Pain management in sheep and goats: Applications and techniques

Joe S. Smith, DVM, MPS, PhD, DACVIM, DACVCP

Assistant Professor of Farm Animal Medicine and Veterinary Clinical Pharmacology, Large Animal Clinical Sciences, University of Tennessee, Knoxville, TN 37996

Abstract

As small ruminants increase in popularity as production and companion animals in North America, clinicians are routinely challenged with determining pain mitigation strategies for sheep and goats. With no FDA or similarly labeled pain medications for sheep or goats currently on the market, small ruminant practitioners are often tasked with developing creative analgesic strategies for these species. Preemptive and multimodal analgesia can be used to mitigate pain, in addition to directed therapies such as ultrasound-guided local anesthesia and focused catheterization such as wound soaker catheters or epidural catheters. Additionally, several non-pharmacologic methods, such as acupuncture, can also be utilized for the mitigation of pain in sheep and goats.

Key words: analgesia, small ruminant, opioid, epidural, acupuncture

Introduction

Sheep and goats are becoming more popular as production and companion animals in North America. As a result of this, there is an increased need to reduce pain from noxious stimuli that can occur from production procedures, surgeries or traumatic injuries. Multiple pharmacologic tools and applications exist for the mitigation of pain in these species, and as veterinarians, creative multimodal solions are often needed to ensure animal welfare when planning pain management strategies.

The pain pathway

When considering the pathophysiology of pain, it is important to consider the four steps in pain transmission (Table 1).[1] Depending on what painful situation is present, specific drugs can be effective at different steps of the pathway. An important consideration is the use of "multimodal" analgesia, where multiple drugs from different classes are used. This has the benefit of working on multiple stages of the pain pathway, as well as reducing the total amount of any single drug needing to be administered.

Pharmacologic options

Currently in the United States, no drugs are labeled for pain in sheep and goats. Practitioners commonly use drugs labeled for other species or people in an extralabel manner in these species. Common drug classes utilized include: nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, dissociatives like ketamine, local anesthetics, and GABA analogs like gabapentin. Tables 2 and 3 list common classes of drugs, doses and routes that are described for use in sheep and goats.[2,3]

Techniques

Another component of the management of pain in sheep and goats is the techniques in the application of the practices. Several key concepts include anticipating painful procedures and preemptively acting (an example of administering an NSAID prior to surgery), using multimodal approaches (combining an NSAID with an opioid) as well as considering local/regional practices where applicable (such as a regional perfusion, soaker catheter, or ultrasound-guided application). Specific techniques are listed below.

Epidural catheters

An extension of epidural anesthesia is the use of an epidural catheter for repeated drug administration. These catheters have recently become more economical in terms of price, and as such are being used more frequently. This technique is most commonly applied for analgesia of orthopedic procedures, an example being pelvic limb fracture repair. While case selection is important, epidural catheterization can provide ease of access for repeated drug administration. Clinicians should identify tractable animals that can be confined to a small pen in the hospital post-procedure for several days.[3] Clinicians should exercise caution in the use of epidural catheterization, as non-tractable animals could be at risk for removal or damage of the catheter. The use of preservative-free drug formulations is encouraged to prevent secondary damage to epidural structures.

Table 1: Components of the pain transmission pathway.

Pain pathway step	Signal	Drugs that act on this step
Transduction	Pain is initiated at the area of injury. Signal is generated and moves toward local nerves.	Local and regional anesthesia, opioids, alpha2 adrenergic agonists, NSAIDs
Transmission	Signal is propagated to larger nerves while en route to the spinal cord.	Local and regional anesthesia
Modulation	Signal is received at the dorsal region of the spinal cord and propagated toward the brain.	NSAIDs, opioids, local anesthetics, sedatives, dissociative anesthetics
Perception	Signal is received and interpreted by the brain as a painful stimulus.	NSAIDs, opioids, injectable anesthetics, sedatives

Table 2: Described analgesic drugs for sheep.

