

HEALTH ZONE

Numbers Game

Gastric Ulcers

BY AMANDA DUCKWORTH



ANNE M. EBERHARDT

Gastric ulcers are a man-made problem

GASTRIC ULCERS AND HIGH-PERFORMANCE HORSES, unfortunately, seem to go hand-in-hand. While gastric ulcers can occur at any age and can happen with any breed, studies have shown that equine gastric ulcer syndrome (EGUS) affects up to 90% of racehorses and 60% of show horses.

Adding to the frustration is that most of the time, it is a man-made problem. Because it is not typically a naturally occurring issue in horses, simple changes to routine care can reduce the odds of a horse developing gastric ulcers. Furthermore, for cases requiring medical attention, there is also a Food and Drug Administration-approved medication, which the American Association of Equine Practitioners encourages owners to use instead of less reliable compounded medicines.

TACKLING ULCERS

EGUS is the result of an imbalance between mucosal aggressive factors—such as hydrochloric acid, pepsin, bile acids, and organic acids—and mucosal protective factors such as mucus and bicarbonate. This leads to the lining of the stomach eroding due to prolonged exposure to normal acids found in the stomach.

“Dietary practices are probably the main culprit,” said Dr. Scott Hay, the vice

president of the AAEP and president of the Fort Lauderdale, Fla.-based race-track practice of Teigland, Franklin, and Brokken.

“There are a lot of different reasons horses get the ulcers, but probably the primary reason is the way we feed Thoroughbred racehorses and high-performing horses. It’s a high-grain diet, but horses are made to be long-term foragers.

“They are supposed to be constantly

Equine gastric ulcer syndrome affects up to 90% of racehorses

eating and having food in their stomachs to deal with the caustic hydrochloric acid secretion in their stomach. We feed them meals, but they still have hydrochloric acid constantly being secreted.”

While the way horses are fed is likely the main reason for gastric ulcers, there are other causes as well, including stall confinement, medication, and stress, which is the reason racehorses are so prone to developing gastric ulcers.

“Horses maintained without direct contact to other horses and horses kept and trained in urban areas are more likely to develop squamous gastric ulcers,” explained Dr. Scott McClure for the AAEP’s Equine Gastric Ulcers: Special Care and Nutrition website section. “Chronic administration of any non-steroidal anti-inflammatory drugs such as phenylbutazone, flunixin meglumine, or ketoprofen, can decrease the production of the stomach’s protective mucous layer, making it more susceptible to the formation of ulcers in the glandular portion of the stomach.”

Because ulcers have become an expected part of racehorse care, sometimes a horse’s connections choose to go straight to medication options, but Hay cautions that they are skipping an important step.

Before choosing a course of treatment, it is key to have an actual diagnosis.

“The gold standard for diagnosing gastric ulcers is a gastroscopy, which is a direct visualization through an endo-

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MESSAGE FROM THE GRAYSON-JOCKEY CLUB RESEARCH FOUNDATION

EQUINE GASTRIC ULCER SYNDROME

Feeding matters (but not in the way
that we previously thought)

DR. BEN SYKES



Grayson-Jockey Club
Research Foundation

It has long been recognized that diet is an important risk factor for equine gastric ulcer syndrome (EGUS). This is particularly true for lesions involving the squamous mucosa in the upper half of the stomach while recent work suggests diet plays little, if any, role in the development of disease in the glandular mucosa of the lower half of the stomach.

Instead it appears lesions in the bottom half of the stomach are affected by other risk factors such as breed, environmental stressors, and the number of days exercising per week.

Regardless, the importance of diet in squamous disease and the importance of roughage in hindgut health have led to the widespread recommendation for the provision of unlimited pasture or hay as a means of reducing the risk and severity of EGUS.

This recommendation is a cornerstone of disease prevention for both the squamous mucosa in the stomach, and the hindgut. However, recent studies funded by the Grayson-Jockey Club Research Foundation have highlighted that feeding, or more specifically overnight fasting, might impact treatment outcome when treating with omeprazole due to impairment of drug absorption.

