Pain Management (Outline)

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**Pain management**
Pre-treatment before painful procedures provides better analgesia than occurs when withholding treatment until 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 including:
  - 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 and the system becomes “sensitized” (windup)

**Central Sensitization**
Involves the neurotransmitter glutamate probably acting through its NMDA receptor. *Ketamine* - antagonist at NMDA receptor and on that basis has analgesic properties

**Drugs used in pain control**
1. Opioids
2. NSAIDs
3. Corticosteroids
4. Alpha-2 agonists
5. Local anesthetics
6. Acupuncture/electro-acupuncture
  - <20 Hz → endorphin release (acute pain)
80 - 120 Hz → serotonin release (chronic pain)
7. Laser prevents/decreases inflammation. Also increases range of motion/soft tissue elasticity
8. 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 with prolonged use
Ataxia – if dose is too big
Excessive motor activity (probably species dependent and depending on circumstances!)
Vomiting, hypothermia, panting,
CNS and respiratory depression

**Transdermal Fentanyl**
75 – 100x more potent than morphine
Skin preparation:
Clip, no alcohol
Avoid skin irritation
Secure lightly 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. Just to emphasize that uptake is very variable

Pharmacokinetics of intravenous and transdermal fentanyl in alpacas.
Transdermal Fentanyl (patch)

Goat
Variable plasma concentrations
Peak at 8 – 18 h
But do not know if these values are therapeutic!

Sheep
peak at 12 h
Inter-individual variations

Pigs
Fentanyl* Synthetic opioid
Transdermal patch: 50 or 100 ug/h (should aim for 2 ug/kg/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 appetite following abdominal surgery

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 and unwillingness to move
Agitation
Inhibition of rumination

Cost analysis for a 30kg goat
Morphine: $0.83/mL (might want to put concentration here -15 mg/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

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

**Tramadol (probably minimal analgesic effects)**
Low abuse potential (not a controlled substance)
Little effect on GI motility
Little to no cardiovascular and respiratory effects

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

**Llamas** (adults)
IV (2mg/Kg): One llama in study 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
Can cause GI or renal toxicity
Inhibit COX synthase and therefore prostaglandins (COX)
Pro-inflammatory cytokines

COX1Inhibitors: responsible for majority of acute and chronic NSAID toxicities
COX2 Inhibitors: 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 disease
Pigs: Prednisone 1 – 2 mg/Kg PO q 24 h

**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- Severe cases**
Treatment
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 or IM 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 /5-15 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**  
Morphine  
0.1 mg/Kg (6 -12 h)  
Lidocaine
1ml/10 kg: blocks perineum and hind legs
1ml/50 Kg: blocks perineum

**Multimodal Analgesia**
NSAID-Opioid prior to surgery
Infiltration with local anesthetic
Epidural
Post-operative NSAID/opioid

**Castration/Disbudding**
Xylazine (0.1 – 0.2 mg/kg IM) Species??
Lidocaine (toxic dose 6-10 mg/Kg) Might be less if given around horn but as it is very vascular and uptake is rapid
Flunixin meglumine
Meloxicam

**Camelid Castration**
Combine and give IM
Ketamine: 5.0 mg/Kg
Xylazine: 0.5 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