunctive analgesia includes tramadol, paracetamol, gabapentin and NMDA receptor antagonists.

Some adjunctive agents have been studied in lab rabbits, but rarely from a perspective of analgesia that is clinically useful to veterinary practice, therefore information is often incomplete. They can and should be used in hospital and at home, but be aware of the limited information on their use in rabbits, and of the prescribing cascade.

In hospital, ketamine at sub-anaesthetic adjunctive doses prevent wind-up pain, and are useful as a CRI (due to the short duration of action) (Varga, 2016).

Tramadol, paracetamol, gabapentin, NMDA receptor antagonists and transmucosal buprenorphine will be discussed in 'Part Three'.

Case studies of successful pain assessment and management

For case study 1, see Figures 8.1 to 8.6.



Figure 8.1. Patient with inadequate pain management after femoral head and neck excision. Current regime: buprenorphine 0.03 mg/kg every 6 hours, meloxicam 0.6 mg/kg Q12 hours.

Name: [redacted] Date: [redacted] Time: [redacted] Initial: [redacted]

History and signalment (complete once)

Species/breed: Rabbit | crossbreed
 Age: 6 years
 Gender/neuter status: FN
 Vaccination status: Vaccinated
 Previous health issues: Recent respiratory disease
 Husbandry: Unknown but spends time outdoors
 Normal personality: Lively interactive
 Presenting problem: Post FHNE R.hind

Whole patient pain assessment

Pain scales
 Scales used: Rabbit Grimace Scale
 Scores: 5/10 Intervention levels: none currently

Analogy
 Would this condition be painful to you? Yes

Behaviour parameters

Position in the kennel/box/consult room/enclosure: Facing the back
 Demeanour: Withdrawn
 Posture: Sternal, stretched out to reduce weight on affected limb, affected limb uppermost
 Interaction with conspecifics/owners/staff: Not interacting
 Reaction to approach: Stops grimacing when approached or observed, shows interest
 Locomotion, mobility and level of activity: Weight bearing but slow postural changes
 Reaction to palpation: Flinching ++
 Reaction to handling: ↑RR
 Any vocalisation?: X
 Any extra abnormal behaviours observed?: X

Physiological/ physical parameters

Respiratory rate/effort/lung sounds: Normal respiratory rate, effort and lung sounds
 Heart rate/rhythm/pulse quality: Mildly tachycardic, pulses not assessed, regular
 Temperature: Normothermic, temp = 38.7°C
 Gut sounds (species applicable): Good gut sounds in all quadrants L + + R + ++
 Mucous membrane colour/quality/CRT: Pink, moist MMs, difficult to visualise CRT
 Mentation: Quiet, alert, responsive
 Blood pressure: Not taken
 Eating?: 0/N Drinking?: Y/N? Any observations: Eating small amounts of kale, herbs
 Urinating?: 0/N Defecating?: 0/N Any observations: Urinated on herself, passing small amounts of small faeces
 General condition and hydration: Good hydration, some weight loss
 Any lesions, wounds, injuries or relevant painful body parts?: Post of FHNE R. hind.

Figure 8.2. Whole patient pain assessment for the painful rabbit featured in Figure 8.1.

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Rabbit Grimace Scale (RbtGS) Score Sheet

Developed by Dr Matt Leach and the Pain and Animal Welfare (PAWS) group at Newcastle University.

Instructions
 The Rabbit Grimace Scale describes five action units that should be scored. These action units have been shown to increase in intensity in response to post-procedural pain (Kitching et al. 2012). These action units should only be used to assess animals. Each animal should be observed for a short period of time to avoid scoring brief changes in facial expressions that are unrelated to the animal's welfare.
 Observe the rabbit considering each of the facial action units outlined in this sheet to assign a score. To assist with scoring, use the scoring sheet alongside the poster and manual which contain visual and text descriptions of each action. This scoring sheet should always be used alongside other validated indices of pain.

