UPDATE ON PAIN MANAGEMENT IN CATTLE

Michael D. Kleinhenz, DVM

Multimodal Analgesia

Credit: http://img.medscape.com/

Which toolbox would you want?

The Dream:
Many tools for many jobs
Right tool for the right job on-demand

Reality:
Few tools, but the tools we are learning how to best use those tools
What “tools” are in the pain management toolbox??

- Number of new analgesic for cattle approved in the US
  - NONE!!

- Number of already approved analgesic drugs in US…
  - NONE!!  Canada: meloxicam

What does this mean???

- We have to use the drugs (tools) available to us under AMDUCA to manage pain in cattle.

Where is he going with this???

- Explore the available drugs
- Same drug different use
- Different drugs and different delivery

Pharmacokinetics of oral gabapentin alone or co-administered with meloxicam in ruminant beef calves

- Gabapentin is a GABA analogue developed to treat epilepsy
- Used to treat chronic and neuropathic pain in humans
- Binds to voltage gated calcium channels (2 μg/mL)
- Decrease excitatory neurotransmitters
- Synergism with NSAIDs
Stress Reduction after long distance transportation?

Impact of oral meloxicam administered alone or in combination with gabapentin on experimentally induced lameness in beef calves.


Effects of meloxicam administration on physiological and performance responses of transported feedlot cattle.

A. F. Cotto, H. L. Capparelli, T. A. Granieri, and B. B. Holcomb.

Effects of meloxicam administration on physiological and performance responses of transported feedlot cattle.

Background

- 65% of calves are shipped to feedlots in Texas, Kansas, Nebraska and Colorado, usually by truck (Swanson and Morrow-Tesch, 2001; USDA, 2009)
- Immunosuppression after transport can lead to Bovine Respiratory Disease (BRD) 45 days after arrival
- BRD is associated with 65 to 80% morbidity and 35 – 55 % mortality (Swanson and Morrow-Tesch, 2001; Cernicchiaro et al, 2012; Edwards, 1996; Speer et al, 2001)
- BRD is estimated to cost the beef industry $500 million annually (NASS, 1996)

Study Rationale

- Non-steroidal anti-inflammatory drugs (NSAIDs) reduce the incidence of BRD in calves following stressful procedures such as castration (Coetzee, 2010)
- Meloxicam is an NSAID with high oral bioavailability and an elimination half-life of 27h after oral administration at 1 mg/kg (Coetzee et al, 2009)
- Generic meloxicam is not licensed for use in cattle but may be used in an extra label manner under AMDUCA and costs 3c/ 15mg tablet or $0.09/ 100 lbs BW


Hypothesis:

Meloxicam administration will decrease the effect of transportation on circulating physiological parameters of stress in beef steers
Materials & Methods

- Arrived at Tri-county Steer Carcass Futurity (TSCSF) Cooperative, Tabor, IA
- Blood sampled at 24 an 144 h post-arrival
- Transported 1,316km (16 Hours)
- Angus, Brahman cross steer calves were sourced from Brown Loam Research Facility in Raymond, MS
- Calves were bled at Time 0 and administered MEL or PLA

Results

Reduction in Cortisol
- Time by treatment interaction (P = 0.04)
- Inverse relationship between Cortisol level and meloxicam (P =0.0017)

Reduction in Stress Neutrophilia
- Time by treatment interaction (P = 0.04).
- Inverse relationship between neutrophil count and meloxicam (P =0.04)

Discussion

- Findings confirm that long distance transport is a stressful event in calves
- Results of hematology are indicative of a stress leukogram; an increase in the number of neutrophils and a decrease in the number of lymphocytes
- Meloxicam diminishes cortisol response and the extent of stress leukogram development
Take home:
After repeated MEL administration a **21 day**
slaughter withhold is adequate

**New tools to consider....**

**Pharmacokinetics of flunixin in preweaned calves after oral and intravenous administration**

- **Dose:** 0.5 mg/kg
- **Time to Maximum Concentration:** 4 h
- **Half-life (T1/2):** 19 h
- **Bioavailability:** 98%
The effects of firocoxib on cauterization disbudding pain and stress responses in preweaned dairy calves

M. L. Stock, 1, 2 T. T. Millman, 1 L. A. Barth, 1 N. K. Van Engen, 1 P. R. Hol, 1 C. Wang, 1 R. Gehringer 1

1 Department of Diagnostic and Production Animal Medicine and 2 Department of Animal Sciences, College of Agricultural Sciences, Iowa State University, Ames, IOWA.

Objectives: We evaluated the effects of firocoxib (Firocoxib) and carprofen (Carprofen) on nociception tests, pain biomarker concentrations, and behavioral responses of preweaned dairy calves undergoing cauterization disbudding.

