

Advances in Equine Nutrition

Volume IV

Edited by

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OVERVIEW OF GASTRIC AND COLONIC ULCERS

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Introduction

Equine gastric ulcer syndrome (EGUS) and right dorsal colitis (RDC) are common in performance horses. Diagnoses are based on history, clinical signs, laboratory findings, gastroscopic examination, and response to altered diet and medical therapy. Effective treatment strategies for EGUS focus on increasing stomach pH by inhibiting or buffering gastric acid, which allows a permissive environment for ulcer healing, and environmental and dietary management. Effective treatment strategies for RDC focus on removing nonsteroidal anti-inflammatory drugs (NSAIDs), decreasing the bulk in the diet, reducing inflammation, coating and lubricating the colon, and decreasing environmental stress. Prevention of these conditions requires long-term dietary and environmental management.

Equine Gastric Ulcer Syndrome

Gastric ulcers are common in performance horses. The term “equine gastric ulcer syndrome” (EGUS) was coined to describe the condition of erosions and ulcerations occurring in the distal esophagus, nonglandular and glandular stomach, and proximal duodenum of horses (Andrews et al., 1999). EGUS is caused by many factors including anatomy of the stomach, exercise, restricted feed intake, diet, environmental stress (stall or transport), and the use of nonsteroidal anti-inflammatory agents (Buchanan and Andrews, 2002). Diagnosis of EGUS is based on history, clinical signs, endoscopic examination, and response to treatment. All ages and breeds of horses are susceptible to EGUS, and current therapeutic strategies focus on blocking gastric acid secretion and raising stomach pH to ≥ 4.0 . To date there is only one Federal Drug Administration (FDA) approved pharmacologic agent for treatment of EGUS: GastroGuard® (Merial Limited, Duluth, GA). However, a more comprehensive approach to EGUS diagnosis and treatment includes determining and correcting the underlying cause, environmental management, dietary manipulation, and pharmacologic intervention.

DIAGNOSIS

The approach to diagnosis of EGUS requires a thorough history, physical examination, and a minimum database (Figure 1). Identifying risk factors and clinical signs is



