Options for Managing Colic Pain

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Introduction

Pain resulting from colic can range from mild discomfort to violent distress. Alleviating pain not only makes the patient more comfortable, but also facilitates examination of the patient. Several options exist for controlling colic pain in the field setting and during transport, if required, to a referral hospital. Many of the drugs covered in this talk are very familiar to the equine clinician, but I will be introducing a new approach we have found to be very useful in managing colic pain. It is important to remember that the level of pain exhibited is an important part of evaluating a colic patient. The effects of analgesic therapy must be considered in subsequent evaluations of the patient. If frequent reevaluation of the patient is desired, drugs with shorter durations of analgesic effect are more appropriate.

Pain control is not limited to drug therapy. Alleviating distension of the stomach (nasogastric tube) or colon (trocarization) can produce appreciable relief. Trocarization of the colon should be reserved for extremely bloated patients.

Patient Evaluation

Equine practitioners are well acquainted with the symptoms of colic pain. The duration, progression and severity of these symptoms are very important in evaluating colic patients. Heart rate is another parameter routinely used by practitioners in evaluating colic patients. Increases in heart rate are generally attributed to pain, but reflexive increases in heart rate in response to decreases in arterial blood pressure are another source that must be considered. Peripheral vasodilation in endotoxic shock patients can produce significant decreases in arterial blood pressure even without major decreases in blood volume. Sequestration of fluid in bowel produces volume deficits that also decrease arterial blood pressure. Evaluating cardiovascular

status should be a routine part of your examinations of colic patients. Checking mucous membrane color and capillary refill time provides useful information, but I find the turgidity and size of the facial artery much more useful for evaluating arterial blood pressure and blood volume, respectively. Familiarizing yourself with the feel of the facial artery in normal patients will help in evaluating colic patients for changes in turgidity or size. Patients with obvious deficits in arterial blood pressure or volume status are more likely to have an abdominal lesion requiring treatment beyond what is realistic in the field setting. Depending on transport time, fluid therapy en route can help deliver a more stable patient to the referral facility.

Phenothiazine tranquilizers

Acepromazine does not possess an analgesic effect. Its alpha$_1$-adrenergic antagonist activity produces vasodilation, which typically decreases arterial blood pressure 15-20 mmHg in normal awake horses. The negative effect is greater when acepromazine administration is combined with hypovolemic or endotoxic shock and/or the cardiovascular depression of inhalant anesthetics. Acepromazine also negates the beneficial effects on cardiac output and arterial blood pressure that can be obtained from administering small, titrated doses of phenyephrine in patients with tachycardic endotoxic shock. Acepromazine should not be administered to colic patients.

NSAIDs

Dipyrone (1.1 mg/kg IV, or 500 mg/450kg) is noted for its antipyretic effects. Dipyrone's modest analgesic effects are capable of alleviating mild colic pain. The lack of a strong analgesic effect removes risk of masking escalating pain, making Dipyrone an ideal initial analgesic agent to administer in horses exhibiting milder colic pain. Dipyrone, perhaps due to its purported antispasmodic effects, is especially effective in the treatment of "gas colic". Unfortunately, Dipyrone is now available only from compounding pharmacies in the United States. The original product was labeled for IV, IM or SQ administration, but is irritating and IV administration is preferable. Dipyrone is a good choice if you are looking for an injectable drug to dispense to knowledgeable horse owners comfortable making IV injections. Intramuscular administration (2.2 mg/kg IM, or 1000 mg/450kg) can be used, but carries the same risks associated with IM administration of banamine. Dipyrone's ability to alleviate mild colic pain can provide the time needed for some benign colic episodes to resolve without a farm call

while not incurring the risk of delaying more appropriate intervention, which can occur when banamine is used in this fashion.

Banamine (flunixin meglumine) (1.1 mg/kg IV, or 500 mg/450kg) produces a moderate analgesic effect that can last for up to 6 hours. The onset of relief provided by banamine is slower than that provided by xylazine or butorphanol, making it somewhat less useful for providing initial relief upon arrival at the stable. Due to its efficacy and duration, banamine has the potential to mask escalating pain, which can delay more appropriate intervention. Banamine should be used cautiously in the early stages of colic where a definitive diagnosis has not been made. Banamine is an excellent choice when a longer duration of relief from mild to moderate colic pain is desired. Though labeled for IV or IM administration, banamine is irritating and IV administration is preferable. Clostridial myositis has occurred following IM administration of banamine.

