Equine gastric ulcer syndrome

Author : Nicola Menzies-Gow

Categories : Vets

Date : October 17, 2011

Nicola Menzies-Gow discusses a common condition in horses, and outlines approaches to diagnostic and treatment methodologies, as well as dietary considerations

Summary

Equine gastric ulcer syndrome (EGUS) is common in horses, with the majority (80 per cent) of ulcers occurring in the squamous portion of the stomach. Risk factors include diet, exercise, stable confinement and stress. A diagnosis is based on history, clinical signs and gastroscopy. Treatment focuses on the use of pharmacologic agents to suppress or neutralise gastric acid, creating an environment that allows ulcer healing to occur. The proton pump inhibitor, omeprazole, is the only drug licensed in the UK. Environmental and dietary management changes are also required as an adjunct to decrease ulcer severity and prevent recurrence.

Key words

omeprazole, ulcer, gastric, diet, management

EQUINE gastric ulcer syndrome (EGUS) is characterised by ulceration in the terminal oesophagus, proximal (squamous) stomach, distal (glandular) stomach and proximal duodenum.

In recent years, EGUS has been increasingly recognised as a common and possibly performance-limiting disease of adult horses. The prevalence of equine gastric ulceration has been reported for a variety of breeds and types of horses, including 70 to 94 per cent of thoroughbreds in race

training (Figure 1), 88 per cent of standardbreds in training, 93 per cent of high-level endurance horses during the competition season, 71 per cent of broodmares and 58 per cent of active show horses.

The stomach is divided into two distinct areas. The proximal portion is lined by stratified squamous mucosa, similar to the oesophageal lining, while the distal portion is lined with glandular mucosa. The distinct junction between the two is called the margo plicatus. Ulceration can occur in either or both regions, but the majority (80 per cent) occurs in the squamous portion. The pathophysiologic mechanisms involved in the two regions differ. An imbalance between inciting and protective factors in the mucosal environment can result in ulcer formation. The major intrinsic factors promoting ulcer formation include hydrochloric acid (HCL), bile acids and pepsin, while the protective factors include:

– the mucus-bicarbonate layer;

– maintenance of adequate mucosal blood flow;

– mucosal prostaglandin E2 and epidermal growth factor production;

– rapid epithelial cellular restitution when injured; and

– gastroduodenal motility.

In the squamous mucosa, there is minimal resistance to HCL provided by the intercellular tight junctions and bicarbonate secretion. Protection is dependent on limited exposure, so excessive acid exposure is the predominant mechanism responsible for ulceration. The glandular mucosa is protected by adequate mucosal blood flow. Alterations in blood flow and the mucus-bicarbonate layer result in ulceration.

Risk factors for gastric ulcer formation include eating behaviour and diet, exercise, stress and excessive use of NSAIDs. The horse is a natural grazer, and grazing results in a constant flow of saliva and ingesta, which buffer acid. When feed is withheld from horses before racing, or when horses are stabled, the absence of this buffering results in the gastric pH decreasing and the squamous mucosa being exposed to acid. Alongside feeding practices, stable confinement has been implicated as a risk factor. This may be related to stabled horses often being fed two large meals daily of feeds, which tend to be high in grain and consumed rapidly. This rapid food consumption leads to a decrease in saliva production and, therefore, less buffering of gastric contents. In addition, serum concentrations of gastrin, a potent stimulus of HCL secretion, are highest in horses fed high-concentrate diets.

High-concentrate diets are high in digestible carbohydrates, which are fermented by resident bacteria to volatile fatty acids (VFA), which are directly capable of causing acid damage. In

contrast, alfalfa hay appears to have a protective and antiulcer effect, possibly due to its high calcium and protein content. Exercise may influence HCL secretory patterns, gastric emptying and mucosal blood flow.

In addition, the mechanical effects of exercise and increased abdominal pressure may prolong squamous mucosal exposure to acid. Furthermore, an increase in serum gastrin concentration has been shown to occur in exercising horses, which may increase HCL secretion, leading to acid damage.

Stress-induced increases in circulating cortisol concentrations and treatment with NSAIDs both result in decreased prostaglandin synthesis, which in turn promotes acid secretion and reduces glandular mucosal blood flow, resulting in ulceration.

While *Helicobacter* infection is implicated in humans and pigs, its role in equine ulcers remains unclear. *Helicobacter equorum* has been isolated from faecal samples from clinically healthy foals (Moyaert et al, 2009) and adult horses (Moyaert et al, 2007).

Helicobacter like DNA has been detected in the stomach of some – but not all – horses with gastric ulcers and/or gastritis (Contreras et al, 2007). Once gastric ulcers are present, evidence from rats suggests that other bacteria, including *Escherichia coli*, may play a role in inhibiting ulcer healing.