Patient Name: [redacted] Sex: [redacted]
 Reason for admission: Post FHNE R.hind (colony)

1	Orbital Tightening	0	0	0	0
	Moderately present	1	1	1	1
	Obviously present	2	2	2	2

• Is there a narrowing of the orbital area with a closing of the eyes? Over 1/2 closed is a score of '2'.
 • A score of '2' can include an eye squint (contraction of muscles around the eye).

2	Cheek Flattening	0	0	0	0
	Moderately present	1	1	1	1
	Obviously present	2	2	2	2

• Have the cheeks lost their rounded (bulging) shape and become flatter? At a score of '2' cheeks have a sunken look.
 • Have the edges of the cheek muscles lost their definition (i.e. visibility)? At a score of '2' they are not very visible.
 • Has the general face shape changed from rounded to angular and have the edges of the cheek muscles become less visible?

3	Nostril (Nose) Shape	0	0	0	0
	Moderately present	1	1	1	1
	Obviously present	2	2	2	2

• Has the upper edge of the nostrils lost its 'U-shaped' profile and formed a more 'V-shaped' profile?
 • Has the lower edge of the nostrils lost its curved profile and become straighter and more vertical?
 • Please note, the openness of the nostrils is NOT related to the nostril shape.

4	Whisker Shape & Position	0	0	0	0
	Moderately present	1	1	1	1
	Obviously present	2	2	2	2

• Have the whiskers lost their relaxed, natural curved profile to become increasingly straight?
 • Have the whiskers clumped together?
 • Do most of the whiskers point in the same direction? At a score of '2', most of the whiskers seem to point downwards.

5	Ear Shape & Position	0	0	0	0
	Moderately present	1	1	1	1
	Obviously present	2	2	2	2

• Have the ear apertures lost their open (dish-shaped) appearance and become folded/curling inwards (more cylindrical)?
 • Has the distance between the lower inside edges of the ears decreased? At a score of '2' they are almost touching.
 • Have the ears moved from standing vertically to the back or side of the rabbit? At a score of '1', the ears are at a 45° angle relative to the back or sides. At a score of '2', the ears are held closer to the back or sides of the body.

Totals		5/10			
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Figure 8.3. Rabbit grimace scale scoring sheet for the painful rabbit featured in Figure 8.1 The decision was to stop buprenorphine and start morphine 1mg/kg IM every 4 hours.



Figure 8.4. Same patient photographed 20 hours after starting morphine.

Name: [redacted] Date: [redacted] Time: [redacted] Initials: [redacted]

History and signalment (complete ones)

Species/breed: [redacted]
 Age: [redacted]
 Gender/neuter status: [redacted]
 Vaccination status: [redacted]
 Previous health issues: [redacted]
 Husbandry: [redacted]
 Normal personality: [redacted]
 Presenting problem: [redacted]

Whole patient pain assessment

Pain scales
 Scales used: Rabbit Grimace Scale
 Scores: 2/10 Intervention levels: none currently

Analogy
 Would this condition be painful to you? **Yes**
 Patient is less painful than before but there is still some discomfort.

Behaviour parameters

Position in the kennel/ box/ consult room/ enclosure: Facing front of kennel
 Demeanour: Brighter
 Posture: Still in sternal, affected leg uppermost
 Interaction with conspecifics/ owners/ staff: Interested in visitors to her kennel, interactive
 Reaction to approach: Interested
 Locomotion, mobility and level of activity: Weight bearing but generally inactive
 Reaction to palpation: Mild flinching on palpation of surgical site
 Reaction to handling: Less stressed
 Any vocalisation?: X
 Any extra abnormal behaviours observed?: X

