



Invited review

Equine gastric ulcer syndrome in adult horses

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ABSTRACT

Many domesticated horses have gastric ulcers which can be diagnosed and graded during gastroscopy. A distinction should be made between equine squamous gastric disease (ESGD), which is caused by exposure of the mucosa to acid, and equine glandular gastric disease (EGGD), thought to occur when mucosal defence mechanisms are compromised. Horses with gastric ulcers may, but do not always, show clinical signs such as poor appetite, mild colic, discomfort during girthing, behavioural changes and reduced performance. The mainstay of treatment is blocking acid production using the proton pump inhibitor omeprazole. Treatment is usually successful in cases of ESGD, but less so for EGGD, where treatment duration is longer and for which sucralfate may be added or alternatives necessary, such as misoprostol, a prostaglandin analogue. To prevent recurrence of ulcers known risk factors, such as high concentrate diets, intense exercise and stress should be avoided or minimized.

Introduction

Gastric ulceration in horses is likely to have been around for as long as horses themselves, given the fact that ulcers are also encountered in feral horses (Ward et al., 2015). However, the prevalence has almost certainly increased considerably following domestication (Ward et al., 2015). Because of the difficulty in confirming a diagnosis of gastric ulcers antemortem, research in this field did not gain momentum until endoscopes long enough to reach the equine stomach became available. In some of the first studies (Murray et al., 1989, 1996) 2 m endoscopes were used which do not allow visualisation of the entire glandular portion of the stomach in all horses. This led to the impression that ulcers in the squamous part of the stomach are much more common than those in the glandular portion (Buchanan and Andrews, 2003; Bezdekova et al., 2007). However, the fact that the gastric region affected was not always specified complicates comparisons between older and more recent literature. The term Equine Gastric Ulcer Syndrome (EGUS) was introduced in 1999 (Andrews et al., 1999a), but the distinction between Equine Squamous Gastric Disease (ESGD) and Equine Glandular Gastric Disease (EGGD), two distinct entities, with different risk factors, pathogenesis and treatment, was not made until considerably later (Luthersson et al., 2009a; Merritt, 2009; Sykes et al., 2015a). This review will focus on the prevalence, pathogenesis, clinical signs and management of erosive and ulcerative diseases of the stomach in the adult horse, and the important distinction between ESGD and EGGD.

Prevalence

The prevalence of EGUS depends on the definition. Many horses with gastric ulcers, identified by gastroscopy, are considered to be asymptomatic (Luthersson et al., 2009a,b). However, Murray et al. (1989) showed that gastric ulcers in adult horses can be clinically significant, with ulceration being more severe in horses with clinical signs. Studies on EGUS are based either on post mortem examinations or on gastroscopy findings, and results of different studies cannot be directly compared. Also, earlier studies were often performed with shorter, 2 m endoscopes, which do not allow visualization of the pyloric region, where most glandular lesions occur (Begg and O'Sullivan, 2003; Luthersson et al., 2009a; Murray et al., 1989).

In an abattoir study, ESGD was found to be far more prevalent in domesticated than feral horses, although ESGD was found in 22% of feral horses (Ward et al., 2015). These results may have been affected by fasting and transport, to which the feral horses were briefly subjected before slaughter. At necropsy, squamous ulcers were found in 64% of wild equids in a safari park, with the highest prevalence in Grant's and Hartmann's zebras which, as opposed to other wild equids, were stabled at night (Lamglait et al., 2017). No clinical signs were observed in any of the animals, supporting the contention that gastric ulcers can occur asymptotically.

Chameroy et al. (2006) found that just 11% of horses in a university riding programme had squamous ulcers, with most ulcers in 3-year-olds. The authors postulated that this was related to the fact that these horses

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did not travel and were not exposed to changing environmental and dietary conditions. This is in contrast to the results obtained by [Prinsloo et al. \(2019\)](#), who found that 56% of horses in a university teaching herd suffered ESGD, where these horses also did not travel.

