Updates in the Medical Management of Colic: Moving Beyond Mineral Oil

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1. Introduction
Colic remains one of the leading reasons for which horse owners consult their veterinarians. While exact numbers are difficult to obtain and vary geographically, reported risks have ranged from 3 to 10 episodes of colic per 100 horse-years. Fortunately, less than 5% of horses with colic have a surgical lesion. Therefore, medical treatment is indicated for the vast majority of horses with colic. While there is unfortunately no new “silver bullet” treatment for colic, this paper will review the main medical treatments currently in use: fluid therapy, laxatives, and analgesics.

2. Fluid Therapy
Fluid therapy is used in horses for a variety of reasons, but the basic goals are to replace losses, support the cardiovascular system, and maintain hydration in the face of ongoing losses. In horses with colic due to intestinal impactions, fluids are commonly given in an effort to promote hydration of the colonic contents. Fluids may be given either intravenously or enterally.

Intravenous fluids are more expensive, require an indwelling intravenous catheter with the associated risk of thrombophlebitis, and may be impractical on the farm. However, horses with diarrhea, signs of hypovolemic shock, or nasogastric reflux greater than 2 to 3 L will generally necessitate IV fluids to maintain hydration. In hospital settings, high volume intravenous fluids (two to three times maintenance rate or 100–150 mL/kg/d) are often given under the premise that there will be net flux of fluid into the gut lumen resulting in softening of impacted material. However, there is conflicting evidence as to the effect of IV fluid volumes on fecal hydration. In one study of normal horses, 5 L/h of IV fluids for 12 hours (approximately 100 mL/kg/d or twice maintenance) did not show any effect on hydration of right dorsal colon contents or feces. In another study comparing fluid rates and means of administration to dehydrated horses, fecal and systemic hydration were restored at twice maintenance IV fluids; however, there was no additional benefit seen when increasing the rate to three times maintenance. In fact, horses given three times maintenance IV fluids had increased urine production and sodium loss, which could contribute to electrolyte abnormalities as well as rebound dehydration when fluids are discontinued. There is in fact too much of a good thing!

Rapid transit of fluids through the small intestine makes enteral fluids a logical option in treatment of large colon impactions. Fluids delivered via naso-
gastric tube will exit the stomach within 15 minutes and reach the cecum and large intestine within 1 to 2 hours in most normal horses. It is also thought that intermittent bolus delivery may result in more fluid being delivered to the colon, as it will overwhelm the small intestine’s capacity for absorption. Nasogastric administration may also stimulate the gastrocolic reflex, thus, aiding with overall gastrointestinal motility. There is evidence that leaving an indwelling nasogastric tube in place for 72 hours does delay gastric emptying, so repeat intubation may be better despite its inconvenience and behavioral effects. Enteral fluids are overwhelmingly less expensive and easier to prepare than IV fluids, as they do not need to be sterile. Enteral fluid therapy is also slightly more forgiving than intravenous fluids in terms of rate and electrolyte composition. However, large volumes of plain water or hypotonic solutions may cause marked electrolyte abnormalities including hyponatremia, hypokalemia, and hypocalcemia. Isotonic fluids, however, are generally well tolerated with no significant effects on plasma biochemistry values except for a mild hemodilution when using a potassium rich solution with 6 g NaCl and 3 g KCl per liter of water. Most average size horses can tolerate 6 to 10 L/h of intragastric fluids; however, there does seem to be some individual variation. Horses with a significant amount of ingesta may show signs of discomfort when large volumes (5 L) of fluid are administered. Fortunately, this generally resolves with time, walking, or decompression via the nasogastric tube. Abdominal distension can also be seen with high volume enteral fluids but is generally well tolerated by most horses. Many horses treated with enteral fluids for an impaction will develop self-limiting diarrheaa due to excretion of fluids as the impaction resolves, and cecal rupture has also been reported.