Drug	Mechanism of action	Dose	Route	Frequency	Comments
Opioids					
Morphine	μ agonist		PO		Not recommended PO
		0.05 - 0.1 mg/kg	IV or SC	q 4-6 hr	
Fentanyl	μ agonist; κ antagonist	2.5 microgram/ kg/hr	TD	Patch applied q 72-96 hr	Careful preparation of patch application site
			IV		Not recommended due to rapid clearance
Tramadol	Weak μ agonist; inhibitor of serotonin reuptake		PO		Not recommended PO
Buprenorphine	Partial μ and κ agonist, δ antagonist	0.01 mg/kg	IV	q 6 hr	Not superior to fentanyl patches for post-operative orthopedic pain; effective based on behavioral score post orthopedic procedure
Butorphanol	μ antagonist to partial agonist; κ agonist	0.2 mg/kg	IM	q 6 hr	
Nalbuphine	Partial μ and κ agonist, δ antagonist	1 mg/kg	SQ	once	Peak analgesia at 30 minutes and started to decline at 120 minutes
NSAIDS					
Phenylbutazone	Nonselective COX inhibitor		IV, SC, PO		Not recommended
Meloxicam	Slight to moderate COX-2 inhibitor	0.5 mg/kg	IV	q 12 hrs	
		2.0 mg/kg	PO	Loading Dose	
		1.0 mg/kg	PO	q 24 hrs following loading dose	
Flunixin Meglumine	Nonselective COX inhibitor	1.1 mg/kg	IV	q 12-24 hrs	
Carprofen	Slight to moderate COX inhibitor	4 mg/kg	IV	once, preoperatively	
Lidocaine	Local anesthetic: sodium channel inhibitor	40mg	IA		
		1 ml/50kg	EP		
			IV	CRI	
Bupivacaine	Local anesthetic: sodium channel inhibitor	10mg	IA		
		1-2 mg/kg	SC		
Ketamine	NMDA receptor antagonist	10 μg/kg/min	IV	CRI	

Table 3: Described analgesic drugs for goats.

Drug	Mechanism of action	Dose	Route	Frequency	Comments
Opioids					
Morphine	μ agonist		PO		Not recommended PO
		0.05 - 0.1 mg/kg	IV or SC	q 4-6 hr	
		0.1 mg/kg	EP		
Fentanyl	μ agonist; κ antagonist		TD		Not supported by EBM
			IV	Not recommended due to rapid clearance	
Butoprhanol	μ antagonist to partial agonist; κ agonist	0.1 mg/kg	IV	4-6 hours	Altered behavior in less painful animals
		0.1 mg/kg	IM	4-6 hours	Altered behavior in less painful animals
Tramadol	Weak μ agonist; inhibitor of serotonin reuptake	2-4 mg/kg	IV	q 6 hours	
		2 mg/kg	PO		Not recommended PO
NSAIDS					
Phenylbutazone	Nonselective COX inhibitor		IV, SC, PO		Not recommended
Meloxicam	Slightly/moderately selective COX-2 inhibitor	0.5 mg/kg	IV	q 8 hours	
		0.5 mg/kg	PO	q 24 hours	
		0.5 mg/kg	IM	q 24 hours	
Flunixin Meglumine	Nonselective COX inhibitor	1.1 mg/kg; 2.2 mg/kg	IV	q 12 hours (1.1 mg/kg)	
		1.1 mg/kg	SC	q 12 hours	
		3.3 mg/kg	TD	once	Low bioavailability
Firocoxib	Highly Selective COX-2 inhibitor	0.5 mg/kg	IV. PO	Once	High volume of distribution could lead to residue risk; limited clinical studies
Lidocaine	Local anesthetic: sodium channel blocker	1 ml/50kg	EP		
		1 m/15kg	EP		
		1-2 mg/kg	SC		
		2.5 mg/kg	IV	Loading dose	Administer slowly
		0.1 mg/kg/min	IV	CRI following loading dose	

CRI: Constant Rate Infusion; EP: Epidural; IA: Intraarticular; IM: Intramuscular; IV: Intravenous; PO: Oral; SQ: Subcutaneous; TD: Transdermal

Epidural catheterization should be used for short-term pain management, as eight days of therapy in goats was demonstrated to cause inflammation at the epidural space after being administered morphine (20 mg total dose) once daily for eight days.[4] Multiple drugs can be considered for administration by an epidural catheter, these include opioids, local anesthetics, as well as dissociative drugs. These catheters are introduced by a Tuohy needle in the lumbosacral space until a "pop" is felt that indicates passage through the ligamentum flavum, and then the catheter is advanced through the needle. Note that this is not a hanging drop technique and strict sterility should be maintained for the entire procedure as well as catheter care afterwards.[3]