Equine gastric ulcers are often under-diagnosed because of the non-specific clinical signs and a lack of markers for laboratory diagnosis. Clinical signs include yawning, bruxism, anorexia, colic, weight loss and reduced performance. Gastroscopy is the only method for accurately diagnosing gastric ulcers (Figure 2).

A four-point scoring system has been developed to help classify the severity of ulcers, in which grades two or above are considered clinically significant. It allows clinicians to compare gastroscopic findings and monitor ulcer healing. There are no haematologic or biochemical alterations specific to the disease. The presence of any alterations would suggest that either another disorder is underlying the clinical signs, or that while there may be gastric ulcers present, they are secondary to another disease.

Treatment

Pain relief, ulcer healing and prevention of secondary complications are the primary goals.

Pain relief

Managing pain in animals with gastric ulceration should ideally be achieved without using NSAIDs. Drugs such as xylazine, detomidine, romifidine or butorphanol are possible alternatives to NSAIDs. The pain should resolve with 48 to 72 hours of initiation of ulcer healing therapy.

Acid suppression or neutralisation

Since acid is implicated as the most important pathophysiologic component of squamous ulcer disease, most antiulcer therapy concentrates on suppressing or neutralising gastric acid. However, it should be remembered that suppressing acidity does not stimulate ulcer healing, but instead is permissive to ulcer healing. Healing mechanisms are initiated with the onset of mucosal injury, and removing the acid allows healing to occur unimpeded.

Since the horse is a continuous secretor of HCL, effective treatment requires pro – longed reduction of gastric acidity. The mechanism of action of the drug used and the dose administered will affect the potency and duration of acid suppression.

Additionally, the bioavailability of orally administered drugs is generally poor, varies between individuals and may be affected by an animal's age. Therefore, deviating from recommended dosages may result in treatment failure.

It is difficult to predict how long a squamous or glandular gastric ulcer will take to heal, but the recommended treatment time for most antiulcer medications is 28 days.

Management changes, in addition to pharmacologic therapy, may speed up ulcer healing. If endoscopy is available, this can be used to monitor healing. However, if this is not available, horses should be treated for at least 28 days.

Early treatment cessation may result in ulcer recurrence. In general, it may take longer to treat large ulcers, more severe ulcers and ulcers in the squamous mucosa. It should be noted that clinical signs might resolve before complete healing has taken place. Signs of poor appetite, colic or diarrhoea usually resolve within a few days after initiating treatment, and improvements in body condition and attitude become apparent within two to three weeks.

The same drugs can be used as preventive medication at times of known greatest risk, such as travelling or high-stress situations. The principal therapeutic options are detailed below.

H2 antagonists

H2 antagonists suppress HCL secretion through competitive inhibition of the parietal cells' histamine receptor; histamine is the most potent stimulus for HCL secretion. Commonly recommended doses are 20mg/kg to 30mg/kg tid PO or 6.6mg/kg qid IV for cimetidine and 6.6mg/ kg tid PO or 1.5mg/kg to 2mg/ kg qid IV for ranitidine. Therapy should continue for at least 28 days, but complete ulcer healing may take longer than 40 days. More scientific literature demonstrates the efficacy of ranitidine in treating equine gastric ulcers compared to cimetidine.

Proton pump inhibitors

Proton pump inhibitors irreversibly bind to the H+/K+-ATPase proton pump of the parietal cell, inhibiting H+ secretion. They have a prolonged anti-secretory effect, allowing for once-daily dosing. Omeprazole has been shown to be more effective than ranitidine, and is the only product licensed for treating equine gastric ulcers in horses more than 30 days of age in the UK, at a dose of 4mg/kg sid PO for 28 days. After the initial treatment, treatment with 1mg/kg to 2mg/ kg sid PO has been shown to decrease or prevent the recurrence of disease in animals maintained in training.

Mucosal protectants

Sucralfate and bismuth subsalcyclate bind to ulcers and promote healing. Sucralfate is effective in treating peptic ulcers and preventing stress-induced ulcers in humans. The mechanism of action in the glandular mucosa is likely to involve adherence to ulcerated mucosa, stimulation of mucus-bicarbonate secretion, enhanced PGE2 secretion and increased concentration of growth factors at the ulcer site.

The mechanism of action in the squamous mucosa is unknown. A dose of 10mg/kg to 20mg/kg every six to eight hours PO is recommended.

However, in a clinical trial in horses, sucralfate (22mg/kg, orally, every eight hours) did not improve subclinical ulcer healing in six and seven-month-old foals (Borne and MacAllister, 1993). Therefore, sucralfate alone may not be beneficial in treating gastric ulcers, but can be used in conjunction with acidsuppressive therapy.