Approximately half (48%) of high-level endurance horses had ESGD during the interseason, but the prevalence increased to 93% during the race season ([Tamzali et al., 2011](#)). Diet, travel, and intensity of exercise, and other, as yet unknown factors, are likely to explain the difference. When gastroscopy was performed in 201 Warmblood horses not in training and considered to be healthy, 58% had an ESGD severity score equal to or greater than two and older horses were more likely to have both glandular and squamous ulcers ([Luthersson et al., 2009a](#)).

Many studies have looked at gastric ulceration in racehorses and most of these appear to have squamous ulcers when they are actively racing, with reported prevalence of around 90% ([Bell et al., 2007](#)). These data indicate that use of horses for competition, especially racing, places them at high risk of development of squamous gastric ulcers. This is not only related to exercise intensity, but also to management and feeding practices employed in the racing industry. Further evidence that a horse's workload is not the only risk factor for ESGD is provided by the fact that roughly half of non-race horses ([Luthersson et al., 2009b](#)), or race horses that are not actively racing, have ulcers ([Murray et al., 1996](#)).

Early endoscopic studies with shorter endoscopes led to the impression that ESGD is more common than EGGD. More recently, and in part due to the understanding that ESGD and EGGD are different disease entities, the prevalence of EGGD has been more extensively studied. This has made it clear that EGGD is also very prevalent, with studies reporting EGGD in 35–72% of various equine populations, and the prevalence was often higher than ESGD in the same study ([Begg and O'Sullivan, 2003](#); [Luthersson et al., 2009a, 2019](#); [Malmkvist et al., 2012](#); [Niedzwiedz et al., 2013](#); [Pedersen et al., 2018](#); [Sykes et al., 2015b](#)). Warmblood horses appear to have an increased risk of EGGD ([Mönki et al., 2016](#)), which often occurs in combination with ESGD ([Luthersson et al., 2009a](#)). An abattoir study found EGGD in 30% of feral horses ([Ward et al., 2015](#)) demonstrating that these do not only occur in domesticated equids.

Etiology/pathophysiology

Squamous ulceration is caused by exposure of the gastric mucosa to acid, mainly hydrochloric acid (HCl), and volatile fatty acids (VFA's), and in vitro studies have demonstrated the detrimental effects of low pH on the squamous mucosa, causing decreased tissue resistance and reduced barrier function ([Widenhouse et al., 2002](#); [Nadeau et al., 2003a, 2003b](#)). Some of these effects were ameliorated by the addition of calcium carbonate, which suggests that a diet with a high calcium content may be protective ([Andrews et al., 2006a](#)).

Researchers were able to induce squamous gastric ulcers with high-concentrate diets, probably because starch leads to increased production of VFA's that reduce mucosal integrity ([Vatistas et al., 1999](#); [Andrews et al., 2006a, 2008](#)), and high starch intake has been identified as risk factor for ESGD ([Galinelli et al., 2019](#); [Luthersson et al., 2009b](#)). The equine gastric microbiota contains a large number of lactate-producing bacteria and lactate concentrations can peak after a meal, contributing to acidity ([Julliand and Grimm, 2016](#)). Serum gastrin concentrations are also higher in horses on high-concentrate diets which further increases acid secretion ([Smyth et al., 1989](#)).

The importance of feeding was demonstrated by the finding that fasting horses had a gastric pH of 1.5, compared to 3.1 in horses that had free access to timothy hay ([Murray and Schusser, 1993](#)), while horses fed ad libitum hay had a lower gastric pH than horses fed hay and concentrates ([Damke et al., 2015](#)). Periods of forage deprivation > 6 h increase the risk of ESGD ([Luthersson et al., 2009b](#)). This is related in part to the amount of saliva produced, which is approximately twice as much when roughage is fed compared to concentrates ([Meyer et al.,](#)

[1985](#)), but may also depend on pellet size ([Bochnia et al., 2019](#)). Forage can also limit or prevent the splashing effect of acid onto the squamous mucosa ([Lorenzo-Figueras, Merritt, 2002](#)). Horses with roughage intake below the recommended minimum were at risk of developing EGUS ([Galinelli et al., 2019](#)).