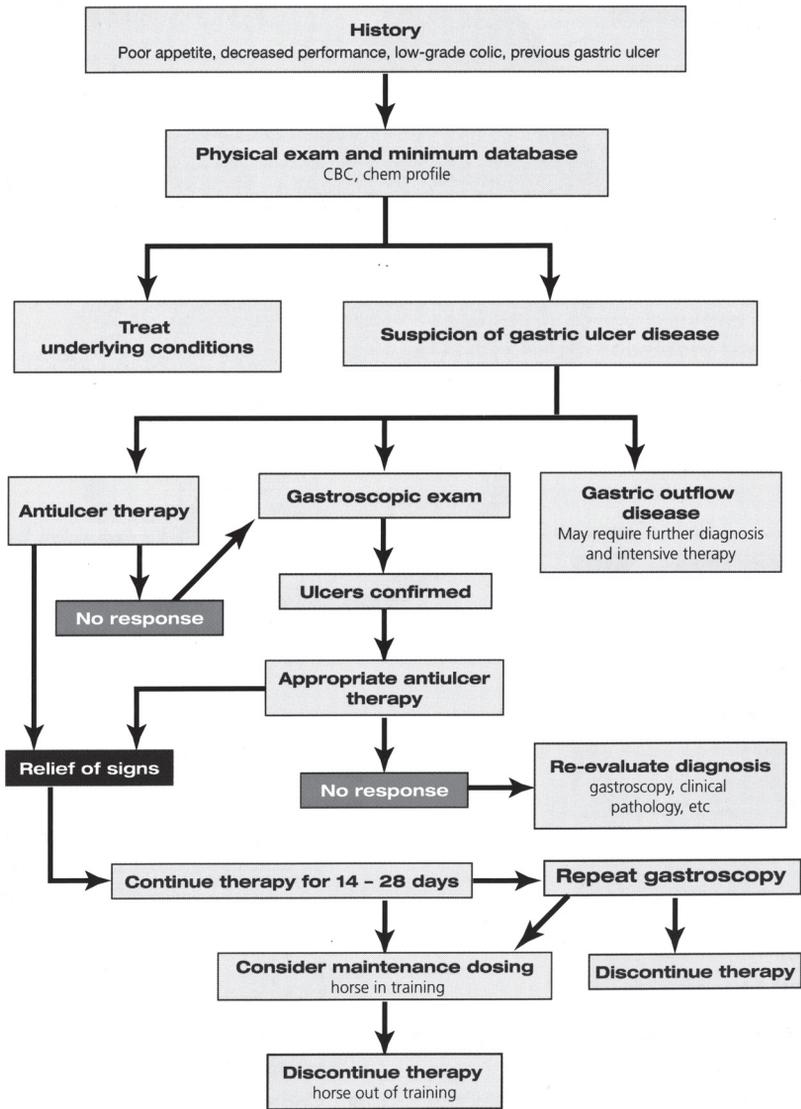


Figure 1. Diagnosis and treatment of EGUS.

helpful in diagnosing EGUS (Table 1). However, gastroscopy is the only definitive diagnostic technique currently available. The procedure for gastroscopy has been described in detail elsewhere, but requires at least a 2-meter endoscope to visualize the nonglandular mucosa and margo plicatus and a 2.5- to 3-meter endoscope to visualize the pyloric antrum and proximal duodenum in most adult horses. Once visualized, ulcers should be rated using a scoring system developed for horses (Andrews et al.,

Table 1. Commonly used antiulcer medications and recommended doses.

<i>Drug</i>	<i>Dosage</i>	<i>Route of Administration</i>	<i>Dosing Interval</i>
Omeprazole	0.5-1.0 mg/kg	Intravenously	Q 24 hrs
Omeprazole (GastroGard™)	4 mg/kg (Treatment of ulcers)	Orally	Q 24 hrs
Omeprazole (GastroGard™)	2 mg/kg (Prevention of recurrence)		
Omeprazole (UlcerGard™)	1 mg/kg (Prevention of ulcers)	Orally	Q 24 hrs
Ranitidine	1.5 mg/kg	Intravenously	Q 6 hrs
Ranitidine	6.6 mg/kg	Orally	Q 8 hrs
Ranitidine	11.0 mg/kg	Orally	Q 12 hrs
Misoprostol	5 mcg/kg	Orally	Q 8 hrs
Sucralfate	20-40 mg/kg	Orally	Q 8 hrs
A1OH/MgOH antacids	30g A1OH/15 g MgOH	Orally	Q 2 hrs
Bethanecol	0.025 - 0.30 mg/kg	Subcutaneous	Q 3-4 hrs
Bethanecol	0.3 - 0.45 mg/kg	Orally	Q 6-8 hrs

1999). Use of a scoring system allows the clinician to compare gastroscopic findings and monitor healing of ulcers to evaluate efficacy of treatment. Currently there are no hematologic or biochemical markers to diagnose EGUS. However, a recent report showed that horses with gastric ulcers had lower RBC counts and hemoglobins than horses that did not have gastric ulcers (McClure et al., 1999). Some horses with EGUS may be slightly anemic or hypoproteinemic, but in my experience the RBC or hemoglobin values are rarely out of the normal range.

O'Connor et al. (2004) recently evaluated the potential of a sucrose permeability test to diagnose gastric ulcers. Urine sucrose concentrations were significantly higher for horses with gastric ulcer scores >1. Using a urine sucrose concentration cutoff value of 0.7 mg/ml or higher revealed an apparent sensitivity of 83% and specificity of 90% to detect ulcers in horses tested using the sucrose permeability test. Thus, this test may provide a simple, noninvasive way to detect and monitor gastric ulcers. Because of the lack of any additional laboratory diagnosis, in situations where ulcers are strongly suspected but gastroscopy is not available, it may be worthwhile to start empirical treatment and observe for resolution of clinical signs. If the horse does not respond to treatment within several days, referral to a facility for gastroscopic examination is indicated (Figure 1).