Bismuth-containing compounds may have a coating effect similar to sucralfate. Additionally, they will inhibit the activation of pepsin and increase mucosal secretion. A compound containing 26.25g of bismuth failed to raise the pH in five horses (Clark et al, 1996).

Bismuth subsalicylate may be converted to sodium subsalicylate in the gastrointestinal tract, which may cause gastric irritation. In addition, salicylates, similar to aspirin, decrease prostaglandin secretion and may further compromise an already damaged mucosa. Therefore, compounds containing bismuth are not recommended for treating equine gastric ulcers.

Antacids

In humans, antacids are primarily used to control symptoms of dyspepsia (heartburn or upset stomach) and are not considered primary therapy for ulcers.

Antacids reduce gastric acidity by neutralising existing acid. Most are based on a combination of aluminium and magnesium hydroxide, or calcium carbonate. One study demonstrated that 30g

aluminium hydroxide per 15g magnesium hydroxide results in an increase in gastric pH for two hours (Clark et al, 1996). Therefore, although antacids may be useful, a dose of 180ml to 200ml at least every four hours is needed for an adult horse. Dietary supplementation with 124.5g of calcium carbonate twice a day increased gastric pH for two hours after feeding, thus it would need to be fed frequently to treat or prevent gastric ulcers (Reese and Andrews, 2009). In addition, the use of an antacid feed additive is counterintuitive, as an acid-neutralising effect is desirable when the stomach is empty and not when it is full, because the gastric pH is naturally high when horses ingest feed.

Synthetic hormones

Misoprostil is a synthetic PGE1 analogue that is effective in treating human gastric ulcers through acid suppression, increased mucosal blood flow, increased bicarbonate secretion and increased mucosal restitution. Reported side effects include diarrhoea, cramping, flatulence and uterine contraction, precluding its use in horses.

A somatostatin analogue, octreotide acetate (0.5mg/kg to 5.0mg/kg) raised the gastric pH level in horses to greater than four for approximately five hours, with no adverse effects noted (Sojka et al, 1992). However, it requires multiple daily dosing and is costprohibitive in horses.

Environmental, nutritional and dietary management

Environmental, nutritional and dietary management changes should be initiated during the pharmacologic therapy to help facilitate healing and prevent recurrence. Intense or long duration exercise, stall confinement, and diet are risk factors for EGUS.

Managing these risk factors can, therefore, decrease ulcer severity and prevent ulcer recurrence.

Modification of exercise

Intense exercise, racing and race training has been shown to contribute to a worsening of squamous gastric ulcers, compared with horses kept at pasture or not in training. In addition, endurance exercise has been shown to play a role in the cause of EGUS in horses. Thus ideally, training and exercise intensity should be reduced – at least until the ulcers have healed – and, although often not practically possible, the exercise regime should be permanently altered to reduce this risk and so prevent recurrence.

Forage feeding

Pasture turnout is the best dietary method of controlling gastric ulcers. However, where this is not possible, horses should be allowed ad-lib hay whenever stabled, as continuous forage

consumption results in a constant flow of saliva and ingesta to buffer the gastric acid.

It appears that alfalfa hay may be better at helping raise gastric pH compared to other hay types, due to the high calcium and/or protein content having a direct effect on gastric secretions. Straw should be avoided, as it appears to worsen ulcer severity compared to hay or haylage.

Concentrate feeding

Ideally, concentrates should be eliminated from the diet, or fed little and often, as bolus feeding of concentrates results in lower saliva production and increased intragastric fermentation, thus producing damaging VFAs.

High-carbohydrate feeds should be avoided due to increased gastrin secretion and VFA production – both are associated with increased acid damage.

The size of the grain meal also has an influence. Large meals are associated with increased VFA production because of the large amount of fermentable carbohydrates and also because larger meals are associated with longer gastric retention times.

Therefore, grain or concentrates should not be fed in excess of 0.5kg/100kg BW every six hours.

Antibiotics versus probiotics

The role of bacteria in EGUS remains unclear, with limited evidence from rats to suggest that bacteria such as *E coli* may play a role in inhibiting ulcer healing.

In a study in horses with spontaneously occurring gastric ulcers, an antibiotic (trimethoprim sulphadiazine) or a probiotic preparation (containing *Lactobacillus agilis, L salivarius, L equi, Streptococcus equinus* and *S bovis*), administered orally, decreased ulcer number and severity compared with untreated controls (Al Jassim et al, 2006), suggesting that resident stomach bacteria are important in the maintenance and progression of squamous gastric ulcers in horses.