Administration of enteral fluids has been evaluated in several studies in normal horses. In one study of adult horses, plain water given at once (50 mL/kg/day), twice (100 mL/kg/day), and three times (150 mL/kg/day) maintenance administered via nasogastric tube over four treatment periods every 6 hours has been shown to be safe and effective at restoring intestinal hydration with a volume-dependent effect on fecal volume. In another study, a balanced electrolyte solution given continuously at a rate of 10 L/h via nasogastric tube was shown to be more effective in hydrating ingesta than an identical rate of fluids given intravenously along with one intragastric dose of magnesium sulfate (1 g/kg in 1 L water). There was also a trend of more fecal production in the horses treated with enteral fluids, and there were less systemic effects. This balanced electrolyte solution contained 5.27 g NaCl, 0.37 g KCl, and 3.78 g NaHCO3 per 1 L of water resulting in a solution with 135 mmol Na/L, 5 mmol K/L, 95 mmol Cl/L, and 45 mmol HO3/C/L. In normal horses, hydration was measured in the feces and right dorsal colon of horses with indwelling fistulas in a crossover design of six treatments. The balanced electrolyte solution and sodium sulfate resulted in the best hydration of right dorsal colon (RDC) contents, while sodium sulfate, magnesium sulfate, and balanced electrolyte solution resulted in the most hydrated feces. Sodium sulfate caused hypocalcemia and hypernatremia while plain water caused hypotremia leaving the balanced electrolyte solution as the safest and most effective option.

Enteral fluids have also been shown to be effective in management of clinical cases of nonstrangulating large colon lesions. In a retrospective analysis of 147 horses with large colon impactions where all were treated with IV fluids (8.2–14.3 mL/kg/h) and only 49 (33.3%) received any enteral treatment, the mean time to resolution of impaction was 48 hours with a range from 1 to 6 days. Additionally, 24 horses (16.3%) required surgical intervention. This contrasts with another study of 108 horses with large colon impactions or displacements where horses were given either enteral fluids alone (8–10 L of a potassium-rich isotonic electrolyte solution every 2 hours) or enteral fluids simultaneously with intravenous fluids (2 mL/kg/h lactated Ringer’s solution). Both groups had a mean time to resolution of approximately 24 hours for impactions and 14 hours for displacements with no significant electrolyte abnormalities. The overall success rate was 99% for impactions and 83% for displacements. Another retrospective study of 53 horses found that impactions treated with enteral fluids resolved faster, had shorter hospitalizations (4 vs 7 days), and lower mean hospital bills (£483 vs £2006) than horses treated with intravenous fluids. The bulk of the evidence supports treatment of colic with enteral fluids whenever possible.

Enteral fluids can also be used to correct mild electrolyte abnormalities. A potassium-rich balanced electrolyte solution safely corrected mild hypokalemia in horses with large colon impactions and displacements. Administration of 1 g/kg body weight of NaHCO3 has been shown to increase cecal pH, which may be useful in the treatment of horses with grain overload.

3. Cathartics/Laxatives

Despite its routine use, there is little literature to support the use of mineral oil in horses. Mineral oil will lubricate ingesta but does not treat dehydration. It is most useful as a marker of transit time, as it should be seen in the feces of a normal horse 12 to 24 hours after administration. Mineral oil has also been advocated for use as a cathartic in cases of intoxication. Recent work, however, suggests that its use in cases of cantharidin toxicity may be contraindicated. Rats treated with mineral oil had increased absorption of cantharidin with increased morbidity and mortality relative to negative controls or those treated with other adsorbents. Careful attention must also always be paid to placement of the nasogastric tube prior to delivery, as deposition...
of mineral oil in the lungs can cause a fatal lipoid pneumonia.\textsuperscript{12,13}

Psyllium is a bulk laxative frequently used in the treatment and prevention of sand colic. There is conflicting evidence as to its efficacy, however. Of twelve ponies with sand surgically placed into the cecum, six were treated with 1 g/kg psyllium and six were untreated. All were euthanized 11 days later with no significant difference in the amount of sand retrieved between the treatment and control groups.\textsuperscript{14} Another trial evaluating psyllium (0.5 g/kg), wheat bran (1 g/kg), and mineral oil (8 g/kg) also failed to prove increased sand evacuation relative to untreated controls.\textsuperscript{15} More recent work showed that horses given psyllium (0.5 kg q12h) in addition to mineral oil (2 L q24h) had increased sand clearance relative to those administered mineral oil alone (51.0\% vs 26.1\% total sand removal)\textsuperscript{16} suggesting that psyllium may improve sand clearance. There is some concern that colonic flora will degrade psyllium after chronic exposure, thus decreasing any laxative properties. This has led to the common practice of only feeding psyllium for 1 week out of every month for sand prevention in endemic areas. The benefit, however, is that when fed routinely (50–100 g daily), fermentation of psyllium by intestinal bacteria results in the production of short-chain fatty acids that may benefit healing of the colonic mucosa in cases of right dorsal colitis.\textsuperscript{17}