Anticholinergics

Buscopan (N-butylscopolammonium bromide) (0.15-0.3 mg/kg IV, or 67.5-135 mg/450kg) is a newer addition to the colic treatment arsenal. Buscopan is used in human medicine to provide relief to patients with Irritable Bowel Syndrome. According to the manufacturer Buscopan relaxes smooth muscles for control of abdominal pain associated with spasmodic colic, flatulent colic and simple impactions. Conversations with the equine field service veterinarians at Ohio State indicates Buscopan is effective in treating "gas colic", but does not provide appreciable relief in other types of colic. Due to the mild relief provided in patients not suffering from spasmodic or flatulent colic, use of Buscopan is not likely to mask escalating symptoms. I am told rectal palpation is much easier in the presence of Buscopan and this is the primary reason for its use. Due to its anticholinergic effects, Buscopan produces an increase in heart rate for up to 30 minutes following administration, making evaluation of the patient's comfort level somewhat more difficult during this period. Buscopan Compositum is a newly released combination of buscopan and dipyrone. The advantage of this combination remains unclear.

Alpha$_2$-adrenergic agonists (alpha$_2$'s)

Xylazine (0.22-0.66 mg/kg IV, or 100-300 mg/450kg) is capable of alleviating mild colic pain and provides noticeable relief in patients with moderate levels of colic pain. Xylazine can provide some relief to patients experiencing severe colic pain, but will not eliminate it when

used alone. The duration of analgesia provided by xylazine is relatively short (20-30 minutes), providing the ability to reevaluate the level of patient discomfort. Xylazine produces dose dependent cardiovascular depression and should be used judiciously in patients with hypovolemic or endotoxic shock. Xylazine also decreases gastrointestinal (GI) motility, which is always a concern in colic patients.

Detomidine (0.011-0.022 mg/kg IV, or 5-10 mg/450kg) is more effective than xylazine in alleviating colic pain. Detomidine is capable of alleviating mild to moderate colic pain. Detomidine can provide appreciable relief to patients experiencing severe colic pain, but typically dose not eliminate it when used alone. Increasing the dose of detomidine (0.044 mg/kg IV, or 20 mg/450kg) has been shown to increase efficacy in combating colic pain, but also increases the level of cardiovascular depression. Using adjuncts such as ketamine and/or opioids is probably a better first choice in patients with more severe levels of colic pain. The duration of relief provided by detomidine is dependent of the severity of the colic symptoms exhibited (60-120 minutes in mild to moderate colic patients, as little as 30-45 minutes in moderate to severe colic patients). Detomidine produces dose dependent cardiovascular depression and should be used judiciously in patients with hypovolemic or endotoxic shock. Detomidine also decreases GI motility, which is always a concern in colic patients. Detomidine's potency has the potential to mask escalating pain, which can delay more appropriate interventions. The field service clinicians at Ohio State only use detomidine to help in controlling severe colic pain (patients where the need for surgical intervention is anticipated).

Opioids

Opioids are not as effective as the alpha$_2$'s in treating moderate to severe colic pain when administered as the sole analgesic agent. The proper use of opioids in treating colic pain is to use them as adjuncts to reduce the amount of xylazine or detomidine required to provide adequate relief, which decreases the adverse effects produced by alpha$_2$ administration. Opioid use should generally be reserved for patients with moderate to severe colic pain during the initial stages of evaluation. Small boluses of ketamine are now my first choice for augmenting the level of analgesia in patients with moderate to severe colic pain.

Butorphanol (0.0067-0.011-0.022 mg/kg IV or 3-5-10 mg/450kg IV) is a *kappa* and *sigma* opioid receptor agonist and a *mu* opioid receptor antagonist (referred to as an opioid agonist-antagonist). One of the

disadvantages of opioid agonist-antagonists is the "ceiling effect", an upper limit on analgesic effect even when larger doses are administered. Used alone butorphanol is effective in alleviating milder colic pain, but is less effective when used to treat moderate to severe colic pain. Probably the most appropriate use of butorphanol and/or banamine is to provide relief in patients with mild to moderate colic pain when a period of "extended observation" is desired. Butorphanol can provide 30-45 minutes of relief in patients with moderate colic pain, and somewhat longer relief in patients with milder symptoms. Butorphanol should not be used in conjunction with *mu* opioid receptor agonists such as morphine.

