AABP FACT SHEET

PRUDENT USE OF SYSTEMIC PAIN RELIEF FOR LAMENESS

Authored by
THE AABP LAMENESS COMMITTEE

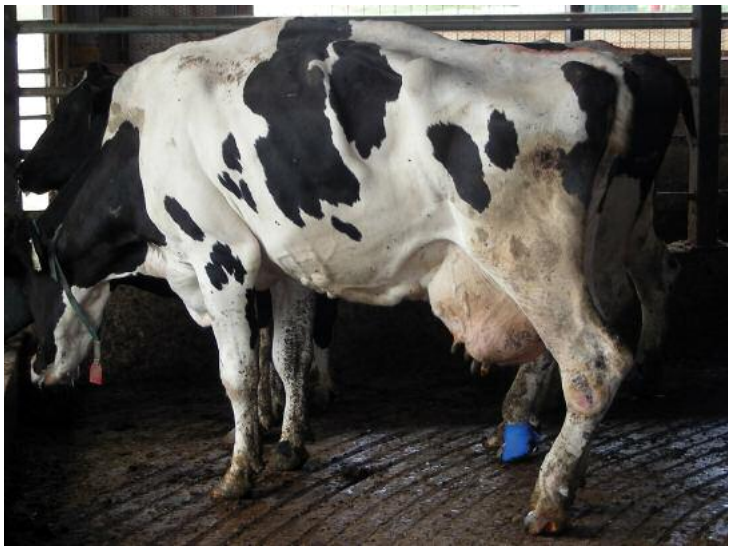
Introduction

Pain can be divided into acute pain associated with surgical procedures, or chronic pain associated with disease processes, and relief of pain in animals is an important part of the practice of veterinary medicine.

Acute pain associated with surgical procedures can in most cases be alleviated with local anesthetics alone or in combination with shorter acting analgesics such as opioids and alpha-2 adrenergics. Occasionally, general anesthesia is necessary. Control of movement through immobilization of the affected joint or limb and provision of a comfortable resting space, such as a bedded pack or area of sheltered pasture, can also be very important for recovery, and cow comfort cannot be underestimated as a means to improve pain management.

Once pain becomes chronic, it is more difficult to control, and local anesthetics are inappropriate for long term pain control. The longer the duration and/or the more intense the pain, the more difficult it is to alleviate, requiring higher and/or more frequent doses of analgesics. Unfortunately, the food animal practitioner has a limited range of drugs with analgesic properties approved for use in bovines available. It is essential that the practitioner follow the guidelines of the Animal Medicinal Drug Use Clarification Act (AMDUCA) in the United States (US) (or other similar acts in other countries around the world), which puts restraints on extralabel drug use for pain management in food animals.

Proper treatment of the underlying disease process causing pain is essential. Hoof block application, where appropriate, is one of the most effective means of providing pain relief in animals with hoof diseases affecting the sensitive corium. This fact sheet will discuss the options for systemic pain relief available to the practitioner. Details of hoof block application, intravenous regional anesthesia, and use of nerve blocks in cattle can be found elsewhere.



Corticosteroids

While commonly used in food animal practice, there is no evidence for a direct analgesic effect for dexamethasone or isoflupredone acetate. Administration of corticosteroids does carry risk for abortion (dexamethasone only) and immune suppression, which must be considered if they are to be used. The anti-inflammatory effects of the drug, mediated through prevention of arachidonic acid release and cyclo-oxygenase-2 inhibition, may carry with them some assumed pain relief, making them potentially suitable in some cases of lameness associated with obvious inflammation.

Opioids

Opioids have a short duration of action and in ruminants have mild analgesic properties. They are controlled substances and are not approved for food producing animals, so the tenets of AMDUCA have to be met before they are selected. Opioids can inhibit rumenoreticular contractions and some may cause abnormal behaviors such as propulsive walking and hypersensitivity/hyperexcitability, which can be dangerous for animals and personnel. However, for very severe pain, short term use of opioids alone or in combination with NSAIDS may be indicated.

Butorphanol is the most widely used opioid in food animal practice. The recommended dose is 0.05 mg/kg subcutaneously every 4 to 6 hours. Suggested meat and milk withdrawals are currently 4 days and 72 hours, respectively in the US as of 08/01/08. Morphine can also be used at a dose of 0.5 mg/kg intramuscularly (or slowly intravenously) every 4 to 6 hours for up to 3 days.