TREATMENT

The goals of EGUS therapy are to relieve pain, eliminate clinical signs, promote healing, prevent secondary complications, and prevent recurrence. The mainstay of EGUS treatment is to increase stomach pH by suppressing stomach HCl acid secretion. Pharmacologic therapy is popular and several agents have proven helpful in EGUS treatment, but the only FDA-approved drug for treatment and prevention of recurrence of gastric ulcers in horses is GastroGard[®]. Because of the high recurrence rate, effective acid control should be followed by altered management strategies and/or long-term treatment to prevent ulcer recurrence. Recently, UlcerGard[®] (Merial LTD, Duluth, GA), a low-dose omeprazole paste, was approved as a nonprescription medication for prevention of gastric ulcers in horses. Many feed additives and nutraceutical agents claim efficacy, but to the author's knowledge there are no published scientific data on the efficacy of these compounds in the treatment or prevention of EGUS. A short time ago we tested an equine supplement (SeaBuck[®] Complete Liquid, SeaBuck Equine, LLC) containing seabuckthorn berry extract. This compound was effective in preventing increased gastric ulcer scores in horses that were stressed. Therefore, this compound may be helpful in preventing recurrence once ulcers have healed.

Compounded formulations of omeprazole lack the stringent efficacy and safety studies that are required for FDA approval and have little chance of efficacy. Also, the chemical properties of omeprazole make it difficult to compound while maintaining efficacy and potency. Many compounded forms of omeprazole are inactivated in the bottle prior to administration and two recent studies confirmed that compounded omeprazole suspensions were ineffective in healing gastric ulcers in racehorses in training (Nieto et al., 2002; Orsini et al., 2003).

ANTIBIOTICS (*HELICOBACTER* SPP.)

Helicobacter has not been cultured from the horse stomach, but DNA from a *Helicobacter*-like bacteria was found in the stomach mucosa of horses using a polymer chain reaction test (PCR) (Scott et al., 2001; Contreras et al., 2007). Although *Helicobacter* has not been cultured from horses, there are some horses that do not respond to conventional acid suppressive therapy. In horses with chronic nonresponsive EGUS, bacteria (primarily *E. coli* and *Streptococcus* sp.) may colonize the ulcer bed and prevent healing. Bacterial colonization of the nonglandular mucosa and gastric ulcer has been shown to occur in horses (Yuki et al., 2000). The use of antibiotics may decrease the bacterial population in these ulcers and allow healing. In horses with gastric ulcers that do not respond to conventional therapy, I recommend combination therapy consisting of omeprazole (4 mg/kg, orally, q 24 h) or ranitidine (6.6 mg/kg, orally, q 8 h), metronidazole (15 mg/kg, orally, q 6-8 h) and/or trimethoprim/sulfa (15 to 25 mg/kg, orally, q 12 h), and bismuth subsalicylate (3.8 mg/kg, orally, q 6 h). An initial 14-day treatment period is prescribed, which should be followed by gastroscopy.

Some horses may require longer treatment. Omeprazole therapy should be continued for the full 28 days if needed.

DIETARY MANAGEMENT

In conjunction with pharmacological therapy, environmental and dietary management may be helpful to facilitate ulcer healing. Limited fasting periods, limited feeding of high-soluble-carbohydrate diets (not to exceed 0.5 kg grain/220 kg body weight) (Andrews et al., 2006) and providing good-quality alfalfa or alfalfa-mix hay can help buffer stomach contents and reduce gastric acidity. Alfalfa hay has been shown to buffer gastric contents and decrease gastric ulcer severity in horses housed in stalls and exercising (Nadeau et al., 2000; Lybbert et al., 2007). Also, pasture turnout when possible can help reduce stress and prevent gastric ulcers.

Right Dorsal Colitis (Colonic Ulcers)

Unlike EGUS, colonic ulcers and right dorsal colitis (RDC) occur less frequently, but may lead to hypoproteinemia and more severe clinical signs. In a necroscopic study of 545 horses, 44% of the nonperformance horses and 65% of the performance horses had colonic ulcers (Pellegrini, 2005). Colonic ulcers are probably associated with inhibition of prostaglandins by stress-induced release of endogenous corticosteroids or the administration of NSAIDs. Early in the condition, horses present with nonspecific signs of mild intermittent or recurring colic episodes, lethargy, and partial anorexia. However, as the condition worsens, clinical signs may include complete anorexia, fever, and diarrhea. Progression of RDC may lead to dehydration, ventral edema, and weight loss. Differential diagnoses for this condition include EGUS, large colon displacement and/or impaction, infectious causes of diarrhea (salmonellosis, Potomac horse fever, *Clostridium*), granulomatous enteritis, eosinophilic enterocolitis, and intestinal neoplasia.