Stress is often cited as a risk factor for gastric ulceration in horses ([Buchanan and Andrews, 2003](#); [Luthersson et al., 2009a](#)), but direct scientific evidence for its role in ESGD is scarce and its importance may differ for squamous and glandular lesions. Young horses that recently started crib-biting had more severe squamous gastric ulcer scores, and significantly lower fecal pH, than noncrib-biting horses ([Nicol et al., 2002](#)) and crib-biting decreased in all horses but tended to decrease more in those given an antacid diet. Cribbing and other stereotypies are associated with ESGD and considered to be coping mechanisms, suggesting a link with stress ([Sykes et al., 2019](#)). Indirect support for the role of stress in ESGD was provided by the finding that hair cortisol concentration was inversely related to the severity of ESGD ([Prinsloo et al., 2019](#)) and it was postulated that high plasma cortisol concentrations associated with stress caused lower hair cortisol through a negative feedback mechanism.

While ESGD is considered to result from increased acid exposure, EGGD is thought to be related to compromise of mucosal defence mechanisms ([Sykes et al., 2015a](#)) and may also be linked to inflammatory bowel disease (IBD), as is the case in humans with Crohn's disease ([Kelly and Hunter, 1995](#)), although there is no evidence to support this hypothesis in horses. Histological examination of glandular gastric lesions showed a lack of ulcerative pathology, but rather of inflammation ([Martineau et al., 2009](#)) and lesion appearance was a poor indicator of underlying severity ([Crompton et al., 2015](#)).

Non-steroidal anti-inflammatory drugs (NSAIDs) at inappropriate doses, especially non-selective cyclo-oxygenase inhibitors, such as phenylbutazone and flunixin meglumine, have been shown to be able to induce EGGD in horses ([MacAlliser and Sangiah, 1993](#); [Ricord et al., 2021](#); [Whitfield-Cargile et al., 2021](#)) and this is thought to be mediated mainly by effects on mucosal blood flow, caused by prostaglandin inhibition ([Wallace et al., 2000](#)), as adequate blood flow is required to remove hydrogen ions. However, the use of NSAIDs does not appear to be common in clinical cases of EGUS. For example, in a study by [Luthersson et al. \(2009a\)](#) only 2/201 horses had a history of NSAID use in the 2 months prior to gastroscopy and only one of these had very mild gastric lesions. Similarly, [Murray et al. \(1996\)](#) found no association between NSAID use and glandular gastric ulcer severity.

Normal use of NSAIDs does not appear to cause EGGD under field conditions and preventive use of omeprazole is not considered necessary ([Fennell and Franklin, 2009](#); [Sykes et al., 2015a, 2019](#)). Although administration of omeprazole ameliorated phenylbutazone-induced EGGD, it was also associated with an increase in intestinal complications and caution should be exercised when co-prescribing NSAIDs and omeprazole in horses ([Ricord et al., 2021](#)).

Salivary cortisol concentrations following ACTH administration were found to be higher in horses with moderate to severe EGGD than in horses with mild EGGD or ESGD, and stress may play a role in the development of EGGD ([Sauer et al., 2018](#); [Scheidegger et al., 2018](#); [Sykes et al., 2019](#)), with horses with severe glandular ulcers being more stress sensitive than controls ([Malmkvist et al., 2012](#)). Both trainer and the number of caretakers were shown to increase the prevalence of EGGD in riding horses and dealing with certain, or many different people may be stressful for some horses ([Mönki et al., 2016](#)). An association between stress and peptic ulcers has also been identified in rodents ([Selye, 1936](#)) and humans ([Levenstein, 2000](#); [Deding et al., 2016](#)) and stress may promote ulcer formation through increased acid load, effects of hypothalamic-pituitary-adrenal axis activation on healing, altered blood flow, or cytokine-mediated impairment of mucosal defences ([Peters and Richardson, 1983](#); [Takeuchi et al., 1986](#); [Kiecolt-Glaser et al., 1995](#); [Arakawa et al., 1998](#)).