Regional infiltration

Regional infiltration catheters allow for release of local anesthetics into specific regions. Longer-acting local anesthetics (bupivacaine, ropivacaine) are preferred for these techniques to reduce the risk of contamination from more frequent administration. While "soaker catheters" can be left in incision sites after amputations or other traumatic procedures, catheters can also be placed to allow for repeated focal nerve blocks. Bupivacaine (1mg/kg) bolused every six hours has been reported for postoperative use in goats via a wound soaker catheter.[5] While care should be taken to not introduce foreign material into these catheters, a cross-species study identified incisional infection rates not higher than incisions that did not have wound soaker catheters applied.[5] The author would like to note that they have not used a wound soaker catheter for more than three days postoperatively in a patient, so this is likely not a long-term application. Wound soaker catheters can be made in clinic with red rubber catheters and then autoclaved (**https://www.veterinarypracticenews.com/how-to-make-a-soaker-catheter-in-6-easy-steps/**). Once sterilized, they can be introduced into a wound (such as an amputation site) during closure. In a recent example of more targeted analgesia, the pain from a mandibular fracture in an alpaca was managed by placement of a catheter into the vicinity of the mandibular foramen. Every six hours local anesthetic was administered via the catheter, and this method proved to be successful in short-term analgesia for the patient where meloxicam and buprenorphine were ineffective.[6]

Another form of regional application is the focused delivery via an ultrasound-guided nerve block. Larger nerves (examples being the femoral and sciatic), as well as muscle compartments can be visualized via ultrasonography to provide guidance for local anesthetic. With this technique, ultrasonography is used to identify a larger nerve and direct the focused distribution of a local anesthetic peripheral to the nerve (extreme care should be taken to not directly inject the nerve with local anesthetic!). This can be performed pre-operatively to decrease nociceptive windup, as well as after a painful injury. These blocks are typically performed with sedation or anesthesia. A 6-13 mHz linear probe was useful in identifying the sciatic and femoral nerves in sheep in one study.[7] In one case series, ultrasound-guided delivery of ropivacaine was used to provide adjunctive analgesia in alpacas undergoing amputation.[8] Ropivacaine could be considered for these procedures due to its longer duration of activity and the decreased tendency to block motor function compared to other local anesthetics.[9]

Acupuncture and electroacupuncture

Becoming increasingly more popular in veterinary medicine, acupuncture with or without the use of electrical stimulus can have applications for small ruminants. With acupuncture, small needles are placed near specific points, anatomic locations, or injured regions of the body, and these needles can be left or have a small electrical current applied (electroacupuncture). Acupuncture can increase endogenous opioid production, increase regional microcirculation, as well as potentially enhancing recovery from nerve injuries.[1] Electroacupuncture has demonstrated analgesia as well as increased beta-endorphin concentrations in sheep studies and has shown decreased hypersensitivity to visceral pain in goats.[10,11] Clinical recommendations have also been made for the use of acupuncture and electroacupuncture in camelids.[12] Electroacupuncture can have a synergistic effect when combined with epidural nerve blocks in goats.[13] In the author's practice, acupuncture and electroacupuncture can be used as a minimally-invasive adjunct as part of a multimodal pain management in sheep and goats. Due to the lack of a drug residues, acupuncture may be of useful for scenarios where a withdrawal time could impact decision making.

Future directions

Several recent developments in pain management for sheep and goats could also be considered. Several studies have recently evaluated the pharmacokinetics of the GABA analogue gabapentin in goats.[14,15] While more data is used, clinicians should be aware that multiple oral administration caused accumulation, indicating that dose-adjustment may be necessary for long-term use.[15] Nalbuphine is an opioid analgesic that is not scheduled in most U.S. states (an exception being Kentucky) that recently had its pharmacokinetic profile described in goats.[16] Nalbuphine levels consistent with analgesia in humans were observed for several hours after SC administration of a 0.8 mg/kg dose, and as such this may present an opioid option that could be administered and left on farm.[16] Recently, prostaglandin receptor antagonists like grapriprant have become commercially available for small animals. These drugs offer the benefit of NSAIDs, without the adverse effects, and have been explored in camelids, and unfortunately they do not appear to be absorbed after oral administration.[17] While not directly analgesic, several drugs have recently been studied for efficacy in the treatment of abomasal ulceration, which can be an adverse effect of the NSAID class. Pharmacodynamic data supports use of pantoprazole in sheep (1.0 mg/kg IV or SC, q 24 hr) as well as esomeprazole in sheep (1.0 mg/kg IV, q 24hr) for the increase of gastric pH, which could aid in the healing of abomasal ulcers.[18,19] Additional reports exist supporting the use of pantoprazole, esomeprazole and famotidine in goats for this purpose.[20,21]

Regulatory concerns

Currently in the U.S. and Canada, there are no drug formulations labeled for the use in sheep or goats for the management or control of pain. The use of all drugs for analgesia in these species would be considered extralabel drug use (ELDU) and fall under the Animal Medical Drug Use Clarification Act (AMDUCA). When treating pain in food animal species practitioners should use the Food Animal Residue Avoidance Databank (FARAD; US; **www.farad.org**) or the Canadian Global Food Animal Residue Avoidance Databank (CgFARAD; Canada; **www.cgfarad.usask.ca**) for edible tissue withdraw recommendations.