DIAGNOSIS

A presumptive diagnosis of RDC can be made on history, clinical signs, changes on CBC (mild anemia, toxic changes in PMNs, left shift), hyperfibrinogenemia, hypoalbuminemia, and hypocalcemia. Peritoneal fluid analysis may show a mild increase in WBC count and increase in total protein concentration. In a recent study, a guaiac-based fecal occult blood test was shown to have a good positive predictive value (72%) and a poor negative predictive value (51%) in the diagnosis of RDC (Pellegrini, 2005). In that study, many horses that had gastric or colonic ulcers had negative tests (i.e., false negatives). Gastroscopic examination of the stomach, if negative, may help diagnose RDC in horses showing typical clinical signs, especially if there is concurrent hypoproteinemia. Abdominal ultrasonography of the right dorsal colon may show

mural thickening (normal = < 4 mm) (Jones et al., 2003). The peripheral wall of the right dorsal colon can be scanned percutaneously through intercostal spaces 11 to 15, ventral to the ventral margin of the right lung field.

Every effort should be made to rule out infectious causes of diarrhea such as salmonellosis and Potomac horse fever (PHF) in horses with diarrhea. Fecal cultures and PHF serology and PCR can be helpful in ruling out these conditions. Horses with salmonellosis will have signs similar to RDC and these diseases may occur together.

TREATMENT

The principal components of treatment for RDC include discontinuing use of NSAIDs, decreasing gut fill to allow the colon to rest, and offering frequent feedings. These steps should lead to reduced inflammation and restoration of normal colon absorptive function (Cohen et al., 1995). Reduction in gut fill can be accomplished by decreasing or eliminating dry hay from the diet and replacing with frequent feeding of alfalfa-based pelleted complete feeds with at least 30% dietary fiber (Purina Senior™, Purina Mills, St. Louis, MO). This reduces gut fill and decreases the mechanical load on the colon. The horse can be allowed to graze small amounts of fresh grass (10- to 15-minute intervals, four to six times daily) to help maintain body weight. The switch to a complete feed diet should be made over several days to a week to allow the gastrointestinal tract time to acclimatize to the feed change. The complete feed diet should be continued for three to four months, at which time hypoproteinemia and hypoalbuminemia should have resolved.

Psyllium mucilloid (Equisyl Advantage™, Animal Health Care Products) or psyllium hydrophilic mucilloid (Metamucil®, Proctor & Gamble, Cincinnati, OH) can be added to the diet to shorten transit time for ingesta and increase water content of the gastrointestinal tract. Also, psyllium increases the concentration of short-chain fatty acids, an effect which has been shown in other species to reduce inflammation, and thus may reduce inflammation in the equine colon also. Furthermore, safflower oil (1 cup, added to feed, q 12 h) can be added to the complete feed to increase omega-3 fatty acids. Omega-3 fatty acids competitively inhibit the activity of the cyclooxygenase enzyme necessary for eicosanoid production. A diet rich in omega-3 fatty acids may reduce the eicosanoid production, thereby decreasing inflammation.

The use of medications routinely used for gastric ulcer treatment (antacids, omeprazole, or ranitidine) would not be expected to be effective in treatment of RDC. However, sucralfate (22 mg/kg, orally, q 6-8 h), a sucrose octasulfate and polyaluminum hydroxide complex, has been used for treatment of RDC. This compound has a strong affinity to bind to gastrointestinal mucosa. It has a greater affinity to bind to ulcer craters when compared to intact epithelial cells. In man, sucralfate is more adherent to duodenal ulcers than gastric ulcers despite the duodenal pH >4.0. Thus, sucralfate may bind to ulcer craters in the colons of horses, forming

a proteinaceous bandage. Furthermore, sucralfate, once bound to the ulcer crater, may stimulate local prostaglandin production, which may exert a “cytoprotective” effect on the colon mucosa.

Minimizing physiologic and environmental stresses can also be helpful in controlling RDC. Stall rest, reduction of strenuous exercise or training, and reduction in transport are ways to decrease stress. Horses should always have adequate amounts of clean, fresh water and should be provided a mineral/salt mix to ensure adequate water intake (Cohen et al., 1995).

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