Selected Aspects of the Clinical Pharmacology of Visceral Analgesics and Gut Motility Modifying Drugs in the Horse

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Comparison of the visceral analgesic effects of xylazine, morphine, butorphanol, pentazocine, meperidine, dipyrone, and flunixin in a cecal distention model of colic pain indicated that xylazine produces the most relief from abdominal discomfort. Repeated administration of xylazine may reduce visceral pain so effectively that the seriousness of abdominal disease is obscured. Xylazine decreased propulsive motility in the jejunum and pelvic flexure of healthy ponies. Morphine and butorphanol also gave relief from visceral pain in the cecal distention model. Morphine may inhibit colonic, and butophanol jejunal, motility. Whether xylazine or opiate mediated decreases in gut motility cause clinically important slowing of ingesta transit is controversial and requires further investigation. The development of behavioral changes (i.e., apprehension and pawing) in horses given opiate therapy may limit the use of these drugs. Combinations of xylazine and morphine or butorphanol produce excellent, safe, visceral analgesia and sedation without untoward behavioral effects. Although flunixin fails to demonstrate good visceral analgesic effects in the cecal distention model, this drug produces analgesia in some cases of colic by blocking prostaglandin mediated induction of pain.

Improvement of propulsive gut motility in patients with ileus may follow administration of neostigmine (which is particularly effective when the large bowel is hypomotile), naloxone (which experimentally stimulates propulsive colonic motility), and metoclopramide (which stimulates stomach and proximal small intestinal motility). (Journal of Veterinary Internal Medicine 1988; 2:85–91)

PHARMACOLOGIC ALTERATION of gut motility and alleviation of visceral pain facilitate definitive surgical and medical management of diseases of the equine gastrointestinal tract. In the past, the choice of an appropriate analgesic or the decision to use a drug to modify gut motility was based largely on personal preference, experience, and subjective assessment of patient response to treatment. The clinical pharmacology of visceral analgesic drugs in horses has recently been investigated under controlled conditions.[1-16] Analgesic potencies of drugs have been most frequently evaluated using visceral pain models (cecal distention with a balloon and cecal impaction)[1,2] and a superficial pain model (threshold to cutaneous heating).[3] In vivo studies of electromyographic and mechanical activity of the small and large bowel in healthy ponies treated with pain modifying drugs have demonstrated that analgesics may also alter gut motility.[7,8,13,16,17] Changes in gut motility produced by these drugs may be deleterious to the patient.

Ileus is an all too frequent complication of celiotomy and intestinal resection in the horse. Pharmacologic methods of safely improving propulsive gut motility early in the postoperative period could greatly benefit the equine patient. Preliminary studies of neostigmine, naloxone, and metoclopramide have demonstrated that these drugs may enhance gut motility in horses.[7,11,18,19] The clinical pharmacology of xylazine, morphine, meperidine, oxymorphone, butorphanol, pentazocine, flunixin meglumine, neostigmine, naloxone, and metoclopramide will be considered relative to their effects on visceral analgesia and gut motility.

Pain

Imidazoles

Xylazine* is a sedative, analgesic, muscle relaxant and local anesthetic.[20] Sedation, which is produced by stimulation of central nervous system $alpha_2$-adrenoceptors, can be antagonized by the $alpha_2$-adrenoceptor antagonist yohimbine.[21] Stimulation of peripheral alpha-adrenoceptors is responsible for several of xylazine's unique pharmacologic effects when administered to clinical patients. These effects include a transient increase in arterial blood pressure, a reduction in gut motility, and hyperglycemia. Bradycardia is produced by an increase in parasympathetic tone and a decrease in central nervous system sympathetic activity, and is generally responsive to anticholinergics (i.e., atropine or glycopyrrolate).[22] One double blind study comparing the analgesic effects of xylazine, pentazocine,† meperidine,‡ and dipyrone§ on cecal balloon induced colic demonstrated that xylazine (2.2 mg/kg intramuscularly [IM] produced the greatest (65 minutes) pain relief, while the other drugs produced little or no visceral analgesia.[1] Xylazine produced superficial analgesia for 3 hours and visceral analgesia for 4 hours (cecal balloon) in a separate study that compared xylazine's analgesic effects with those of butorphanol,|| flunixin,¶ and morphine.#[4] This study demonstrated that xylazine was the best visceral analgesic. Xylazine (2.2 mg/kg IM) was also the best analgesic for relief of superficial, deep, and visceral pain when compared with fentanyl,**-meperidine, methadone,†† oxymorphone,‡‡ and pentazocine.[3] Xylazine's visceral analgesic effects lasted 90 minutes in one experimental study of cecal balloon induced colic in horses,[5] but may be of shorter duration in clinical patients.[6] Davis questioned the clinical usefulness of xylazine for relief of colic in horses based upon its brief duration of action.[23] However, repeated administration of xylazine is well tolerated and may reduce visceral pain so effectively that the seriousness of abdominal disease can be obscured.[24] When xylazine is used for relief of abdominal pain, the patient must be closely monitored for progression of the disease process.