Morphine (0.1-0.2 mg/kg IV, or 45-90 mg/450kg) is a *mu* opioid receptor agonist that can be used to alleviate colic pain. The level of analgesia provided increases with the dose of morphine, but so do the adverse effects on GI motility. I now use ketamine as my first choice to augment the level of analgesia provided by alpha$_2$'s in patients with moderate to severe colic pain. When morphine use is required to augment the level of relief provided the patient likely requires care beyond what can be provided in a field setting and plans for referral and the management of that process should be undertaken.

Meperidine (Demerol) is a *mu* opioid receptor agonist I have used to treat pain in horses when morphine is not available. I have used meperidine (0.5 mg/kg IM q4h) in conjunction with small doses of acepromazine to effectively treat moderate levels of pain in equine patients. Back in the late 1970's as an equine ambulatory practitioner I used meperidine (IM) to augment analgesia provided by xylazine to help control severe colic pain, but unfortunately cannot remember how much I administered. Textbooks indicate meperidine (0.5-1.0 mg/kg IV) has been used in standing chemical restraint techniques.

***Mu* opioid receptor agonists decrease GI motility and their use should be limited to colic patients with more severe levels of pain (where the need for surgical intervention is anticipated).**

NMDA antagonists ("ketamine stun")

Ketamine is a NMDA receptor antagonist. Ketamine possesses amazingly potent analgesic properties at sub-anesthetic doses. Ketamine boluses (0.22 mg/kg IV, or 100 mg/450 kg) given to effect* provide a surprising amount of short-term relief of moderate to severe colic pain. These small doses of ketamine seem to be much more effective in alleviating colic pain when layered over a mild background

effect of xylazine or detomidine. Adding ketamine allows much smaller levels of xylazine or detomidine to be used, which reduces their adverse effects on cardiovascular function and gastrointestinal motility. A single IV bolus generally provides about 15-20 minutes of relief. If the initial ketamine bolus does not provide sufficient relief a second dose can be administered 2 minutes later. The relief provided by the small doses of ketamine is dramatic and the short duration of effect facilitates frequent reevaluation of the patient's level of comfort. I have successfully managed colic pain for up to two hours prior to surgical intervention using repeated small boluses of ketamine. Small doses of xylazine (0.22-0.44 mg/kg IV, or 100-200 mg/450kg) may be required periodically to maintain the effectiveness of these small doses of ketamine over time.

(*) The onset of ketamine is approximately 60-90 seconds – allow time for the prior dose to achieve onset before administering subsequent doses. In cases of really severe colic pain a larger initial bolus (0.66 mg/kg IV, or 300 mg/450kg) may be appropriate, with subsequent increments (0.22 mg/kg, or 100 mg/450kg) given as needed. Caution must be employed when aggressively treating colic pain with ketamine – recumbency can result in some patients from administration of as little as 1.5 mg/kg IV (~700 mg/450kg), which can be reached with several larger doses given close together. Ketamine redistributes from the CNS to skeletal muscle fairly rapidly (anesthetic doses resolve in approximately 15 minutes), so the amount administered over any given 15-minute interval is the value you want to focus on when using this technique.

Combination Therapy

Combining smaller doses of two or more analgesic drugs to provide relief in patients with mild to moderate pain can reduce the level of side effects produced. Combining larger doses of two or more drugs may be required to provide relief in patients with severe pain.

Transport options

Providing relief from colic pain during transport of the patient to a referral hospital is a very important consideration. Injury and/or respiratory compromise can occur when horses go down in the trailer. The expected duration of the trip and potential for pain to escalate during transport must be considered in making therapeutic choices. Banamine and/or detomidine can often provide sufficient coverage for patients exhibiting moderate colic pain if transport time is not

excessive. If transport time is expected to be long or the patient's level of pain is likely to worsen, options for providing additional pain relief during transport should be included in the plan. A dose of morphine (0.1-0.2 mg/kg IV or IM can be administered to augment the level of analgesia. With adequate instructions drugs can dispensed to the owners for use during transport, if needed. Alternatively, you can follow behind the transport rig to provide assistance, if required. For patients experiencing more severe colic pain an IV infusion of detomidine (2-5 mg/450kg/hr) and ketamine (270 mg/450kg/hr) can provide a stable level of analgesic support. Morphine (15-30 mg/450kg/hr) or butorphanol (10 mg/kg/hr) can also be added to this infusion to increase the level of analgesia provided. A loading bolus of morphine (0.1 mg/kg IV) or butorphanol (0.022 mg/kg IV) can be administered to quicken the onset of relief.

