Pain Management
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Importance

• Welfare
• Reduce complications
• Increase chances of favorable outcome
• Increase client satisfaction

• “I solemnly swear to use my scientific knowledge and skills for the benefit of society through the protection of animal health, the relief of animal suffering, the conservation of livestock recourses,...”
Signs of pain

• Stoic
• Depression
• Decreased appetite
• Hide, avoid interactions; isolation
• Reluctant to move; lay down
• Lameness
• Abnormal posture
• Vocalization
• Cush, reluctant to get up; lateral
• Rapid/ Open mouth breathing
Challenges

• Assessing pain
• Changing attitudes
• Drugs
• IV access (pigs)
Pain management

• Pre-treatment before painful procedures provides more analgesia than after robust pain sensations develop

• Difficult/ impossible to manage pain associated with chronic disease such as lameness
  – Combination treatment approach required
Pathology of Pain

• Responses of the nervous system to noxious stimuli are not static “hard-wired” events

• Repeated noxious stimuli can:
  – Change the ability of the peripheral receptor to respond to a stimulus
  – Change the perception of that response at the level of the brain
Peripheral Sensitization

- Results from agents released from damaged tissues
  - Cytokines, kinins, arachidonic acid derivatives, K⁺, H⁺, peptides & other agents (e.g. histamine)
  - Cause an increase in the sensitivity of the nerve endings
  - The thresholds that are perceived as painful become lower
    - The system becomes “sensitized” (windup)
Process of Central Sensitization

• Involves the neurotransmitter glutamate
  • Probably acting through its NMDA receptor

• Clinical significance of NMDA receptor!
  • *Ketamine* - antagonist at NMDA receptor
  • *Ketamine* - has analgesic properties
Drugs

• Opioids
• NSAIDs
• Corticosteroids
• Alpha-2 agonists
• Local anesthetics
Integrative Medicine

• Acupuncture/electro-acupuncture
  • <20 Hz $\rightarrow$ endorphin release (acute pain)
  • 80 - 120 Hz $\rightarrow$ serotonin release (chronic pain)

• Laser
  • Prevent/decrease inflammation
  • Increases range of motion/soft tissue elasticity

• Physical therapy
Opioids: Morphine

• Mostly for *acute* pain
• Inexpensive
• SC or IM 0.25 – 0.5mg/kg 4-6 hourly
• Epidural
  – 0.1mg/kg q12h
• Side effects:
  • Decreased gastro-intestinal motility (Prolonged use)
  • Ataxia
  • Excessive motor activity
  • Vomiting, hypothermia, panting,
  • CNS and respiratory depression (given IV)
Transdermal Fentanyl

- 75 – 100x more potent than morphine
- Skin preparation
  - Clip, no alcohol
  - Avoid skin irritation
  - Secure with elasticon
Fentanyl in alpacas

• Mean residence time (range) after i.v. dosing (2μg/kg) was 1.30 hr (0.65-4.00 hr).
• Bioavailability of fentanyl from t.d. fentanyl in alpacas was 35.5% (27-64%).
• Fentanyl absorption from the t.d. fentanyl patch into the central compartment occurred at a rate of approximately 50 μg/hr (29-81 μg/hr) between 8 and 72 hr after patch placement.
• Emphasizes the variability

Pharmacokinetics of intravenous and transdermal fentanyl in alpacas.
Lovasz M¹, Aarnes TK¹, Hubbell JA¹, Bednarski RM¹, Lerche P¹, Lakritz J¹ Department of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, Ohio, USA
Transdermal Fentanyl (patch)

• Goat
  • Variable plasma concentrations
  • Peak at 8 – 18 h

• Sheep
  • peak at 12 h
  • Inter-individual variations
Opioids

• Pure mu agonist

• Fentanyl* Synthetic opioid
  • Transdermal patch: 50 or 100 ug/h
    • Plasma concentrations 6.5-8.5h post-application (interscapular)
    • Differences in plasma concentrations between pigs may lead to signs of toxicity
      • probably unlikely as pigs are fairly insensitive to opioid effects and under dosing more likely!
  • Combination of morphine epidural (0.1mg/kg) and fentanyl patch (50ug/h) resulted in increased activity and apatite following abdominal surgery)

Opioids

• Buprenorphine (Very expensive)
  • Partial mu agonist
  • 0.01-0.05 mg/kg IM and 0.005-0.01 mg/kg IV q8-12h
  • Effect last 8-12 hours
  • Mild to moderate acute pain
  • No respiratory depression
  • Side effects
    • Inappetence
    • Unwillingness to move
Clinical pharmacology of buprenorphine in healthy, lactating goats.