Xylazine decreased propulsive motility in the distal jejunum, cecum, and pelvic flexure of normal ponies for up to 140 minutes.[7,16,25] Interestingly, the effect of xylazine on myoelectric activity of the pelvic flexure is similar to that of atropine, but is of shorter duration. The use of repeated doses of xylazine for the treatment of impaction colic may not be desirable, as normal motility is essential to move the impacted ingesta aborally. The effect of repeated doses of xylazine administered before anesthesia on the development of postoperative ileus has not been assessed. In addition, the infusion of pharmacologic doses of xylazine into isolated perfused pony jejunum resulted in simultaneous increases in jejunal vascular resistance, increased jejunal motility, and increased oxygen consumption.[8] This combination of effects might decrease bowel motility and viability, particularly if the bowel is already compromised by an obstructive process. The clinical relevance of these observations, however, remains to be determined. Other potential side effects of xylazine include hypotension following the initial transitory hypertension (alpha-adrenoceptor stimulation). Hypotension is caused by bradycardia, decreases in cardiac output, and peripheral vasodilation.[22] First and second degree atrioventricular (AV) block are also commonly encountered. Despite these side effects, xylazine is a clinically useful drug. Healthy horses can tolerate up to ten times the recommended dose.[20] Repeated small doses of xylazine usually provide excellent, relatively predictable, analgesia in volume depleted, metabolically compromised colic patients.

Detomidine,§§ a drug pharmacologically similar to xylazine, produces dose-dependent analgesia and sedation in horses.[9,10,26,27] Like xylazine, detomidine produces pronounced sedation by stimulating central nervous system $alpha_2$-adrenoceptors. Detomidine produced excellent analgesia for superficial pain (controlled electric current model) at doses of 20 μg/kg.[9] The visceral analgesic effects of four doses of detomidine (5, 20, 80, or 160 μg/kg intravenously [IV]) were evaluated in ponies using a cecal balloon pain model. Detomidine produced excellent dose-dependent analgesia that ranged from 13.5 ± 5.17 minutes at 5 μg/kg to 45.5 ± 7.13 minutes at 20 μg/kg, up to 239 ± 31.53 minutes at 160 μg/kg.[10] Detomidine produced a longer duration of analgesia than xylazine (1.1 mg/kg IV) at all but the lowest dose. Both sedation and analgesia were fully established within 15 minutes following detomidine administration. Higher doses (80 or 160 μg/kg) produced excessive sedation (i.e., swaying or ataxia). Although cecal contractions ceased after detomidine administration, none of the experimental ponies had side effects from this interference with motility. The precise effects of this drug on large bowel motility remain to be documented, and repeated doses may be constipating. A dose of 20 to 40 μg/kg is recommended for alleviating ab-

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* Rompun, Haver, Bayvet Division, Miles Laboratories, Shawnee, KS.

† Talwin-V, Winthrop Veterinary Division of Sterling Drug, New York, NY.

‡ Demerol, Winthrop Laboratories, Division of Sterling Drug, New York, NY.

§ Novin, Haver, Bayvet Division, Miles Laboratories, Shawnee, KS.

|| Torbugesic, Bristol Veterinary Products, Division of Bristol-Myers Co., Syracuse, NY.

¶ Banamine, Schering Veterinary, Schering Corp., Kenilworth, NJ.

Morphine, Eli Lilly and Co., Indianapolis, IN.

** Sublimaze, Janssen Pharmaceutica Inc., Piscataway, NJ.

†† Dolophine, Eli Lilly and Co., Indianapolis, IN.

‡‡ Numorphan, DuPont Pharmaceuticals, Inc., Manati, PR.