The distance from the fluid bag to the patient's catheter influences the delivery rate when using a conventional solution administration set, so an IV flow control device such as a Dial-A-Flo (a) should be utilized to prevent a marked increase in the drug delivery rate should the patient become recumbent during transport. A coiled extension set (b) can be used to provide additional free-play. Using a Dial-A-Flo type device to control CRI delivery adds approximately $7 to cost. Dial-A-Flo settings (ml/hr) OFF, 20, 30, 40, 50, 60, 70, 80, 100, 125, 165, 210, 250, and OPEN allow a "stock 450kg detomidine/ketamine/opioid mixture" to be safely delivered to a wide range of patient sizes (Table 1). The ability to adjust flow also provides greater flexibility in the drug mixtures used without resorting to dilution. One disadvantage of the Dial-A-Flo approach is the line can become tangled and occluded if the patient rolls in the trailer.

Delivery rate determines the drug concentrations required in the carrier solution. Drug concentrations are then used to determine the amount of each drug required for a pre-selected volume of carrier solution. There are a limited number of flow settings available. First you select a flow setting to use. I prefer 70 ml/hr because I use similar flow rates in many other CRI applications. There are several setting on the Dial-A-Flo device near this value to facilitate adjustments in delivery, if necessary. Next, select a desired duration for the infusion (provide a cushion in case transport takes longer than planned). The combination of flow rate and intended duration determine the amount of carrier solution required (e.g. for a 3-hour duration at 70ml/hr a 210 ml volume of carrier solution is required). Empty a bag of electrolyte solution to a final volume of 200 ml (mild rounding is allowed). Then add, in this example, three hours worth of each drug based on the

doses provided above. Adjust for patient weight using ratios (e.g. 337kg is 75% of 450kg, 0.75 x 270 mg/kg/hr = 200 mg/hr x 3 hr = 600 mg of ketamine). The Pentafusion section of the Hagyard Formulary contains information on creating and delivering analgesic CRI solutions.

Lidocaine (50 mcg/kg/min, or 68 ml/450kg/hr) can be safely substituted as the carrier solution in this CRI technique, enhancing the analgesia provided and also adding anti-inflammatory activity that recent studies indicate may be important in minimizing the incidence of post-colic laminitis. When lidocaine is used as the carrier solution its safe delivery rate determines the flow that must be used. I have consulted a number of experts and none have experience with delivery significantly higher in equine patients than the dose provided in these notes. To minimize risk of overdose the calculated delivery rate for lidocaine should "correspond" with one of the settings provided by the Dial-A-Flo device. Some latitude is allowed, but extremely large or obese patients (greater surface area/body weight divergence), hypoproteinemia, and inaccurate weight estimates can reduce whatever cushion exists. For a 450kg patient the 70ml/hr setting is used. Safe delivery rates for lidocaine are provided for a number of body weights (Table 1). If patient size does not permit straight lidocaine to be used, a dilution can be created to fit one of the settings of the Dial-A-Flo device (e.g. for a 337kg patient a mixture of 75% 2% lidocaine and 25% electrolyte solution could be used to allow safe delivery at 70 ml/hr). Other drug concentrations would be calculated using the 70 ml/hr delivery rate as described previously. When lidocaine is used as the base solution for the CRI, a loading bolus of lidocaine (1.3 mg/kg IV, given slowly) should be administered just prior to starting the CRI to counter its rapid clearance rate.

Sample Protocol using the Dial-A-Flo method (450kg patient, 70ml/hr, 3hr duration):

Attach solution administration set and empty bag of electrolyte solution to a final volume of 200ml. Add 10 mg of detomidine, 800 g ketamine (and, optionally, 45 mg of morphine or 30 mg of butorphanol). Attach Dial-A-Flo device and coiled extension set (optional, though recommended). Fully open the flow adjustment of the solution administration set and the Dial-A-Flo device to fill fluid lines with drug containing solution. Adjust Dial-A-Flo to desired 70ml/hr delivery rate and attach to IV catheter.