Magnesium sulfate is frequently dosed at 0.5 to 1.0 g/kg enterally for treatment of impactions. Systemic absorption of MgSO\textsubscript{4} is believed to be limited; however, slight increases in plasma magnesium have been noted.\textsuperscript{6} Renal excretion should prevent hypermagnesemia; however, magnesium toxicity has been reported in dehydrated horses.\textsuperscript{18} Simultaneous administration of enteral magnesium sulfate with intravenous fluids is thought to promote secretion of fluids into the intestinal lumen by increasing the intraluminal osmolality. However, as previously discussed, there is work to support that a balanced electrolyte solution given enterally is superior to IV fluids plus MgSO\textsubscript{4} in promoting hydration of ingesta.\textsuperscript{2} Enteral MgSO\textsubscript{4} (1 g/kg in 1 L water) is superior to either plain enteral water or IV fluid therapy at 5 L/h for 12 h in improving fecal water content.\textsuperscript{6}

Diocyl sodium sulfosuccinate (DSS) is an anionic surfactant, which decreases surface tension, thus, facilitating water penetration. Historically, it has been used to treat impactions at 4 to 8 oz in 8 L of water; however, it is not superior to the use of magnesium sulfate and water.\textsuperscript{19} Toxicity (colic, diarrhea) has also been reported at a dosage of 50 mg/kg, and DSS is, therefore, of questionable use when there are other safer alternatives.

Activated charcoal and/or di-tri-octahedral smectite (DTOS) may be used when the colic is thought to be due to ingestion of a toxin. Di-tri-octahedral smectite is a natural hydrated aluminomagnesium silicate that adsorbs positively charged organic cations in the intestinal tract. It is used to treat and prevent enteritis in a variety of species and is now frequently used for the prevention and treatment of colitis in horses. It was first reported to prevent lincomycin-induced colitis in four horses, speculatively due to absorption of clostridial toxins.\textsuperscript{20} It has since been shown that DTOS effectively absorbs Clostridium difficile toxins A and B, C perfringens enterotoxin and exotoxins, Bacteroides fragilis toxin, and gram-negative endotoxin in vitro.\textsuperscript{21–23} DTOS does not inhibit the effect of metronidazole, which is fortunate as both drugs may be used simultaneously for treatment of clostridial infections. Horses treated with DTOS after surgery for large intestinal disease had a significant reduction in the prevalence of postoperative diarrhea (10.8\%) compared with negative controls (41.4\%).\textsuperscript{24} The previously discussed research on cantharidin, rats administered activated charcoal or smectite had survival times similar to the negative controls, suggesting that these treatments may be preferred over mineral oil in cases of blister beetle toxicity.\textsuperscript{11} Horses may also be exposed to toxins intragenerically due to misreading of labels on gallon sized jugs. Propylene glycol has been accidentally administered to horses due to the similarity of the label to mineral oil. Propylene glycol toxicity can result in D-lactic acidosis with severe depression and ataxia or death.\textsuperscript{25,26} Isopropyl alcohol has also been accidentally administered resulting in central nervous system depression and colic. Supportive medical therapy, gastric lavage, and repeated administration of activated charcoal is advocated in these cases as significant amounts of isopropyl alcohol and acetone are adsorbed by charcoal in vitro.\textsuperscript{27}

Gastric and enteric phytobezoars due to persimmon ingestion may also be treated successfully with medical treatment. Intragastric or oral administration of carbonated cola or diet cola has been reported successfully.\textsuperscript{28} The mechanism of dissolution is not well understood but is likely due to a combination of mucolysis, dissolution from carbon dioxide bubbles, and acidification.