References

1. Smith JS, Mulon PY. Management of Pain from Surgery and Lameness in Goats. *Principles of Goat Disease and Prevention.* 2023:251-265.

2. Smith JS, Schleining J, Plummer P. Pain management in small ruminants and camelids: analgesic agents. *Vet Clin North Am Food Anim Pract.* 2021;37:1-16.

3. Smith JS, Schleining J, Plummer P. Pain Management in small ruminants and camelids: applications and strategies. *Vet Clin North Am Food Anim Pract.* 2021;37:17-31.

4. Larsen JJ, Svendsen O, Andersen HB. Microscopic epidural lesions in goats given repeated epidural injections of morphine: use of a modified autopsy procedure. *Acta Pharmacol Toxicol (Copenh).* 1986;58:5-10.

5. Abelson AL, McCobb EC, Shaw S, et al. Use of wound soaker catheters for the administration of local anesthetic for post-operative analgesia: 56 cases. *Vet Anaesth Analg.* 2009;36:597-602.

6. Stathopoulou T, Seymour C, McSloy A, et al. Pain management of a mandibular fracture in an alpaca (*Vicugna pacos*) via epidural catheter placement in the mandibular foramen. *Vet Rec Case Reports.* 2019;7:e000863.

7. Waag S, Stoffel MH, Spadavecchia C, et al. Ultrasound-guided block of sciatic and femoral nerves: an anatomical study. *Lab Anim.* 2014;48:97-104.

8. Foster A, McSloy A, Monticelli P. Ultrasound-guided psoas compartment and sciatic nerve blocks for pain management of hind limb procedures in the alpaca (*Vicugna pacos*). *Open Vet J.* 2020;10:120-127.

9. Simpson D, Curran MP, Oldfield V, et al. Ropivacaine: a review of its use in regional anaesthesia and acute pain management. *Drugs.* 2005;65:2675-2717.

10. Bossut DF, Stromberg MW, Malven PV. Electroacupuncture-induced analgesia in sheep: measurement of cutaneous pain thresholds and plasma concentrations of prolactin and beta-endorphin immunoreactivity. *Am J Vet Res.* 1986;47:669-676.

11. Shah MK, Ding Y, Wan J, et al. Electroacupuncture intervention of visceral hypersensitivity is involved in PAR-2-activation and CGRP-release in the spinal cord. *Sci Rep.* 2020;10:11188.

12. Robinson NG, Holt TN. Acupuncture in the Camelid. *Llama and Alpaca Care*: Elsevier. 2014;628-648.

13. Cui LY, Guo NN, Li YL, et al. Analgesic and physiological effect of electroacupuncture combined with epidural lidocaine in goats. *Vet Anaesth Analg.* 2017;44:959-967.

14. Kleinhenz MD, Davis D, Weeder MM, et al. Pharmacokinetic report: Pharmacokinetics of a single oral dose of gabapentin in goats (*Capra hircus*). *J Vet Pharmacol Ther.* 2024.

15. Jessie C Ziegler MH, Sherry Cox, Joe S Smith. Pharmacokinetics of single and multidose oral gabapentin in goats. *2024 ACVIM Forum*. Minneapolis: American College of Veterinary Internal Medicine. 2024;62.

16. Garcia JD, Smith JS, Minich D, et al. Pharmacokinetics of nalbuphine administered intravenously and subcutaneously in goats (*Capra aegagrus hircus*). *J Vet Pharmacol Ther.* 2024.

17. Wilson KE, Leventhal, Hannah R, Council-Troche,McAlister R, Davis, Jennifer L. Lack of oral absorption of grapiprant in adult alpacas. *2021 ACVIM Forum.* 2021;3005.

18. Smith JS, Bennett K, Flynn R, et al. Pharmacokinetics and pharmacodynamics of intravenously and subcutaneously administered pantoprazole in sheep (*Ovis aries*). *PLOS ONE.* 2024;19:e0304533.

19. Smith JS, Gebert J, Bennett K, et al. The pharmacokinetics and pharmacodynamics of esomeprazole in sheep after intravenous dosing. *Front Vet Sci.* 2023;10.

20. Fladung R, Smith JS, Hines MT, et al. Pharmacokinetics of esomeprazole in goats (*Capra aegagrus hircus*) after intravenous and subcutaneous administration. *Front Vet Sci.* 2022;9:968973.

21. Escher OG, Smith JS, Christopher K, et al. Pharmacokinetics of famotidine in goats after intravenous administration. *J Vet Pharmacol Ther.* 2024.