Physiological/ physical parameters

Respiratory rate/ effort/ lung sounds: Slightly high respiratory rate, normal lung sounds
 Heart rate/ rhythm/ pulse quality: Still mildly tachycardic, regular, pulses not assessed
 Temperature: Not taken at this time point
 Gut sounds (species applicable): Good gut sounds in all quadrants L ++ | ± R ++ | ++
 Mucous membrane colour/ quality/ CRT: Pink mms, difficult to visualise CRT
 Mentation: Bright, alert, responsive
 Blood pressure: Not taken
 Eating? Drinking? Any observations: Eating hay, greens, pellets
 Urinating? Defecating? Any observations: Seen posturing correctly to urinate (not on herself this time), passing small amount of normal faeces.
 General condition and hydration: Good
 Any lesions, wounds, injuries or relevant painful body parts?: Post FHNE R.H.

Figure 8.5. Whole patient pain assessment, following swapping analgesia from buprenorphine to morphine.

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Rabbit Grimace Scale (RbtGS) Score Sheet

Developed by Dr Matt Leach and the Pain and Animal Welfare (PAWB) group at Newcastle University.

Instructions
 The Rabbit Grimace Scale describes five action units that should be scored. These action units have been shown to increase in intensity in response to post-procedural pain (Hoisinger et al. 2012). These action units should only be used in awake animals. Each animal should be observed for a short period of time to avoid scoring brief changes in facial expressions that are unrelated to the animal's welfare.
 Observe the rabbit considering each of the facial action units outlined in this sheet to assign a score. To assist with scoring, use the scoring sheet alongside the poster and manual which contain visual and text descriptions of each action. This scoring sheet should always be used alongside other validated indices of pain.

Observer: [redacted] Date: [redacted] Time: [redacted] Initials: [redacted]

Species: [redacted] Sex: [redacted] Age: [redacted]

Procedure: Post FHNE R. hnd (20hrs)

Time of assessment: [redacted]

Site / Animal number: AM

Score	Description	0	1	2
1	Orbital Tightening	Not present	Moderately present	Obviously present
	0	1	2	
	0	1	2	
2	Cheek Flattening	Not present	Moderately present	Obviously present
	0	1	2	
	0	1	2	
3	Nosil (Nose) Shape	Not present	Moderately present	Obviously present
	0	1	2	
	0	1	2	
4	Whisker Shape & Position	Not present	Moderately present	Obviously present
	0	1	2	
	0	1	2	
5	Ear Shape & Position	Not present	Moderately present	Obviously present
	0	1	2	
	0	1	2	
Totals		2	10	

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Figure 8.6. Rabbit Grimace Scale scoring sheet, following swapping analgesia from buprenorphine to morphine. On reflection: pain levels improved post- morphine. There is also a factor of time post-surgery. This patient would have benefited from: an epidural for the procedure; full μ -agonists or a CRI peri- and post-operatively; thermotherapy.



Figure 9.1. Patient had a thoracotomy and thymoma removal surgery by median sternotomy the day previous. At 4am the patient was described as 'doing well'; the CRI rate was reduced by half. Photograph was taken at 8am, four hours after the CRI rate reduction.

In case study 2, the patient had a thoracotomy and thymoma removal surgery by median sternotomy the day previous. At 4am the patient was described as 'doing well'; the CRI rate was reduced by half. **Figure 9.1** was taken at 8am, four hours after the CRI rate reduction.

Current analgesia: fentanyl (5µ/kg/hr) and ketamine (0.1mg/kg/hr) CRI. The local block had worn off by this time point.

- positioned in the corner of his kennel but facing outwards
- inactive
- slightly miserable demeanour
- not interested in interaction
- not moving
- respiratory rate was 130 (potentially due to condition/ surgery)
- heart rate: 200
- mucous membranes pink
- normothermic
- very quiet gut sounds
- scoring 4.5/8 on the Rabbit Grimace Scale, is visibly grimacing in the photo
- taking weight off the surgical site by slightly arching his upper back
- reacted to palpation around the surgical site by an increase in respiratory rate only
- since the CRI was reduced at 4am, had stopped eating and defecating.