4. Pain Management

The signs of pain seen with colic can be due to distension of a viscous, tension of the root of the mesentery, or inflammation. Pain management is an important part of managing colic as pain itself can cause motility inhibition. While many of the drugs used to treat colic may cause transient decreased motility, the beneficial effects typically outweigh those consequences. Multiple analgesic agents are often used for the treatment of colic: non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and α\textsubscript{2}-adrenergic agonists (Table 1). As distension is a frequent source of pain, nasogastric intubation to relieve gastric distension may also be an important part of pain control. Cecal trocharization may be performed in horses with marked large colon or cecal gas distension when
surgery is not an option; however, there is a risk of causing peritonitis.

NSAIDs inhibit cyclooxygenase, which has two isoforms: COX-1 and COX-2. COX-1 is constitutively expressed and is important for physiologic activities such as renal perfusion and mucosal blood flow; therefore, most of the detrimental side effects of NSAIDs are due to its inhibition. COX-2 is inducible and causes the release of pro-inflammatory prostanooids, making it the suggested preferred target of action to minimize toxic effects. Toxicity is unlikely when NSAIDs are given for short duration at appropriate doses, but repeated administration to dehydrated horses may result in serious side effects, such as acute kidney injury (medullary crest necrosis), right dorsal colitis, and gastric ulceration. Using multiple NSAIDs concurrently is also contraindicated as it increases the risk of toxicity. Flunixin meglumine, phenylbutazone, and ketoprofen are nonselective NSAIDs. Carprofen, meloxicam, firocoxib, and etodolac are preferential COX-2 inhibitors but have limited evaluation for their use in the medical treatment of colic. There is some evidence that they have less effect on mucosal repair and will likely continue to increase in use.

Flunixin meglumine is the most frequently used analgesic in cases of colic. Dosed at 1.1 mg/kg IV, onset of action should occur in approximately 20 minutes and last for 8 to 12 hours. This dose should be repeated no more frequently than every 12 hours. While labeled for use either intravenously or intramuscularly, potentially fatal clostridial myositis has been reported secondary to intramuscular flunixin injection, so IV or oral use is recommended. Flunixin can also be used to treat endotoxemia at a dose of 0.25 mg/kg IV q8h. Phenylbutazone and ketoprofen are used predominantly to treat musculoskeletal pain but can provide fair analgesia for visceral pain.

The COX-2 preferential NSAIDs have been evaluated more extensively for musculoskeletal use and in models of intestinal ischemia, which are beyond the scope of this presentation. However, several studies have included evaluation of their effects on visceral pain. With ischemic-injured jejunum, firocoxib was found to provide equivalent analgesia to flunixin meglumine based on postoperative pain scores. It is worth noting that firocoxib cannot be administered in an aqueous solution, so if given through an intravenous catheter, patient blood should be drawn back into the catheter and extension set first or it should be given via direct venipuncture. Another study evaluating horses after small intestinal surgery found that those treated with meloxicam showed more signs of gross pain than those treated with flunixin suggesting less potential visceral analgesia with meloxicam.

Alpha2-adrenergic agents are frequently used for both their sedative and analgesic properties. Their onset of action is more rapid and analgesia is more potent than NSAIDs. Xylazine has a short duration of action of 20 to 60 minutes. Detomidine is 100 times more potent than xylazine and lasts for 40 to 120 minutes. One multicenter clinical trial found that detomidine at either 20 μg/kg or 40 μg/kg provided better subjective analgesia than flunixin or butorphanol. Side effects of the α2-agonists include transient hypertension followed by hypotension and bradycardia. They also cause transient ileus that lasts longer than the sedative and analgesic effects. Detomidine may mask surgical lesions, so judicious use is recommended.