Exercise

Vatistas et al. (1999) were able to induce and maintain squamous gastric ulcers for 6 weeks by subjecting horses to simulated race training, although only one of 30 horses demonstrated signs of abdominal discomfort. Serum cortisol concentrations were lower at the end of the trial, which could be seen as a reduced stress response, but could also be a result of over-training (Golland et al., 1999). During exercise intra-abdominal and intragastric pressure increased from walk to trot to gallop which reduces the intragastric lumen to almost zero at trot and gallop (Lorenzo-Figueras, Merritt, 2002), pushing the acidic gastric contents up against the squamous mucosa. The serum gastrin concentration was higher in exercising horses and this may stimulate HCl secretion and further increase the risk of ulcer development (Furr et al., 1994,1992). The importance of exercise is supported by fact that the prevalence of ESGD increases during the race season (Tamzali et al., 2011) and is very high in racing horses.

Exercising during 5 or more days per week also considerably increased the risk of horses developing EGGD (Pederson et al., 2018; Sykes et al., 2019) and may be related to altered gastric blood flow or (physiological) stress (Rendle et al., 2018). However, in a study of 201 horses not in race training, workload was not identified as a risk factor, demonstrating that exercise intensity is certainly not the only factor (Luthersson et al., 2009b).

In humans, *Helicobacter pylori* plays an important role in the development of gastric ulcers and *Helicobacter*-like DNA was detected in gastric antral tissue samples of horses, although microscopic examination failed to show spiral bacteria, typical of gastric *Helicobacter* species (Murray, 2003). In 2007, Moyaert et al. identified a novel bacterium species, named *Helicobacter equorum*, in fecal samples of two horses, although it has not been shown to play a role in intestinal disease (Moyaert et al., 2009,2007). *Helicobacter*-like DNA was found in gastric ulcers of two out of seven horses, but also in one horse with normal gastric mucosa (Contreras et al., 2007). The equine glandular mucosa harbours an abundant and diverse microbiota, that varies per individual and contains significantly more *Streptococcus* species in the glandular region of the stomach, but *Helicobacter* may not be an important inducer of EGGD (Husted et al., 2010; Perkins et al., 2012; Dong et al., 2016).

Clinical signs

Many horses with gastroscopic evidence of gastric ulceration have no obvious clinical signs, or signs are subtle and not recognized by owners, and are considered to be healthy, although prevalence and severity were higher in horses with mild compatible signs (Murray et al., 1989; Niedźwiedz et al., 2013). Signs most commonly associated with EGUS are poor appetite, weight loss, poor body condition, colic and discomfort when tightening the girth strap (Camacho-Luna et al., 2018). Early research on EGUS focused on racing Thoroughbreds and the signs these horses displayed. As other types of horses were studied additional signs that can result from gastric ulceration were observed. These include altered behaviour, such as nervousness, aggression, coat changes, teeth grinding and self-mutilation (McDonnell, 2008; Varley et al., 2019). Decreased performance may also be a result of both ESGD (Franklin et al., 2008) and EGGD (Sykes et al., 2019). Thoroughbreds in which squamous gastric ulcers were induced by a combination of feed withholding and treadmill exercise showed decreased performance, as evidenced by decreased VO_{2max} and VCO_{2max} (Nieto et al., 2009). However, determining the clinical relevance and which clinical signs are related to ESGD and which to EGGD is often difficult, as the location of ulcers is not always specified and because ESGD and EGGD occur concurrently.

Diagnosis

Gastroscopy remains the only way to confirm the presence of ulcers antemortem, using an endoscope at least 2.5–3 m long, to allow

visualization of both the squamous and glandular portion of the stomach (Andrews et al., 2002; Sykes et al., 2015a). Visualization also enables grading of EGUS, to allow comparisons between horses and within horses over time. In 1997, MacAllister et al. developed a scoring system, mainly used for research purposes, based on lesion number and severity and graded squamous and glandular ulcers separately. The other commonly used grading system was described by the Equine Gastric Ulcer Council (EGUC) in 1999 (Andrews et al., 1999a) and has proven particularly useful for the grading of ESGD.