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§§ Domosedan, Farmers Group Ltd., Turku, Finland.

dominal pain.[10] Lower doses (10 to 20 µg/kg) provide adequate sedation in most horses.[28] Analgesic effects are reported to disappear before sedative effects, and analgesic effects may be minimal or short-lived at the 10 µg/kg dose.[10]

Side effects following detomidine administration to experimental horses were dose-dependent and included sweating, occasional tremors, increased urine production, ataxia, profound decreases in heart rate (as low as 10 to 15 beats per minute), and transient hypertension persisting for more than 15 minutes and, in some cases, for up to 60 minutes.[28] Second degree AV and sinoatrial block were noted in some experimental horses.[9,27-29]

Further research is required to determine the optimum clinical dosage of detomidine, however, preliminary studies suggest excellent visceral analgesia and sedation for standing diagnostic and minor surgical manipulations. Detomidine's prolonged duration of sedative and analgesic effects may make it an attractive alternative to xylazine in clinical practice. Prolonged sedation, however, could mask signs of worsening abdominal distress and might delay appropriate medical or surgical intervention. Detomidine is not yet approved for use in the United States.

Opioids

The opioids are centrally and peripherally acting analgesics that produce behavioral changes. These drugs act at specific opiate receptors throughout the body, in the brain, and in the spinal cord. The analgesic potency of opiate drugs varies. If morphine sulfate is arbitrarily assigned a visceral analgesic potency of 1, methodone has equal or slightly greater potency; pentazocine 0.25 and butorphanol 7 (Table 1).[4,23]

Administration of 1.0 mg/kg of morphine IV relieved abdominal pain in a colicky pony. In this case, morphine was shown to have an antispasmodic action on the jejunum.[30] Kalpravidh assessed the analgesic potency of morphine as a superficial (focused heat source on the skin above the coronet band) and visceral (cecal distention by balloon) analgesic.[4] Morphine (0.66 mg/kg IM) produced good analgesia for superficial pain and acceptable analgesia for visceral pain (xylazine was better for visceral pain). Some ponies showed behavioral changes including apprehension, pawing, and increased locomotor activity such as pacing, headshaking, restlessness, and shivering. Similar behavioral changes were seen by Muir et al. and Combie after administration of morphine (0.66 mg/kg IV) to horses.[22,31] Tobin et al. have suggested that these effects are due to the release of norepinephrine and dopamine from central nervous system nerve terminals.[32] An alternative explanation for the production of these behavioral effects is the preferential stimulation of specific opiate receptor subtypes. Opiate pharmacologic actions are believed to be mediated via a heterogeneous class of receptors termed mu,

TABLE 1. Visceral Analgesic Potency of Selected Drugs in Horses*

Drug	Relative Potency
Xylazine	3.5
Morphine	1
Meperidine	0.5
Methadone	1.5
Oxymorphone	2.0
Fentanyl	0.5
Butorphanol	2.5
Pentazocine	0.25
Flunixin†	0.1–1
Dipyrone†	<0.1–0.5

* Data modified from Pippi and Lumb.[3]
† Dependent upon the cause of colic.

kappa, sigma, and delta receptors. Stimulation of mu and kappa receptors produces ataxia, sedative effects, and decreases in gastrointestinal transit time. Morphine is reported to act preferentially at mu receptors.[33] Stimulation of sigma receptors causes central nervous stimulation and psychotomimetic effects. The significance and distribution of opiate receptors in the horse remains to be determined. Roger studied the effects of morphine (0.5 or 1 mg/kg IV) on pony large colon motility.[11] An initial short-lived period of stimulation of the colonic muscle was followed by a dose related inhibitory phase in which overall mechanical and electrical activities were abolished for a mean of 300 minutes. These studies suggest that endogenous opiates might be part of the regulatory mechanism for control of equine colonic motility.

Morphine-like drugs have long been used as constipating agents. Roberts and Argenzio (1986) demonstrated that administration of morphine to experimental ponies decreased gut sounds, delayed defecation, and promoted fecal drying.[33] Whether the use of morphine as a preoperative analgesic would potentiate postoperative ileus is unknown, but must be considered based upon its long duration (7 hours) of action in horses.[17] There are anecdotal reports of ileus and abdominal pain in equine patients following standing laparotomy when xylazine and morphine have been used for restraint or analgesia. In one study of cecocolic motility in healthy ponies, morphine (0.66 mg/kg IV) was administered 5 minutes after xylazine (0.55 mg/kg IV). Xylazine caused almost complete loss of cecocolic motility. Morphine infusion resulted in uncoordinated right ventral colon motility, but no cecal motility. Progressive motility in the cecocolic region returned 85 to 125 minutes after morphine administration.[25]

Opiate antagonists might be useful in countering the potentially undesirable effects of endogenous opiates in impaction states and in antagonizing the constipating effects of opiate analgesics. The narcotic antagonist naloxone blocked the transit-slowing effects of morphine in

rat small intestine.[33] However, in Roberts and Argenzio's study of intestinal transit in ponies, cited above, a dose of 10 μg/kg of naloxone administered before or up to 2 hours after morphine (0.4 or 1 mg/kg IM) failed to prevent the defecation delaying and fecal drying effects of morphine.[33] In view of these findings, further research is indicated to investigate appropriate dosage regimens for narcotic antagonists as stimulants of large bowel motility and as drugs to antagonize the constipating side effects of narcotic analgesics.