Therefore, antibiotic treatment may be indicated in horses with chronic nonresponsive gastric ulcers, and probiotic preparations containing *Lactobacillus* and *Streptococcus* may be helpful in preventing gastric ulcers – or may be used as an adjunct to pharmacologic treatment.

Dietary supplements

A large number of dietary supplements are available for treating and preventing equine gastric ulcers. Many of these products have not been tested in horses and scientific evidence related to their efficacy is lacking.

Those that have some scientific testing include seabuckthorn berry extract, corn or rice bran oil, and a pectin-lecithin complex. Seabuckthorn berry extract did not heal ulcers in horses, but it may prevent squamous ulcers from getting worse during times of stress or feed deprivation (Reese et al, 2008).

While one study showed that dietary corn oil significantly lowered gastric acid output and increased prostaglandin concentration in the gastric juice (it was suggested that corn oil supplementation could be an economical approach to the therapeutic and prophylactic management of glandular ulcers in horses, especially those associated with the use of NSAIDs [Cargile et al, 2004]), in another study, corn oil and rice bran oil did not prevent squamous ulceration (Frank et al, 2005).

Similarly, a pectin-lecithin complex – which is reported to be important in gastric mucosal protection – was associated with improved healing of gastric ulcers (Venner et al, 1999) in one study, but not in a second study (Murray and Grady, 2002).

Concentrated electrolyte pastes or solutions are often given as a dietary supplement to endurance horses. Repeated oral administration of such electrolyte solutions has been shown to increase the number and severity of gastric ulcers (Holbrook et al, 2005). These products should be used with caution in horses and may be best given after exercise with feed to minimise their effects on the gastric mucosa.

Other

Other management changes that should be considered include allowing horses to exhibit normal behaviour to minimise stress, such as allowing visibility to horses that they normally socialise with when stabled.

References

- Al Jassim R A M, Scott P T, Trebbin A L et al (2006). The genetic diversity of lactic acidproducing bacteria in the equine gastrointestinal tract, *FEMS Microbiol Lett* **248**: 75-81.
- Borne A T and MacAllister C G (1993). Effect of sucralfate on healing of subclinical gastric ulcers in foals, *J Am Vet Med* **202**: 1,465-1,468.
- Cargile J L, Burrow J A, Kim I et al (2004). Effect of dietary corn oil supplementation on equine gastric fluid acid, sodium and prostaglandin E_2 content before and during pentagastrin infusion, *J Vet Intern Med* **18**: 545-549.
- Clark C K, Merritt A M, Burrow J A et al (1996). Effect of aluminum hydroxide/ magnesium hydroxide antacid and bismuth subsalicylate on gastric pH in horses, *J Am Vet Med* **208**: 1,687-1,691.
- Contreras M, Morales A, Garcia-Amado M A et al (2007). Detection of *Helicobacter*-like DNA in the gastric mucosa of thoroughbred horses, *Lett Appl Microbiol* **45**: 553-557.
- Frank N, Andrews F M, Elliott S B et al (2005). Effects of dietary oils on the development of

gastric ulcers in mares, *Am J Vet Res* **66**: 2,006-2,011.
- Holbrook T C, Simmons R D, Payton M E et al (2005). Effect of repeated oral administration of hypertonic electrolyte solution on equine gastric mucosa, *Equine Vet J* **37**: 501-504.
- Moyaert H, Decostere A, Vandamme P et al (2007). *Helicobacter equorum sp nov*, a urease-negative *Helicobacter* species isolated from horses faeces, *Int J Syst Evol Microbiol* **57**: 213-218.
- Moyaert H, Haesebrouck F, Dewulf J et al (2009). *Helicobacter equorum*is highly prevalent in foals, *Vet Microbiol* **133**: 190-192.
- Murray M J and Grady T C (2002). The effect of a pectin-lecithin complex on prevention of gastric mucosal lesions induced by feed deprivation in ponies, *Equine Vet J* **34**: 195-198.
- Reese R E and Andrews F M (2009). Nutritional and dietary management of equine gastric ulcer syndrome, *Vet Clin North Am Equine Pract* **25**: 79-92.
- Reese R E, Andrews F M, Elliott S B et al (2008). The effect of seabuckthorn berry extract (Seabuck Complete) on prevention and treatment of gastric ulcers in horses, *Proceedings of the 9th International Equine Colic Research Symposium*, Liverpool.
- Sojka J E, Weiss J S, Samuels M L et al (1992). Effect of the somatostatin analogue octreotide on gastric fluid pH in ponies, *Am J Vet Res* **53**: 1,818-1,821.
- Venner M, Lauffs S and Deegen E (1999). Treatment of gastric lesions in horses with pectin-lecithin complex, *Equine Vet J Suppl* **29**: 91-96.