These findings suggest the feeding management of horses during the therapeutic phase, and when omeprazole is used as a preventative, should differ from that when non-pharmacological strategies are being employed for disease management.

The poor healing response of glandular lesions and sub-maximal healing rates of squamous lesions with oral omeprazole have been known for some time. This has led to questions whether acid suppression is the most appropriate treatment of both forms of disease, espe-

cially glandular disease. However, recent studies with new generation, more potent acid suppressors have shown that very good rates of healing are observed for both the squamous and glandular mucosa when appropriate magnitude and durations of acid suppression are achieved. This has reinforced the need to maximize acid suppression when treating with oral medications such as omeprazole.

THE IMPACT OF DIET ON DRUG ABSORPTION

Until recently the role of diet on the efficacy of oral omeprazole has been understated and the potential for feeding recommendations to interact with drug efficacy largely ignored.

However, it has been shown that, when compared with the fasted state, feeding reduces the absorption of buffered omeprazole formulations by approximately 50-66%, meaning that two to three times as much drug would be required to produce a similar effect when the horse is eating unlimited roughage vs. being administered the drug after an overnight (10 hour) fast.

Consistent with this finding, it has been shown, in a study funded by the Grayson-Jockey Club Research Foundation and using indwelling pH probes in horses' stomachs, that the magnitude and duration of acid suppression achieved in animals receiving an unlimited hay diet is less than horses receiving a high-grain/

low-fiber diet used as a proxy for a race-horse/performance horse diet. The magnitude of this effect was pronounced in some animals with minimal, if any, acid suppression demonstrable in horses consuming unlimited hay even at the "full" omeprazole dose of four mg/kg once a day.

Considering this, the author believes current recommendations that do not distinguish between feeding management during pharmacological treatment and dietary prevention are inappropriate. Instead recommendations should be updated to include that, where possible, omeprazole be administered after an overnight (8-10 hour) fast and approximately 60 minutes prior to the morning feed. This small management change has significant potential to increase the efficacy of oral omeprazole in many patients. Once omeprazole treatment is completed the current recommendation for unlimited roughage as part of prevention management is appropriate, as long as ongoing oral omeprazole therapy is not required for prevention.

The idea of "starving" horses overnight is somewhat counterintuitive and flies in the face of previous recommendations for EGUS prevention.

However, several important factors in the recommendation should be recognized; firstly, horses naturally consume 70-80% of their roughage during the day with the remaining 20-30% consumed overnight. Studies have shown that horses stabled and fed hay from a single hay net typically cease eating around 10 p.m. (although some animals clearly don't subscribe to this rule!) and then spend the remainder of the evening/night resting. As

such, the proposed enforced fast does not dramatically alter the eating behavior of most horses beyond preventing them from accessing their breakfast the following morning until there is a chance to administer the medication. Secondly, a horse consuming unrestricted roughage takes eight to 10 hours to empty its stomach of roughage so it is only a narrow window that the stomach is empty, not the full eight-to-10-hour fasting window.

THE IMPACT OF TIMING OF FEEDING

Like the impact of feeding as a whole, to date little attention has been paid to the timing of feeding in regard to omeprazole administration. Although horses are constant acid secretors, there is also a significant effect of meal

feeding on acid secretion.

Proton pump inhibitors (PPIs), such as omeprazole, are prodrugs, meaning that they are absorbed in an inactive form that requires conversion to an active form following absorption.

For PPIs it is gastric acid secretion that is the stimulus for the drugs to be converted to their active form (in effect, and somewhat ironically, the acid producing proton pumps need to be turned on and producing acid to be inactivated and stop producing acid), and it is important the stimulation of pumps occur while drug concentrations are present.