The patient was painful: The CRI rate was increased again back to fentanyl at 10µg/kg/hr and ketamine at 0.2mg/kg/hr. He was administered meloxicam at 0.6mg/kg SC BID.

Figure 9.2 shows the patient three hours after increasing the fentanyl and ketamine CRI rate back to 10 µg/kg/hr and 0.2mg/kg/hr respectively, and post-meloxicam injection at 0.6mg/kg.

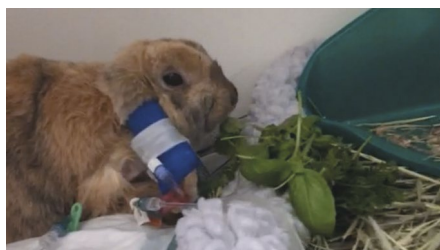


Figure 9.2. Patient photographed three hours after increasing the fentanyl and ketamine CRI rate back to 10 µg/kg/hr and 0.2 mg/kg/hr respectively, and post-meloxicam injection at 0.6 mg/kg.

- demeanour: 'quiet, alert and responsive'
- still mildly tachypnoeic (RR 120) (potentially due to condition/ surgery)
- heart rate 180
- normothermic
- audible gut sounds
- pink mucous membranes
- scoring 2.5/8 on the Rabbit Grimace Scale
- no reaction to palpation around the surgical site
- eating fresh herbs
- rousable and interactive with staff on approach (came to greet you)
- was able to hop about normally to access food and water
- posture was more normal (no longer arching his back)
- defecating well, and urinating.

As he had improved clinically and pain wise, it was decided to maintain the CRI at this rate, as this rate appeared to be successful in treating his pain.

Plan: visually observe respiratory rate/ effort and demeanour every two hours, and pain score every four-six hours. As stable, TPRs were reduced to BID, to reduce handling and stress.

Reflection: pain levels improved when CRI rate was increased back to what it was originally and administered an NSAID. Patient was doing well on the original CRI rate, therefore it was not necessary to have reduced the rate.

This patient would have benefited from:

- a chest drain or wound soaker catheter for on-going local analgesia, (and on-going air or fluid removal)
- having the NSAID earlier on
- thermotherapy.

Managing the stressed rabbit

Veterinary nurses are very good at identifying signs of stress in their patients. Recognising and managing stress from a handling and environmental perspective has been covered in Foote (2020).

The painful patient is likely to be stressed and anxious, or the anxious or stressed patient will respond more extremely to painful stimulus.

Pain should be treated first, then reassessed and reimplemented based on assessment.

If the patient continues to exhibit behavioural signs of stress despite pain being perceivably controlled, add in anxiolytics or low dose sedation. These often work synergistically with other anaesthetic agents or opioids:

- Midazolam: 0.2–0.5 mg/kg IM/IV as required (suitable for patients that may be cardiovascular-unstable)
- Butorphanol 0.1–0.5 mg/kg IM/IV every 4 hours
- Medetomidine or dexmedetomidine micro-doses at 1–3 µ/kg (suitable for healthy patients that are cardiovascular-stable) every 4–6 hours or as required (Biascoechea, 2019; Lichtenberger & Lennox, 2008; Varga, 2016) (**Figure 10**).

Both midazolam and butorphanol can also be life-saving anxiolytics in certain respiratory distress rabbit cases.

Newer tablet form anxiolytics used in pet cats and dogs are generally studied in laboratory rabbits, but only from toxicology or pharmacological perspectives. However,

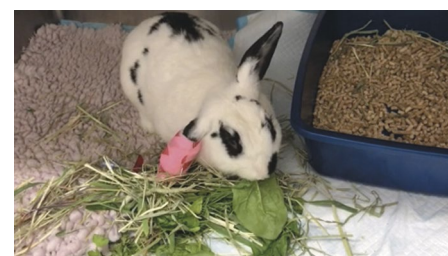


Figure 10. Alfie was exhibiting signs of stress when admitted to hospital, such as trying to escape and being averse to handling. A dose of 0.5mg/kg midazolam IM (or 0.3mg/kg IV) every 6-8 hours greatly reduced his anxiety, and also served as an appetite stimulant. With kind permission from Linda Osborne.

trazadone has had successful preliminary studies in laboratory rabbits for the purpose of anxiety reduction (Rickerl et al., 2020) and may be a future anxiolytic for pet rabbits.