Butorphanol is a synthetic morphinan derivative chemically related to naloxone. This drug has narcotic agonist and antagonist properties. Muir and Robertson, and Kalpravidh et al. examined the analgesic effects of butorphanol in horses using the same models for the production of visceral (cecal balloon) and superficial pain (focused heat source) as previously described.[4,5,12] Analgesia was dose related and a dose of 0.4 mg/kg IV produced analgesia that persisted for 30 minutes for superficial pain and 90 minutes for visceral pain.[12] Butorphanol (0.2 mg/kg) produced adequate visceral analgesia for approximately 60 minutes in one study[5] and up to 4 hours in another.[4] Butorphanol's visceral analgesic effects were of shorter duration than xylazine's in one study.[5] The pain threshold for both visceral and superficial pain was higher with xylazine (2.2 mg/kg IM) than butorphanol (0.2 mg/kg) in another study.[4] Arterial blood pressure increased after administration of butorphanol (0.2 mg/kg IV) to horses with cecal balloon induced colic pain.[5] In general, butorphanol blunted the hemodynamic response to experimental colic pain. This blunting effect might mask important prognostic indicators in colic patients treated with butorphanol. Although a dose of 0.2 mg/kg of butorphanol IV produced good to excellent visceral analgesia, this dose also induced apprehension, increased locomotor activity, and caused ataxia in some horses.[5,12] In 66 equine patients with abdominal pain that were treated with 0.1 mg/kg of butorphanol IV, analgesic response was considered excellent (pronounced analgesic effect for a time period adequate to permit specific therapy) or good (noticeable analgesic effect with minor indications of pain).[34] Personal experience suggests that total IV doses of 4 to 10 mg in a 450-kg horse provide clinically useful analgesia. Xyalzine (1.1 mg/kg IV) followed by butorphanol (0.1 mg/kg IV) produced excellent visceral analgesia in one study.[14] Butorphanol (0.1 mg/kg IV) has been reported to decrease jejunal, but not pelvic flexure, propulsive motility in ponies.[13] Butorphanol (0.1 mg/kg IV) produced minimal effect on intestinal sounds, time to first defecation after treatment, and fecal consistency in one study.[33]

Pentazocine is a synthetic narcotic agonist–antagonist that has some visceral analgesic properties. The visceral analgesic effects of this drug have been investigated by Lowe,[1] Pippi,[3] and Kalpravidh[4] in ponies and by Muir

and Robertson[5] in horses using a cecal balloon distension pain model. Pentazocine (0.99 mg/kg IV) produced visceral analgesia with a duration of about 30 minutes in one study.[5] Pentazocine was clearly inferior to xylazine as a visceral analgesic.[1,3,4] By comparison, butorphanol was demonstrated to be 10 to 17 times as potent as pentazocine on a dose to body weight basis (see Table 1). Pentazocine (0.3 mg/kg IV) has been demonstrated to inhibit pony jejunal, but not pelvic flexure, motility.[13] Pentazocine blunted hemodynamic effects of cecal balloon induced colic pain and may mask the severity of obstructive disease in clinical patients.[5]

Meperidine is a synthetic narcotic analgesic that produces approximately 20 to 40 minutes of analgesia in horses and ponies with cecal balloon induced abdominal pain.[1,3,5] Meperidine's analgesic effects are inferior to those of xylazine for visceral and superficial pain.[1,3] Meperidine (1.0 mg/kg IV) has been demonstrated to inhibit pony jejunal, but not pelvic flexure, motility.[13] Meperidine (3.0 or 4.0 mg/kg IM) produced little effect on intestinal sounds, time to first defecation after treatment, and fecal consistency.[33] Oxymorphone is a potent morphine analogue. Oxymorphone has been used successfully by some practitioners to manage colic.[23] Methadone is a synthetic narcotic that produces excellent analgesia without excitement in horses.[23]