If gastroscopy is going to be used to identify and grade gastric ulcers it is important to know how it compares to histology. When results of endoscopy, necropsy and histology were compared it became obvious that endoscopy may underestimate ulcer number and severity (Andrews et al., 2002). This was confirmed by the poor correlation between the number and severity of lesions and clinical signs, although horses with clinical signs had more and more severe squamous ulcers than those without (Murray et al., 1989). A positive response to therapy suggests that any ulcers present were clinically significant. When both ESGD and EGGD are present and one type of disease heals but the other does not, the significance of both becomes clearer.

When using any grading system, it is relevant to know how large the inter- and intra-observer variability is. When the original EGUS grading system was developed, there was significant variability between observers for the lesion number score in the squamous epithelium, but not in the other parameters (MacAllister et al., 1997). Using the EGUC system, inter- and intra-observer reliability were substantial for squamous mucosa (Wise et al., 2021). When a visual analogue scale (VAS) was used inter- and intra-observer reliability were moderate for squamous mucosa, although reliability improved with familiarity and observer experience (Wise et al., 2021). A limitation of the use of grading systems, with a limited number of categories, is that gastric ulcers of different total surface area, and thus presumably a different clinical significance, can be assigned the same grade and assessing improvement and/or healing over time may be more useful (Varley et al., 2019).

Inter- and intra-observer reliability were substantial for glandular mucosa using the EGUC scale (Wise et al., 2021) and when a visual analogue scale (VAS) was used both inter- and intra-observer reliability were moderate (Wise et al., 2021). These findings confirm that variability is large for grading of EGGD (Tallon and Hewetson, 2021) and emphasize the difficulties in reducing a biological continuum, in this case in severity, to a single grade. Current recommendations are to use descriptive terminology for EGGD (Sykes et al., 2015a), but further refinement, possibly through the use of verbal rating scales, seems desirable (Tallon and Hewetson, 2021) and a modified version of the EGUC system may be appropriate for EGGD (Wise et al., 2021).

It has been suggested that mucosal biopsies can aid a diagnosis of EGGD (Murray et al., 2004). Crumpton et al. (2015) showed that lesion appearance was not useful in predicting severity in EGGD. The fact that glandular lesions extend into the deeper layers of the mucosa in some cases (Murray et al., 2003) may explain why gastroscopic findings do not always correlate with severity of signs, as inflammation and/or healing in deeper tissues cannot be visualized by gastroscopy.

Because gastroscopy is invasive and requires fasting and fairly expensive equipment, other diagnostic methods have been investigated. Sucrose permeability testing, first reported around the turn of the century (O'Conner et al., 2002, 2004), is based on the fact that sucrose cannot cross the healthy gastrointestinal mucosa, but when the epithelium is injured, as in EGUS, it can, leading to increased blood sucrose concentrations following enteral administration (Meddings et al., 1993; O'Conner et al., 2004). This absorption of sucrose is possibly more pronounced in cases of ESGD (Hewetson et al., 2017). Blood sucrose testing had a high sensitivity for the detection of gastric ulcers in weanling foals but the specificity was low and it was found to be neither sensitive nor specific in adult horses with EGUS (Hewetson et al., 2017, 2018). Therefore, this technique is unlikely to replace gastroscopy, but

may be useful in selecting horses that would benefit from gastroscopy.

The fecal occult blood test also has a low sensitivity for detecting gastric ulcers (Pellegrini, 2005; Andrews et al., 2015) and an owner questionnaire was not helpful in predicting the presence of gastric ulcers, although some questions did correlate with an increased risk of EGUS (Busechian et al., 2021). Recently, a number of serum biomarkers were found to be increased in horses with EGUS and may prove useful as an initial screening tool (Shawaf et al., 2020).

Treatment

Very few squamous ulcers heal spontaneously, especially when horses remain in (race) training, and most require medical therapy (Murray et al., 1996; Andrews et al., 1999a). However, spontaneous healing can occur, as demonstrated by the fact that three of eight vehicle-treated control horses showed ulcer resolution in 14–25 days, although healing occurred more often and more rapidly in horses treated with omeprazole (Murray et al., 1997). Also, 55% of dietary induced squamous ulcers healed when horses were turned out to pasture (McGowan et al., 2011).