Dose: 1.4 mg/kg

Tendency to be less sensitive to nociception tests

Minimal decreases in pain biomarkers

Impact of carprofen administration on stress and nociception responses of calves to cauterization dehorning

M. L. Stock, 1, 2 L. A. Barth, 1 N. K. Van Engen, 1 T. T. Millman, 1 R. Gehringer 1, 2

C. Wang, 1 E. A. Voets, 1 L. W. Waldroup, 1 L. A. Lohman, 1 W. H. Hu, 1 and J. F. Costello 1, 2


Can I have a price check on aisle 3??

<table>
<thead>
<tr>
<th></th>
<th>Meloxicam</th>
<th>Carprofen</th>
<th>Firocoxib</th>
<th>Gabapentin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>1 mg/kg</td>
<td>1.4 mg/kg</td>
<td>0.5 mg/kg</td>
<td>15 mg/kg</td>
</tr>
<tr>
<td># pills/100 lb</td>
<td>3</td>
<td>1</td>
<td>0.5</td>
<td>2.25</td>
</tr>
<tr>
<td>Cost per pill</td>
<td>$0.02</td>
<td>$0.93</td>
<td>$1.57</td>
<td>$0.07</td>
</tr>
<tr>
<td>Cost to treat 100 lb calf</td>
<td>$0.06</td>
<td>$0.93</td>
<td>$0.78</td>
<td>$0.16</td>
</tr>
</tbody>
</table>
At the end of the day may I suggest a nice red????

![Wine with Red Meat](image)

Finadyne® Transdermal

- Dose of 1ml/15kg Body wt.
- Topical/pour-on application
- EU approval for the treatment of fever and endotoxemia
- Under US-FDA consideration? Canada?
- Anti-pyretic effect at 4 h

Pharmacokinetics of transdermal flunixin in Holstein calves

- Bioavailability: 48%
- Half-life: 6.42 h
- Tmax – 2 h
- Range (1.5-4 h)
Always read and follow label directions

- Localised dermal inflammatory reactions and necrosis have been reported at 5 mg/kg.
- Erosive and ulcerative abomasal lesions were observed in animals administered the product at 3 times the recommended treatment dose.
- Occult fecal blood was observed in some animals administered the product at 5 times the recommended treatment dose.

Human Safety Warnings!!

- Personal protective equipment consisting of impermeable gloves, protective clothing and approved safety glasses should be worn when using this product.
- The product has been shown to cause severe and irreversible eye damage.
- Avoid contact with the treated area (allowing for spreading of the product) without protective gloves, for at least 3 days or until the application site is dry (if longer)

EFFECTS OF TRANSDERMAL FLUNIXIN MEGLUMINE ON PAIN BIOMARKERS AT DEHORNING

M. D. Kleinhenz; N. K. Van Engen; P.G. Gorden; J. F. Coetzee
Study Animals

- 24 Holstein Bull Calves
  - Single source farm
  - 6-8 weeks of age
  - Weight: 68.2 ± 6.7 kg
- 10 day acclimation
  - Trained for restraint with a halter and lead rope

Effects of transdermal flunixin at dehorning

24 Holstein Calves

Randomization

Dehorn + Flunixin (n=8)  Sham Dehorn + Flunixin (n=8)  Dehorn + Placebo (n=8)

Study Design

<table>
<thead>
<tr>
<th>Dehorn + Flunixin</th>
<th>Sham + Flunixin</th>
<th>Dehorn + Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot iron dehorning</td>
<td>Sham procedure</td>
<td>Hot iron dehorning</td>
</tr>
<tr>
<td>10 sec contact time</td>
<td>Cold identical</td>
<td>10 sec contact time</td>
</tr>
<tr>
<td>Copper ring present</td>
<td>dehorner</td>
<td>Copper ring present</td>
</tr>
<tr>
<td>Finadyne Transdermal</td>
<td>3.33 mg/kg</td>
<td>Placebo</td>
</tr>
<tr>
<td>Applied along topline</td>
<td>Applied along topline</td>
<td>Equal volume for dosing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Applied along topline</td>
</tr>
</tbody>
</table>
Plasma Cortisol

Mechanical Nociception Threshold

Implications

• Transdermal flunixin had minimal effects on pain mitigation
• Some effects on centralized pain at 48 h

• Like carprofen and firocoxib, more work needs to be done studying the effects of different types of pain.
A HUGE THANK YOU!!!!

- Dr. Hans Coetzee
- Nick Van Engen
- The PhAST lab group
  - Jackie Peterson
  - Dr. Pat Gorden
  - Dr. Suzanne Rawjewski
  - Dr. Joe Smith
- Vet Students
  - Katie Plozel
  - Kris Hayman
  - Adlai Schuler
  - Dan Breuer
  - Cassy Klostermann
  - Brenna Grey
  - Aislinn Pomfret

Questions

mkleinhe@iastate.edu