Clinical use of the opiate drugs in equine practice has not become common due, in part, to the behavioral changes described earlier.[17,31,32,35] Combie et al. demonstrated that narcotic analgesics produce a characteristic and quantifiable dose-dependent increase in spontaneous locomotor activity.[31] Muir, Skarda, and Sheehan demonstrated increases in heart rate, arterial blood pressure, and cardiac output with no changes in arterial pH, $PaCO_2$, or PaO_2 in pain-free adult horses given recommended doses of morphine, meperidine, oxymorphone, and pentazocine.[35] Robertson, Muir, and Sams demonstrated that butorphanol given to pain-free adult horses in doses up to 0.4 mg/kg IV had minimal cardiopulmonary depressant effects. In this study, horses given doses equal to or greater than 0.2 mg/kg became excited and ataxic.[36] Improved analgesia with reduced behavioral side effects has been demonstrated after administration of xylazine and morphine[22] or xylazine and butorphanol.[14] Xylazine has also been demonstrated to provide improved, extended analgesia when combined with fentanyl, meperidine, oxymorphone, or pentazocine. Administration of these drug combinations was not associated with significant cardiopulmonary abnormalities.[14] Xylazine drug combinations may also achieve immobilization of equine patients. Under xylazine–butorphanol sedation–analgesia, horses tolerated the placement of towel clamps in the skin, skin incision, and the grid approach to the abdomen through the left flank without benefit of local anesthesia.[14] Recommended IV doses for these drugs and combinations are

listed in Table 2. Safety at recommended doses and the synergistic analgesic effects of these drug combinations make them useful in the restraint of the equine colic patient.

Non-Steroidal Anti-Inflammatory Drugs

Dipyrone, phenylbutazone,‖ ‖ and flunixin meglumine are peripheral acting analgesics that prevent pain by inhibiting biosynthesis of prostaglandins in injured tissues. Flunixin has been reported to reduce pain associated with colic in 68% of 118 horses tested.[15] In another study, flunixin relieved clinical signs of colic for 30 to 60 minutes in ponies with experimental pelvic flexure impactions.[2] Flunixin failed to demonstrate analgesic effects in the cecal balloon distention pain model, and dipyrone decreased pain in one of 20 trials.[1] Experimental failure to demonstrate efficacy of these drugs may result from limitations of the model that produces acute pain by direct stimulation of the stretch receptors in the abdomen, not via induction of prostaglandin synthesis.[4] In the clinical setting, administration of dipyrone and flunixin meglumine resulted in relief of mild abdominal pain.[24] At a dose of 0.5 to 1.0 mg/kg, flunixin meglumine may provide visceral analgesia for up to 8 hours.[15] Flunixin meglumine may mask signs of intestinal ischemia-endotoxemia and result in an undesirable delay of surgical intervention.[24] Flunixin and dipyrone had no effect on mechanical or myoelectrical activity of pony jejunum and pelvic flexure.[2,7]

Modification of Motility

Ileus is a major complication of many intestinal resections and may occur following an uncomplicated exploratory celiotomy. The search for a safe and effective pharmacologic means to hasten the return of propulsive gut motility, which would allow horses to begin to drink and eat soon after surgery, is clinically relevant and ongoing.

Neostigmine,¶¶ an anticholinesterase, increases the concentration of acetylcholine at smooth muscle receptors.[23] Neostigmine also directly stimulates cholinergic receptors.[23] Experimental doses of 0.022 mg/kg of neostigmine IV produced defecation and increased propulsive activity of the cecocolic area[25] and pelvic flexure.[7] Neostigmine decreased propulsive motility in the pony jejunum[7] and has recently been shown to delay gastric emptying of particulate markers in horses.[18] This drug has been used to promote colonic motility, but small intestinal ileus may not respond to this drug. Neostigmine caused abdominal discomfort in experimental ponies.[7] The drug should be withdrawn if signs of severe

TABLE 2. Dosages of Drugs and Drug Combinations Commonly Used to Produce Visceral Analgesia

	IV Dose Range (mg/kg)
Drug	
Xylazine	0.6–1.0
Morphine	0.02–0.10
Meperidine	0.2–0.6
Oxymorphone	0.01–0.06
Pentazocine	0.4–0.8
Butorphanol	0.02–0.04
Drug combinations	
Xylazine/morphine	0.6/0.2–0.6
Xylazine/meperidine	0.6/0.2–1.0
Xylazine/butorphanol	0.6/0.02–0.04
Xylazine/pentazocine	0.6/0.2–0.8

IV: intravenous.

abdominal pain follow its use. Overdose of neostigmine in humans is associated with abdominal cramps, diarrhea, salivation, bradycardia, hypotension, and bronchoconstriction.[37] The present authors observed one horse in which asystole developed. This horse died after a neostigmine overdose. The clinical importance of neostigmine's effect on gastric emptying remains to be evaluated.