Following administration of oral omeprazole maximal serum concentration occurs at around 45-90 minutes and it is important that maximal stimula-

tion of the proton pumps occur within this period. Further, the type of meal might be important as gastric distention appears to play a role in gastrin release, and subsequent acid production, in the horse. Larger amounts of gastrin, which stimulates acid production, are released more rapidly in response to voluminous, roughage-based meals when compared with smaller grain meals.

Considering this, the author recommends feeding a large, highly palatable, roughage-based meal (i.e. alfalfa hay) 60 minutes after administration of oral omeprazole followed by any required grain/supplement feeding. ^{BH}

Dr. Ben Sykes is an adjunct associate professor at the University of Queensland.

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scope,” he said. “It becomes a little bit of a struggle for a veterinarian to get owners and trainers to do serial gastroscopy on horses to get a diagnosis and then a follow up when they are pretty sure they already have ulcers because they are race-horses. We have a lot of people we work for who try to save money by not having the endoscopy done. The downside of that is you don’t get a baseline diagnosis.”

The problem with not having a baseline diagnosis, according to Hay, is that in some cases the horses do not have gastric ulcers to begin with so treating them for the condition is a waste of money, and for those that do have ulcers, it is impossible to know how well treatment is working without a baseline.

“There are certainly some subjective signs you can put your finger on that would say your horse might be suffering from gastric ulcers,” said Hay. “You can get a pretty good idea that they might be dealing with some ulcers due to other factors like poor appetite, colic, poor hair coat, and generally poor demeanor. Still, if you really want to get down to the bottom of it and be more efficient in how you spend your money and how you treat your horse, you would be doing a lot more gastroscopy.

“In my mind, you have three times you want to scope them: before you start treatment, after you have been through the initial phases of treatment, and then about 90 days down the road to see if your maintenance therapy is holding.”

PREVENTION AND CURE

Although prevention might not be possible in all cases, the AAEP recommends several steps to lessen the chance of gastric ulcers.

“I am not sure it is totally avoidable in high-performing horses, but there are ways that people could feed their horses better to have a better, more natural gastric ulcers-fighting effect,” said Hay. “Certainly, having hay in front of them all of the time is a big deal. That seems intuitive, but not all people do that. If they can have something in their stomach fairly



ANNE M. EBERHARDT

Horses trained in urban areas are more susceptible to gastric ulcers

constantly, it battles the effects of those gastric acid secretions.”

In addition to free-choice access to grass or hay, the AAEP recommends that if a horse must be stalled, arrange for the horse to see other horses and consider offering a ball or some other object that the horse can enjoy in his stall; feed the horse more frequently to help buffer the acid in the stomach; and decrease grains that form volatile fatty acids.

“Medication to decrease acid production is only necessary in horses showing clinical disease or when the predisposing factors cannot be removed, such as with some horses in race training or aggressive show campaigning,” said McClure. “There are many supplements on the market that claim to prevent squamous gastric ulcers. Many are ineffective and lack validation. Horse owners should utilize products for prevention of squamous gastric ulcers that have been validated in competent scientific studies.”

Because gastric ulcers remain an issue in horses, research is routinely being done to see how best to approach the problem. For example, in 2017, Hagyard Equine Medical Institute submitted a study that was published in the *Journal of Equine Veterinary Science* that showed treatment with a polysaccharide blend reduced gastric ulceration in active horses.

For the study, gastroscopy was used on

10 horses for diagnosis and scoring of existing ulcers. They were given 1-2 ounces of a polysaccharide blend, and the study showed that a polysaccharide blend of high-molecular-weight hyaluronan and schizophyllan, a beta-glucan, administered daily for 30 days demonstrated ulcerative healing.

“Ulcers can be found in as many as 80-100% of horses,” said Dr. Nathan Slovis, the director of the McGee Medical Center at Hagyard. “Our objective in this research was to determine whether a natural treatment would help in the healing process. From the data gathered, we were able to determine that horses can be successfully treated with a naturally safe and effective polysaccharide blend of hyaluronan and schizophyllan.”