For both of the aforementioned drugs, guidance from the Food Animal Residue Avoidance Databank (FARAD) should be sought regarding appropriate and current meat and milk withholding times in the US. The website is www.farad.org and the contact telephone number is 1-888-USFARAD.

Alpha-2 Adrenergic Agonists

The drug most commonly used in this class in food animals is xylazine. It has both analgesic and sedative effects. The analgesic effects are very short lived (<1 hour), but the sedative effects can last greater than 24 hours, which makes

Lameness Pain Relief *continued*

them poor choices for long-term pain management. Xylazine may be indicated alone or in combination with butorphanol for post-operative pain, especially if sedation is desired. However it should be noted that it has little analgesic effects on the digits and lower limbs. The recommended dose is 0.1–0.3 mg/kg given as an intramuscular injection. Recumbency is more likely as the dosage increases. The label meat and milk withdrawal times are currently 5 days and 72 hours respectively in the US for the dose listed as of 08/01/08. Longer withdrawals are required at higher doses.

NSAIDs

Non steroidal anti-inflammatory drugs (NSAIDs) are used for their analgesic, antipyretic, and anti-inflammatory properties. They produce most of their therapeutic effects through inhibition of prostaglandin synthesis, via inhibition of both cyclo-oxygenase 1 and 2. There is also some evidence that they produce analgesic effects by central mechanisms other than inhibition of prostaglandin synthesis.

Of the NSAIDs commonly used in large animal practice, only flunixin meglumine is approved for use in food-producing animals in the US. While flunixin is approved for pain due to musculoskeletal disorders in horses, it has no written claim for analgesia in cattle. It is approved for use in beef and lactating dairy cattle for the control of pyrexia associated with respiratory disease, endotoxemia in mastitis, and inflammation associated with endotoxemia. Aspirin, while commonly used in practice, is not approved for use in bovines in the US. However, given the paucity of analgesics available to the veterinary profession, some regulatory discretion is currently being exercised in its use. Other veterinary products used in an extra-label manner in food animals in the US are phenylbutazone and ketoprofen. Phenylbutazone use in female dairy cattle 20 months of age or older is *prohibited*. Dipyrone use in food animals is also *prohibited*.

The approved dose range for flunixin meglumine is 1.1 mg/kg twice a day to 2.2 mg/kg once a day administered *intravenously* for up to three days. The label slaughter and milk withdrawal times are 4 days and 36 hours respectively, provided that the drug is administered per label directions intravenously. Intramuscular use should be avoided due to residue concerns.

Higher doses of aspirin are required on a per kg basis in ruminants compared to other species due to a high clearance and low volume of distribution, hence effective pain relief probably only occurs for 3-4 hours between doses. The 240 grain bolus is most convenient for use in adult cattle (1 grain equals 65mg) and the recommended dose rate is 100 mg/kg, so 4 boluses twice daily is appropriate for a mature Holstein cow. Current slaughter and milk withdrawal periods should be sought from FARAD prior to use in the US.

Ketoprofen is similar to flunixin meglumine with the advantage of an intramuscular route of administration which can help with increased client compliance in countries where its use is approved in food animals. It is not currently approved for use in food animals in the US. In Canada, the approved dosage is 3 mg/kg by IV or IM injection, once a day for up to 3 days. In Canada, the meat withdrawal is 24 hrs and there is no milk withdrawal required. Note that according to AMDUCA, Ketoprofen may NOT be used instead of flunixin in the US.

Because of human health concerns and requirement for extended meat withdrawal times due to its long half life (~30-80 hours), phenylbutazone should only very rarely be considered for use in valuable beef breeding stock, or dairy bulls with chronic osteoarthritis where slaughter for human consumption is not an option. The recommended dose in cattle based on pharmacokinetic and clinical trials in lame bulls is 17-25 mg/kg loading dose, followed by 4-6 mg/kg once a day, or 10-14 mg/kg every other day.

Gastrointestinal (GI) ulceration is the most commonly described side-effect from NSAID therapy, but it is rare as long as animals are eating. The first sign of GI side effects are anorexia, followed by mild diarrhea, which should subside when the NSAID is discontinued. Renal toxicity has also been described following NSAID administration. This usually only occurs if the animals are severely hypovolemic, or are also receiving other potentially nephrotoxic drugs concurrently. As long as animals are rehydrated before or immediately after administration, nephrotoxicity should not be a concern.

Other Considerations

As veterinarians, it is important that we bring to the producer's attention the option of euthanasia in cases where there is suffering that cannot be alleviated. AABP

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