Roger, Bardon, and Ruckebush investigated the effect of naloxone,## an opiate antagonist, on the myoelectrical and mechanical activity of the equine jejunum and large colon.[11] Naloxone (0.5 mg/kg IV) elicited pronounced propulsive activity of the left ventral and dorsal colons that lasted approximately 45 minutes. Defecation was observed and no untoward side effects were reported. These results suggest that opiate antagonists may be useful in stimulating colonic motility in patients with postoperative ileus or impaction. The clinical usefulness of this class of drugs requires further investigation.

Metoclopramide*** (methoxychloroprocainamide) stimulates and coordinates motility of the stomach and proximal small intestine, but has little effect on the large intestine in humans.[38] The drug acts by direct stimulation of smooth muscle, by augmenting acetylcholine release from post-ganglionic cholinergic nerve terminals, by sensitizing muscarinic receptors in gastrointestinal smooth muscle, and by alpha$_2$-adrenergic blockade.[38,39] It appears to require intrinsic stores of acetylcholine to exert its effect. Metoclopramide also antagonizes the inhibitory effects of dopamine on gut smooth muscle.[38–40] Metoclopramide accelerates gastric emptying and shortens transit time through the small intestine via its ability to stimulate and coordinate gastric, pyloric, and duodenal motor activity.[40,41] This drug has been used successfully in dogs to treat gastric stasis following surgical correction of acute gastric dilatation or pyloric ste-

nosis.[40] Metoclopramide, however, did not increase duodenal motility in eight human patients after abdominal surgery.[38] Metoclopramide restored normal stomach to anus transit time and restored coordinated gastric and small intestinal motility in a model of postoperative ileus in ponies.[39] The use of metoclopramide within 4 days of bowel anastomosis in human patients is not recommended.[39] The safety of this drug in the early postoperative period in horses with bowel anastomoses remains to be investigated.

A safe dose for metoclopramide in horses has not yet been established. Infusion of 0.5 mg/kg of metoclopramide over a 30-minute period to a normal pony and to ponies with experimental postoperative ileus resulted in periods of excitement.[16,19,39] A dose of 0.25 mg/kg administered over a 30-minute period in the same experiments produced periods of restlessness, alternating with sedation and yawning. Side effects varied in intensity from pony to pony and lasted for about 15 minutes after the infusion ended.[19] Doses of 0.06 and 0.15 mg/kg of metoclopramide IV resulted in intermittent colic in one healthy pony.[16] A dose of 0.03 mg/kg IV in four healthy ponies resulted in no changes in motility of the distal jejunum or pelvic flexure, although ponies showed mild discomfort for 10 minutes after administration.[16] Further investigation is required to develop a safe and effective therapeutic regimen for the use of metoclopramide in horses. Whether this drug will be useful in stimulating proximal intestinal motility in postoperative equine colic patients remains to be determined.

Panthenol,††† an alcohol analogue of pantothenic acid, is a precursor of coenzyme A. Its use for stimulating intestinal motility has been advocated on the grounds that it increases the formation of acetylcholine. Panthenol (5.5 mg/kg IV) had no effect on intestinal motility in a study of six ponies.[7] The drug has no known pharmacologic uses.

Conclusion

Although much remains to be learned about the pathophysiology of abdominal obstructive diseases in horses and about the pharmacology of visceral analgesics and motility modifying drugs, significant progress has been made in these areas of investigation in the last few years. Reliable models for abdominal obstruction and postoperative ileus in horses have been developed. Most controlled studies indicate that xylazine is the most effective analgesic available for visceral pain in horses. The clinical significance of the gut motility inhibiting effects of this drug needs further investigation. Preliminary studies of neostigmine and metoclopramide suggest that, once safe dosage regimens have been developed, these drugs hold promise for the treatment of postoperative

ileus in horses. Development and use of reliable models to test response to analgesics and effects of drugs on gut motility will, hopefully, allow rapid advancement in our ability to pharmacologically modulate gastrointestinal pain and motility in horses.

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††† Ilopan, Adria Laboratories, Columbus, OH.

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