• Dose used: 0.02 mg/Kg IV
• Half life: 73.8 +/- 19.9 min
• Agitation
• Inhibition of rumination
Cost analysis for a 30kg goat

- Morphine: $0.83/mL
  - $3.30 to $5.00 per day q4-6h

- Fentanyl patch: $27 each
  - Application for 3 days

- Buprenorphine: $17.40/mL
  - $52.00 per day for 0.01 mg/kg q8h
Opioids

- Butorphanol
  - Short acting, analgesic effect not as potent as other opioids
  - 0.05 to 0.5 mg/Kg for sedation and analgesia (SR and camelid)

- Tramadol
  - Low abuse potential (now a controlled substance)
  - Little effect on GI motility
  - Little to no cardiovascular and respiratory effects
Tramadol

**Alpacas** (adults):
- PO (11mg/Kg): poor bioavailability (5.9 – 19.1 %)

**Llamas** (adults)
- IV (2mg/Kg): 1 llama had adverse effects (neurologic)

**Goats** (6-9 months)
- IV (2mg/Kg): no adverse effects
- PO (2mg/kg): no adverse effects, active metabolite not detected
NSAIDs

Advantages
• Do not alter behavior or level of consciousness
• Synergistic effect with opioids
• Analgesia, anti-inflammatory, antipyretic

Disadvantages
• Rarely control severe pain
• GI or renal toxicity
FIGURE 1. Algorithm of the biochemical pathway shows that the formation of prostaglandins occurs via both cyclooxygenase enzymes (COX-1 and COX-2).
NSAIDs

• Inhibit COX synthase and therefore prostaglandin
• Prostaglandins (COX)
  • Stimulates mucosal production and bicarbonate secretion (gastric acid protection)
  • Pro-inflammatory cytokines

• Cox1: responsible for majority of acute and chronic NSAID toxicities

• Cox2: main one responsible for overproduction of PG after injury or infection
NSAIDs

• Flunixin meglumine:
  • 0.5 - 1.1 mg/Kg, IV, q 12 – 24 h

• Meloxicam: Cox 2 selective
  • IV, IM, SC
  • Pigs: 0.3 – 0.5 mg/kg, PO, q 24 h
  • Sheep: 1mg/Kg, PO, q 24 h
  • Goats: 1 mg/Kg, PO, q 24 h
  • Llamas: 1 mg/Kg, PO, q 48 – 72 h

• Firocoxib: Cox 2 selective
  • No studies in small ruminants, pigs, or SAC
Corticosteroids

- Chronic pain, immune mediated
- Pigs: Prednisone 1 – 2 mg/Kg PO
Osteoarthritis

• Treatment
  • Combination therapy
    • NSAID
    • Tramadol
    • Gabapentin
    • Cosequin. 2 tabs OD Contains glucosamine; chondroitin; Vit C; Mg
    • MSM 2 tabs OD
    • Conquer HA gel. 2cc OD
    • PSGAG 250mg/ml (polysulfated) 1ml im every 4 days for 2-4 weeks then once a week
Osteoarthritis

- Treatment - Severe cases
  - Intra-articular depomedrol plus amikacin
- Prednisolone tabs 1mg/kg
  - Pigs - “Corticosteroid resistant”
- PSGAG once a week
- Alternate between prednisolone and meloxicam every 6-8 weeks
Alpha-2 Agonists

• Effects: sedation, muscle relaxation, analgesia
• Analgesic effect is synergistic with opioids
• Cardiovascular side effects: sinus bradycardia and bradyarrhythmias
• Mild respiratory depression
• Decrease in insulin → hyperglycemia → promote diuresis (ADH inhibition)
• Can trigger labor (uterine contractions)

• Xylazine:
  • 0.05 – 0.2 mg/Kg IV or IM
Alpha-2 Antagonists

- Contraindicated in debilitated animals or if cardiovascular disease
- Consider giving these IM

- Tolazoline: 1.5 to 2 mg/Kg IV to reverse xylazine
  - Give slowly, watch for reactions

- Yohimbine: 0.125 mg/Kg IV to reverse xylazine
  - Give slowly, watch for reactions
  - Weak effect in ruminants
Systemic Lidocaine

Potential Benefits:
• Anti-inflammatory
• Analgesic
• Neuropathic pain
• SC, IM or regional IV block
• Prevent depolarization of sensory nociceptors
  • primarily by blocking Na channels
Systemic Lidocaine

• Rapid clearance
• Loading dose of 2-3mg/kg /20 minutes
• Followed by 3-6 mg/kg/hour CRI
• Alternatively, bolus every 2-3 hours
  • Bolus = 3 mg/kg in fluid bag over 20-30 minutes
Epidural Analgesia in Small Ruminants

• Caudal (sacro-coccygeal)
• Cranial (lumbosacral)
• Cheap, longer effect

• Morphine
  • 0.1 mg/Kg (6 -12 h)

• Lidocaine
  • 1ml/10 kg: blocks perineum and hind legs
  • 1ml/50 Kg: blocks perineum
Regional Limb Perfusion SR

- Cheap
- Lidocaine (to achieve high hydrostatic pressure)
- Diagnostic value
- Can be difficult to perform
- Useful to assess/treat wounds
- Easier if tourniquet is placed
  - Proximal to elbow: cephalic vein
  - Proximal to tarsus: recurrent tarsal veins
Multimodal Analgesia

- NSAID-Opioid prior to surgery
- Infiltration with local anesthetic
- Epidural
- Post-operative NSAID/opioid
Castration/Disbudding

• Xylazine
• Lidocaine (toxic dose 6-10 mg/Kg) Might be less if given around horn as it is very vascular and uptake is rapid
• Flunixin meglumine
• Meloxicam
• Ket stun
Camelid Castration

• Combine and give IM
  • Ketamine: 4.6 mg/Kg
  • Xylazxine: 0.46 mg/kg
  • Butorphanol: 0.1 mg/Kg

• Alternative
  • 1ml (10mg) of butorphanol
  • 1 ml (100mg) xylazine
  • 1 bottle (1 gram) Ketamine
  • Alpacas: 1ml/18 kg
  • Llamas: 1ml/23 kg

• Intratesticular lidocaine

Pig veins
Pig veins