As exposure to acid is the most important etiological factor for ESGD, histamine antagonists have been used extensively in horses, as histamine stimulates acid secretion by the parietal cells (Kitchen et al., 1998). In horses, ranitidine was found to be approximately four times more potent than cimetidine, increasing gastric pH for 8 h (Sangiah et al., 1988), and effective in limiting ulcer development in a feed deprivation model (Murray and Eichorn, 1996), but owner compliance is a problem with the required dosing interval.

As there are other triggers for acid secretion, blocking the actual production of acid is more effective and the proton pump inhibitor (PPI) omeprazole has become the drug of choice for treating gastric ulcers in horses. Omeprazole works by blocking hydrogen-potassium-ATPase, the enzyme that catalyzes the final step of HCl production in parietal cells, but it is inactivated by stomach acid and needs to be protected to pass the stomach. This can be achieved by using either a buffered paste or an enteric coated formulation, with the bioavailability being higher for enteric coated omeprazole (Andrews et al., 1992; Jenkins et al., 1992; Birkmann et al., 2014). Not all compounded omeprazole products will be effective and efficacy may be dependent on vehicle pH, with vehicle pH > 8 associated with effectiveness (Merritt et al., 2003). Recently, a novel in feed omeprazole formulation was shown to be as effective as a commonly used enteric coated omeprazole product (Wise et al., 2021). As may be expected, omeprazole is more effective than cimetidine for the treatment and prevention of recurrence of gastric ulceration in racehorses maintained in active training (Nieto et al., 2001).

After 5 days the once daily administration of oral omeprazole increases gastric pH for 27 h (Andrews et al., 1992; Jenkins et al., 1992) which means it need only be given once a day, increasing owner compliance. However, it has been suggested that omeprazole should be administered 4–8 h before race training for optimal effect (Merritt et al., 2003). Bioavailability was higher in fasted horses (Daurio et al., 1999), whereas in another study bioavailability was higher in horses fed *ad libitum* hay compared to when they were fasted (Recknagel et al., 2020). Current recommendations for racehorses are to administer omeprazole early in the morning, before the first feed (Sykes et al., 2015a). The problem of omeprazole degradation in the stomach and differences in oral bioavailability can be circumvented by using intravenous omeprazole (Campbell-Thompson et al., 1988; Sangiah et al., 1989; Andrews et al., 2006b) or a long-acting intramuscular preparation (Sykes et al., 2017; Gough et al., 2020).

When used in horses with naturally occurring squamous ulcers enteric coated omeprazole healed all ulcers in 10–21 days (Murray et al., 1997). These horses were maintained in individual stalls and when omeprazole treatment was assessed in Thoroughbreds in race training healing was achieved in 57%, 67% and 77% after 2, 3 and 4 weeks of omeprazole treatment respectively (Andrews et al., 1999b) and clinical

signs often improve within 48 h of starting treatment (Murray, 1991). Once weekly injections of long-acting, intramuscular omeprazole were more effective at 4 weeks for ESGD than daily oral omeprazole, with healing rates of 97% and 67% respectively (Gough et al., 2020), although the study included only a small number of horses. A few injection site reactions were associated with the use of intramuscular omeprazole, but these were self-resolving (Gough et al., 2020).

In human medicine there are some concerns with the long-term use of PPI's and given that some horses are on these drugs for extended periods of time this may also be something to consider in this species, although no side effects were noted in horses treated with omeprazole for up to 90 days (Buchanan and Andrews, 2003). Recently however, oral omeprazole has been shown to induce hypergastrinemia in horses (Pagan et al., 2020) and severe ESGD can develop within several days of discontinuation of omeprazole (Sykes, 2021). Although omeprazole did not induce major changes in the composition of fecal or gastric glandular microbiota, certain microbial genera became more predominant in the gastric glandular mucosa after administration (Cerri et al., 2020).