The Dial-A-Flo settings allow a "450kg stock" mixture (with or without lidocaine) to be safely used in a variety of patients of weights (Table 1). Delivery rate is adjusted using a ratio (e.g. for a 337 kg patient

delivery rate would need to be 0.75 x 70 ml/hr = "50" ml/hr). Greater latitude in selecting a delivery setting is acceptable when lidocaine is not used as the carrier solution. A table can be created detailing the drug amounts needed to prepare "450kg stock" solutions of varying durations to ease implementation.

"Elastomeric Infusion System"

Another option for controlling an analgesic CRI is the use of an "elastomeric infusion system", such as the Homepump Eclipse or C-Series(c). A variety of pre-set delivery rates and volumes are available. The "elastomeric infusion system" is attached directly to the patient so the risk of delivery interruption should the patient roll during transport is reduced. "Elastomeric infusion systems" are more expensive than the Dial-A-Flow (Homepump Eclipse E40100 cost $15.50) and the limited number of fixed delivery rates and volumes require a more customized approach. Certain "elastomeric infusion systems" (I-Flow Homepump) use the diameter and length of the attached tubing to control delivery rate. Others (MILA 7100, 100ml volume) use a variety of extension sets containing a flow limiter to control delivery (0.8, 2.5, 5, 20, & 40 ml/hr delivery rates are available). The flow limiters located in the tubing are temperature sensitive. They are designed to operate at skin temperature, so the distal portion of the tubing containing the flow limiter should be in contact with the skin to ensure accurate delivery.

Creating a mixture to be delivered using an "elastomeric infusion system" is identical to the process used for Dial-A-Flo controlled delivery. Delivery rate determines the drug concentrations required in the carrier solution. Drug concentrations are used to determine the amount of each drug required for a pre-selected volume of carrier solution. The Homepump Eclipse E401000 delivers 100ml/hr with a nominal capacity of 400ml (package insert provides information on minimum and maximum fill volumes, which are 200ml and 500 ml respectively for this unit, and their impact on delivery rate, which varies slightly). When filled with 400ml this unit provides a 4-hour duration of delivery. In this example you would add a 4 hr amount of each drug (based on the doses provided above adjusted for patient weight using ratios) to the device and then fill remaining volume with carrier solution (which again can be a properly adjusted lidocaine solution if desired). Attach to IV catheter.

Sample protocol using a Homepump Eclipse E401000 "elastomeric infusion system" (450kg patient, 4 hr duration):

Inject 12 mg of detomidine, 1000 mg of ketamine, (and, optionally, 60 mg of morphine or 40 mg of butorphanol) into the device. Fill device to 400 ml with carrier solution (which in this case could be "394" ml of electrolyte solution or 270 ml of lidocaine (68 ml/hr x 1.0 x 4 hr) plus "124" ml of electrolyte solution – minor rounding is allowed). Attach device to IV catheter and patients neck (bandage to secure and protect device and line).

General anesthesia

We periodically receive colic patients that have become so painful during transport that they must be anesthetized soon after arrival. These horses are recumbent, extremely violent and not responding to aggressive analgesic therapy. General anesthesia makes further evaluation safer for both the patient and personnel involved and can also be used to provide humane relief while owners make a decision regarding surgical intervention. General anesthesia can be used to provide the same benefits in the field setting, if necessary. Loading an anesthetized horse into a trailer for transport to a hospital is no easy task, though it can be accomplished.

(a) LifeShield Regulator IV Extension Set, Dial-A-Flo with Option-Lok, list # 11742-48, Hospira, numerous manufacturers produce similar devices

(b) Coiled Extension Set, CE8010, International Win, Ltd.

(c) Homepump Eclipse E401000, I-Flow Corporation, numerous manufacturers produce similar devices, a variety of pre-set delivery rates and volumes are available

Appendix

Table 1: patient weight (kg) and corresponding Dial-A-Flo settings for safe delivery of undiluted 2% lidocaine. Table can also be used as a guide in determining the appropriate setting for a patient when using a "stock 70ml/450kg/hr" analgesic mixture

Setting (ml/hr)	20	30	40	50	60	70	80	100	125
Weight (kg)	130	200	265	330	400	450	530	660	830