Conclusion

This article acknowledges the difficulty in assessing and managing pain in rabbits, but new information is coming through all the time: we can keep raising the standards.

It is important to be able to assess pain in order to manage it. Part 1 described pain assessment. Part 2 (this article) provided information on pain management in hospital. Part 3 (next article) will look at managing a chronic pain rabbit at home.

In managing pain, the solutions described are simple to achieve but will have a significant improvement on patient welfare (such as making a local block part of a routine protocol), or perhaps require more practice (such as doing an epidural or a dental block). Multi-modal approaches and opioid drug doses, constant rate infusions, local agents and adjunctive agents are described. These cover all aspects of the pain pathway (Tables A1–A5 in supplementary materials).

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References

- Benato, L., Rooney, N. J., & Murrell, J. C. (2019). Pain and analgesia in pet rabbits within the veterinary environment: A review. *Veterinary Anaesthesia & Analgesia*, 46(2), 151–162. <https://doi.org/10.1016/j.vaa.2018.10.007>
- Biascochea, J. (2019). Anaesthesia and analgesia in exotic companion mammals. PVMA https://cdn.ymaws.com/www.pavma.org/resource/resmgr/docs/kvc/2019/biascochea_jose/1.analgesia_and_anesthesia_i.pdf
- Carpenter, J. W., & Marion, C. J. (2018). *Exotic animal formulary* (5th ed). Elsevier.
- Deflers, H., Gandar, F., Bolen, G., Farnir, F., & Marlier, D. (2018). Influence of a single dose of buprenorphine on rabbit (*Oryctolagus cuniculus*) gastro-intestinal motility. *Veterinary Anaesthesia & Analgesia*, 45(4), 510–519.
- D'Urso, E. S., Zani, D. D., Dacerno, M., Gioeni, D., Rabbogliatti, V., Ravasio, G. (2018). Locoregional anaesthesia for peri-operative pain management in rabbits undergoing total ear canal ablation and lateral bulla osteotomy (TECALBO): Case series. *International Journal of Health, Animal Science and Food Safety. Proceedings of the Veterinary and Animal Science Days 2018*, 6th–8th June, 72–73.
- Foley, P., Henderson, A., Bissonette, E., Wimer, G. R., & Feldman, S. H. (2001). Evaluation of fentanyl transdermal patches in rabbits: Blood concentrations and physiologic response. *Comparative Medicine*, 51(3), 239–244.
- Foote, A. (2020). Evidence-based approach to recognising and reducing stress in pet rabbits. *The Veterinary Nursing Journal*, 35(6), 167–170.
- Freijs, E. (2016). Comparison of plasma levels and analgesic effect between oral transmucosal and subcutaneous administration of buprenorphine in rabbits. https://stud.epsilon.slu.se/9518/1/freijs_e_160922.pdf
- Hawkins, M. G. (2015). Advances in exotic mammal clinical therapeutics. *The Veterinary Clinics of North America: Exotic Animal Practice*, 18(2), 323–337. <https://doi.org/10.1016/j.cvex.2015.01.008>
- Hedley, J. (2020). BSAVA small animal formulary, Part B: Exotics (10th ed.). BSAVA.
- Hollwarth, A. (2020). Evidence-based analgesia in exotic pet medicine. *Today's Veterinary Practice*. <https://veterinary-practice.com/article/evidence-based-analgesia-in-exotic-pet-medicine>