Because of the cost of omeprazole, the desire to not treat horses medically if not necessary and restrictions regarding its use in some equestrian competitions, alternative treatments have been investigated. Aloe vera appeared have some positive effect on squamous gastric ulcers, but was not as effective as omeprazole paste (Bush et al., 2018). A prebiotic dietary supplement was non-inferior to omeprazole, but many horses were taken off omeprazole during the trial because of racing legislation and this likely reduced omeprazole efficacy (Kerbyson et al., 2016). Probiotics may provide some protection against ESGD and could be used as an adjunct to therapy to maintain gastrointestinal health (Camacho-Luna et al., 2018; Yuki et al., 2000). However, prebiotics, such as fructo-oligosaccharides, are degraded to short chain fatty acids, such as butyric acid, by microbes and may be harmful to both squamous and glandular mucosa (Cehak et al., 2019).

Neither dietary oils, nor a pectin-lecithin complex feed supplement, which increases gastric juice mucus concentration (Köller et al., 2010), prevented squamous gastric ulceration in a feed-deprivation model (Murray and Grady, 2002; Frank et al., 2005; Sanz et al., 2014). Conner et al. (2018) reported that a proprietary blend of buffering agents decreased squamous ulcer severity in university riding horses, although they did not include a control group and the gastric lesion score after treatment in one group was still greater than two, and thus potentially clinically relevant.

Finally, because of high recurrence rates treatment should be accompanied by management changes, to try to avoid those factors that are known to increase the incidence of EGUS, and long-term medical therapy is often necessary (Buchanan and Andrews, 2003). The importance of management factors is illustrated by the fact that it was possible to reduce the recurrence of ESGD following omeprazole therapy, by reducing the starch intake of affected horses (Luthersson et al., 2019). The prophylactic use of omeprazole reduces the risk of horses developing ulcers when in active race training, but there is no consensus on the required dose; 1 mg/kg of the buffered paste seemed as effective as 2 mg/kg (Mason et al., 2019). Horses prone to ulcers may be given omeprazole for several days around transportation and show competition (Buchanan and Andrews, 2003).

Omeprazole is less effective in the treatment of EGGD than ESGD and treatment duration is longer, with a minimum of 8 weeks being recommended before adjunctive therapies are considered (Sykes et al., 2015a). In cases of EGGD it is often recommended to combine omeprazole with sucralfate, a hydroxyl aluminium salt of sucrose octasulfate that binds to the negatively charged ulcer bed, forming a proteinaceous protective barrier. It increases bicarbonate and mucus secretion, stimulates prostaglandin production and inactivates pepsin and bile salts (Borne and MacAllister, 1993). Although it may not promote ulcer healing on its own, the combination of omeprazole and sucralfate led to better healing of EGGD than omeprazole alone (Kranenburg et al., 2020). This likely reflects the different pathogenesis of EGGD, which is

less dependent on exposure to gastric acid than ESGD. Misoprostol, a prostaglandin analogue, that stimulates mucus and bicarbonate production, was shown to be superior to omeprazole and sucralfate for both healing and improvement of glandular lesions in horses, although it also inhibits acid secretion (Sangiah et al., 1989; Varley et al., 2019), but should not be used in pregnant or nursing mares because of its effect of increasing uterine contractions (Buchanan and Andrews, 2003).

The addition of trimethoprim sulfonamide to omeprazole was not shown to be superior in the treatment of EGGD and cannot be recommended given the lack of conclusive evidence for the role of bacteria in the pathogenesis of EGUS, or from an antimicrobial stewardship point of view (Sykes et al., 2014). Also, antimicrobials may influence the gastric microbiome, which has been shown to differ between horses with and without EGGD, but a potential cause or effect relationship has not been demonstrated (Paul et al., 2021). Whether horses should have rest days or complete rest from training during treatment of EGGD warrants further study (Sykes et al., 2019).

Conclusions

Equine gastric ulcers are common, probably as a result of common management and use of horses. They can be diagnosed by gastroscopy and the presence of ESGD and/or EGGD should be specified, but determining their clinical significance remains difficult. Although treatment with omeprazole is effective in many cases, we should not rely solely on medical therapy to manage gastric ulcers, but must continue to investigate potential etiological factors and address husbandry practices and other known risk factors.

Conflict of interest statement

The author of this paper has no financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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