Butorphanol is the most commonly used opioid and is a mixed agonist-antagonist. It provides adequate analgesia falling between NSAIDs and α2-agonists. While butorphanol is less likely to cause excitement than other opioids, it should be administered concurrently with an α2-adrenergic agonist to minimize those effects. Butorphanol will also cause some ileus, which can be decreased by administering it as a continuous rate infusion (23.7 μg/kg/h). Horses given a 24-hour infusion of butorphanol after colic surgery had a significant reduction in pain scores. N-butylscopolammonium bromide blocks the muscarinic acetylcholine receptors of the gastrointestinal tract. It is frequently used for its spasmylytic effects in horses with gas colic and impactions. It can also be useful for facilitating rectal examinations. In a duodenal and colorectal distension model, there was no effect on duodenal distension or motility; however, the colorectal distension thresh-

<table>
<thead>
<tr>
<th>Drug</th>
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<tr>
<td><strong>Nonselective NSAIDs</strong></td>
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<tr>
<td>Flunixin meglumine</td>
<td>0.25–1.1 mg/kg IV or PO q8–24h</td>
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<tr>
<td>Phenylbutazone</td>
<td>2.2–4.4 mg/kg IV or PO q12–24h</td>
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<tr>
<td>Ketoprofen</td>
<td>2.2 mg/kg IV q24h</td>
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<td><strong>COX-2 Preferential NSAIDs</strong></td>
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<tr>
<td>Meloxicam</td>
<td>0.6 mg/kg IV q12h</td>
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<tr>
<td>Firocoxib</td>
<td>0.27 mg/kg loading dose then 0.09 mg/kg IV q24h</td>
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<td>Carprofen</td>
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<tr>
<td>Etodolac</td>
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<tr>
<td><strong>α2-Adrenergic Agonists</strong></td>
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<tr>
<td>Xylazine</td>
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<tr>
<td>Detomidine</td>
<td>10–40 μg/kg IV, IM</td>
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<td><strong>Opioids</strong></td>
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<tr>
<td>Butorphanol</td>
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<tr>
<td><strong>Other</strong></td>
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<tr>
<td>N-butylscopolammonium bromide</td>
<td>0.3 mg/kg IV</td>
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<tr>
<td>Lidocaine</td>
<td>1.3 mg/kg over 5–10 minutes, then 0.05 mg/kg/min IV CRI</td>
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old did increase.\textsuperscript{34} Effects last 20 to 30 minutes; however, tachycardia may persist for 50 minutes.

Lidocaine is a local anesthetic that binds to voltage-gated sodium channels, thus, preventing propagation of action potentials. It is frequently used as an intravenous continuous rate infusion in horses for its potential analgesic, anti-inflammatory, and prokinetic effects; however, there is a large amount of conflicting evidence. Lidocaine at 5 mg/kg loading, followed by 100 \( \mu \text{g/kg/min} \) CRI was shown to be a visceral analgesic using EEG changes as a measure of nociception in anesthetized ponies undergoing castration.\textsuperscript{35} However at a dose of 2 mg/kg loading followed by 50 \( \mu \text{g/kg/min} \) CRI, lidocaine had no significant effects on duodenal distension pressures and minimal effect on colorectal distension pressures suggesting minimal visceral analgesia.\textsuperscript{36}

Lidocaine has also been shown to improve mucosal healing in experimentally induced small intestinal ischemia due to a presumptive decrease in the production of inflammatory cytokines.\textsuperscript{37} While lidocaine has not been shown to have direct prokinetic properties, it is used commonly by many practitioners as such for postoperative ileus. In normal horses, however, lidocaine administration has been seen to decrease mean fecal output and increase fecal transit time.\textsuperscript{38} Therefore, practitioners using lidocaine for its analgesic effects need to be aware that it may prolong transit time, and this may be exacerbated when combined with other drugs that decrease motility (opioids, alpha-2 agonists). In addition, lidocaine toxicity may occur at serum concentrations between 1.65 and 4.53 \( \mu \text{g/mL} \),\textsuperscript{39} and these concentrations can be affected by other drugs, liver disease, and general anesthesia. Signs of toxicity include muscle fasciculations, anxiety, ataxia, collapse, and electrocardiographic changes. Fortunately, the half-life of lidocaine is short, so discontinuing the infusion generally results in resolution of clinical signs.

5. Conclusion

Medical therapy continues to be an appropriate and effective treatment for most cases of colic. It is important to remember, however, that any horse that remains painful despite appropriate medical therapy and analgesia should be referred for possible surgical intervention.

Acknowledgments

Conflict of Interest

The Author declares no conflicts of interest.

References and Footnote


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