- Huynh, M., Boyeaux, A., & Pignon, C. (2016). Assessment and care of the critically ill rabbit. *The Veterinary Clinics of North America: Exotic Animal Practice*, 19(2), 379–409. <https://doi.org/10.1016/j.cvex.2016.01.011>
- Lafferty, K., Cital, S., & Goldberg, M. E. (2015). Analgesia in exotic animals. In: M. E. Goldberg & N. Shaffran (Eds.), *Ch 13 in Pain management for veterinary technicians and nurses* (pp. 216–263). Blackwell Publishing.
- Lennox, A. M. (2008). Clinical technique: Small exotic companion mammal dentistry: Anaesthetic considerations. *Journal of Exotic Pet Medicine*, 17(2), 102–106.
- Lennox, A. M. (2013). The use of constant rate infusion analgesia in exotic companion mammals. *Proc Assoc Exot Mamm Vet Conf*.
- Lichtenberger, M., & Lennox, A. (2008). The critical mammal disaster: Part one. *NAVCC Conference* (pp. 1840–1847).
- Nugent-Deal, D. J. (2016). Quality exotic small mammal anaesthesia. <https://lafeber.com/vet/quality-exotic-small-mammal-anaesthesia/>
- Nugent-Deal, D. J. (2019). Exotic small mammal anaesthetic techniques. <https://www.vetfolio.com/learn/article/exotic-small-mammal-anaesthetic-techniques>
- Pignon, C. (2018). Emergency and critical care of rabbits. <https://lafeber.com/vet/emergency-and-critical-care-of-rabbits/>
- Pollock, C., Echols, M. S., Lichtenberger, M. (2013). Epidural anaesthesia in small mammals. <https://lafeber.com/vet/epidural-anaesthesia-in-small-mammals/>
- Rickerl, K., Reed, J., & Brundage, C. (2020). Physiological effect of trazadone hydrochloride use for anxiety and sedation in rabbits (*Oryctolagus cuniculus*). *The FASEB Journal*, 34(S1), 1–1.
- Schnellbacher, R. W., Carpenter, J. W., Mason, D. E., KuKanich, B., Beaufrière, H., & Boysen, C. (2013). Effects of lidocaine administration via continuous rate infusion on the minimum alveolar concentration of isoflurane in New Zealand White rabbits (*Oryctolagus cuniculus*). *American Journal of Veterinary Research*, 74(11), 1377–1384. <https://doi.org/10.2460/ajvr.74.11.1377>
- Schnellbacher, R. W., Divers, S. J., Comolli, J. R., Beaufrière, H., Maglaras, C. H., Andrade, N., Barbur, L. A., Rosselli, D. D., Stejskal, M., Barletta, M., Mayer, J., Rodriguez, P., & Quandt, J. E. (2017). Effects of intravenous administration of lidocaine and buprenorphine on gastrointestinal tract motility and signs of pain in New Zealand White rabbits after ovariohysterectomy. *American Journal of Veterinary Research*, 78(12), 1359–1371. <https://doi.org/10.2460/ajvr.78.12.1359>
- Tearney, C. C., Barter, L. S., & Pypendop, B. H. (2015). Cardiovascular effects of equipotent doses of isoflurane alone and isoflurane plus fentanyl in New Zealand White rabbits (*Oryctolagus cuniculus*). *American Journal of Veterinary Research*, 76(7), 591–598. <https://doi.org/10.2460/ajvr.76.7.591>
- Touzot-Jourde, G., Nino, V., & Holophème-Doran, D. (2015). Comparison of methadone and morphine sedation and analgesia in the NZW rabbit. *Workshop analgesics. Journal of Veterinary Pharmacology & Therapeutics*, 38, 73–74.
- Varga, M. (2015). Emergency management of gut stasis in rabbits. *Companion Animal*, 20(1), 20–25.
- Varga, M. (2016). Analgesia and pain management in rabbits. *Veterinary Nursing Journal*, 31(5), 149–153.