In all, 90% of the horses treated with the blended therapy showed complete resolution or improvement in ulcerative areas, increased appetite, weight gain, and positive behavioral changes.

THE GO-TO

Historically the most effective way of medically treating gastric ulcers in horses has been by inhibiting gastric acid secretion. There are a number of treatment options, but GastroGard, which was given FDA approval in 1999, remains the only federally approved omeprazole treatment for horses.

“There are certainly things like fa-



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motidine and ranitidine, and those are drugs that have been used over the years to treat gastric ulcers,” said Hay. “But as far as the one that actually does the best job, there is only one omeprazole out there that is FDA-approved, and there has never been a generic produced.”

GastroGard consists of omeprazole, which is an acid pump inhibitor that hinders gastric acid secretion regardless of the stimulus. It is one of the most studied medications in horses. Omeprazole is also familiar to many people, as it is the same medication found in Prilosec, which is a popular treatment for human ulcers.

Together, GastroGard, which treats ulcers, and its medication-cousin UlcerGard, which prevents ulcers, are the only FDA-approved animal drugs for the treatment or prevention of equine gastric ulcers. One of the reasons people tend to skip gastroscopy is to save money because treating gastric ulcers with GastroGard is not a cheap endeavor.

“It is expensive to treat them,” said Hay. “You are going to be spending \$1,000 to treat a horse with GastroGard over a month’s time. If you are looking to save a couple of hundred dollars by not doing the gastroscope because you have a pretty good idea the horse has gastric ulcers, I understand that men-

tality, but the problem is you are treating them blindly. You don’t know if you are curing them, and you don’t know if they are staying cured.”

Although GastroGard is the only FDA-approved omeprazole on the market, it does not mean it is the only one available. However, the AAEP cautions against using off-label medication. When it comes to using compound medications, multiple studies have shown a lack of active ingredient and/or lack of effectiveness.

“Certain compounding pharmacies will produce omeprazole in all kinds of different combinations, but none of them are approved,” said Hay. “The risk of going with compounded medications is they undergo a much less stringent level of scrutiny.

“There have been a lot of studies looking at how stable these drugs are over time, and the FDA-approved product has performed admirably while the compounds have not in most cases. Even something as simple as if there is medication actually filling the tube has been looked at.”

One example of this was a poster presented by Dr. Mark Wallace of Carolina Equine Hospital in Browns Summit, N.C., during the 2017 American College of Veterinary Internal Medicine Forum. For his study, “Radiographic evaluation of compounded and illegal over-the-counter omeprazole products,” Wallace took radiographs of compounded and non-FDA-approved omeprazole products and compared them to GastroGard.

While GastroGard syringes were completely full with no air pockets, the over-the-counter products were not completely filled and had air pockets.

“The use of compounded omeprazole and illegally produced over-the-counter omeprazole products in the equine industry is widespread. Compounded and illegal omeprazole paste products often have production quality-control problems as documented by incomplete filling of syringes, air pockets, and variations in homogeneity,” Wallace concluded.

Through the years the FDA has sent out warnings to companies marketing unapproved equine gastric ulcer products, but they can still be found fairly regularly.

“We are always pretty skeptical about if some of these compounders have actually treated a horse,” said Hay. “Some compounders probably have gotten close enough in some cases to be close to the real thing, but that doesn’t make it legal. It’s an interesting phenomenon, and I am surprised it has gone on as long as it has.

“Believe me, I am not trying to make money on GastroGard, and over the years you invest a lot more in GastroGard than you really want to if you are prescribing to clients, but at the end of the day, it is frustrating to me to see horsemen spending so much money on alternate medications that may or may not be effective. Depending on what lawyer you talk to, it is arguable whether they are even legal, and I would say most are not.” **BH**

Amanda Duckworth is a freelance writer based in Lexington.

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