Clinical Commentary

Gastric juice pH measurement in horses: Three-quarters of a century of history!

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Summary
Inhibition of gastric acid and increased stomach pH>4.0 is currently accepted as the mainstay of treatment for gastric ulcers in horses. Measurement of gastric pH is complicated and requires placement of a cannula and collection of gastric juice or placement of pH electrodes in the stomach. Since the distance from the nares to the stomach is approximately 200 cm, finding a system with a pH electrode with this length is difficult, not to mention difficult to maintain. There has been a fascination with the measurement of gastric juice pH in horses that has covered three-quarters of a century starting with a fistula model in 1933 and culminating in a recent technique described in this issue. Placement of gastric cannulas and various pH electrodes have been used to measure gastric juice pH in horses in the past and present, but the future may require more sophisticated methods as we look at the efficacy of different formulations of acid suppressive drugs for treatment of equine gastric ulcer syndrome.

Introduction
Inhibition of gastric acid secretion and the maintenance of a pH of >4.0 is the mainstay of antiulcer treatment in horses. The reason for this is that nonglandular gastric mucosa exposed to pH<4.0, induced functional damage in the tissues manifested by decreased sodium transport and histological evidence of cellular swelling in Ussing chamber experiments (Widenhouse et al. 2002; Nadeau et al. 2003a, b; Andrews et al. 2006a). Damage was most evident in the nonglandular stratum transitionale and stratum spinosum, deep to the superficial cornified layer where there is an abundance of sodium-potassium ATPase pumps. These in vitro studies confirmed the earlier assumptions that pH in the stomach was a significant risk factor for nonglandular gastric ulcers. In previous studies using a feed-deprivation model, ranitidine treatment (6.6 mg/kg bwt, per os, q. 8 h) resulted in a stomach pH of >4.0, which decreased nonglandular ulcer surface area when compared with untreated controls (Murray and Schusser 1993; Murray and Eichorn 1996). Later studies showed that administration of omeprazole increased gastric juice pH, which resulted in improvement in gastric ulcer scores and ulcer healing (Andrews et al. 1999a,b; Dauroi et al. 1999; MacAllister et al. 1999). These experiments clearly showed that stomach pH (>4.0) was a risk factor for nonglandular gastric ulcers; however, the role of pH in glandular ulcer disease is not known, but maintaining pH >4.0 in the stomach is still an acceptable goal.

In the past, several methods have been used to measure stomach pH in horses. As early as 1933, a gastric fistula was made in a 13-year-old mare and data reported described the horse as a continuous acid secretor and found that the horse secreted 10–30 L of acidic fluid per day (Egorov and Chehredciov 1933). In 1974, pH electrodes inserted through incisions made in the cranial and caudal halves of the stomach of horses at necropsy showed a similar mean pH (pH ~4.5–6.0) when fed a control diet (hay-grain ration containing 12% crude protein); whereas mean pH was lower (pH ~2.0–4.0) in the digesta of horses fed a pelleted high cellulose diet (a pelleted, high-cellulose, low-protein diet containing 3% urea) (Argenzio et al. 1974). This study illustrated that pH electrode position in the digesta yielded a pH, but might not represent gastric or mucosal pH in other regions of the stomach. The pH found in this study suggested that hay had a buffering effect on gastric acids compared to a high carbohydrate diet. This was one of the first studies to report differences in pH values in horses fed pelleted high carbohydrate diet vs. a hay diet.

Thirteen years later, Campbell-Thompson and Merritt (1987) fitted horses with gastric cannulas and the subsequent experiments formed the basis of our modern understanding of gastric secretion in horses (Merritt 2003). Stomach cannulas allowed continuous collection of gastric juice and measurements of pH, acidity, total acid output (TAO), electrolytes and prostaglandins under basal and stimulated conditions (Campbell-Thompson and Merritt 1990; Merritt et al. 1996; Kitchen et al. 1998; Sandin et al. 2000; Cargile et al. 2004). Initial studies, using the cannula model, showed that ranitidine (5 mg/kg bwt, i.v.) inhibited gastric acid secretion and confirmed that endogenous histamine was involved in the stimulation of gastric acid secretion in horses. However, in these early experiments, hourly TAO in gastric fluid was significantly decreased without an increase in gastric juice pH (Campbell-Thompson and Merritt 1987). This showed that TAO measurement was more sensitive than pH in determining effects of acid suppressive drugs, as pH is expressed as a log scale. The cannula model expanded our understanding of gastric secretion in horses under basal and pentagastrin and histamine stimulation and was later used to improve our understanding of equine gastric ulcer syndrome (EGUS).

In the 1990s, the cannula model was the ‘model of choice’ for investigation of omeprazole as a treatment for EGUS. Preclinical trials performed in horses fitted with gastric cannulas showed that omeprazole was a potent inhibitor of gastric acid secretion in horses with a long duration of effect (Andrews et al. 1992; Jenkins et al. 1992, 1997; Dauroi et al. 1999).
In this issue of EVE, a new technique for implantation of indwelling pH electrodes is described by Sykes et al. (2015). According to the authors, the described technique is similar to the abomasal toggle technique described in cattle (Grymer and Sterner 1982) and was easy to perform without special surgery skills. The procedure was modified from a percutaneous endoscopic gastrostomy tube placement technique recently reported in horses (Toth et al. 2014). The procedure was performed in two standing horses under sedation and required a 3 m endoscope, an ultrasound unit and a commercially available 20 French percutaneous endoscopic gastrostomy (PEG) tube. A video link describing the technique was included with the article as supplementary information. Once placed, 2 pH electrodes were placed through the PEG tube so that they were approximately 5 cm apart in the ventral fundus. The positioning was confirmed by endoscopic examination in the fasted state. The procedure was well tolerated by both horses, although a few minor complications were observed as noted in the article. Typical plots of pH over time for high grain/low forage or hay diet were reported. Predictable pH spikes were reported in the high grain/low forage-fed horses after the morning and late afternoon feedings, whereas pH in the hay-fed group was low throughout the measurement period with less variation observed.

I applaud the authors for developing this method for measuring continuous gastric pH in fed horses and this technique might provide a useful model for investigating the efficacy of acid suppressing drugs during the fed and fasting state. The placement of the pH electrodes was confirmed in the fasting state and not in the fed state, so shifting and displacement could occur with feeding, which could result in aberrant pH readings, although the electrodes were anchored. In addition, unlike the cannula-model, TAO cannot be measured and significant changes in TAO might occur with acid suppressive drugs without appreciable changes in pH, although pH is noted as a risk factor for EGUS, not TAO.

Sykes et al. (2015) recorded pH from the ventral fundus of the stomach and the data collected show a typical pH profile seen in horses fed a hay diet (Merritt 2003). Gastric fill in horses fed forage is described as a matt or ball of feed in the stomach at the level just above the oesophageal opening. The matt has coarser contents layered at the top of the stomach and finer particulate components filtered to the bottom toward the ventral fundus. The upper, coarser matt, being the furthest from the acid secreting region of the stomach, is more accessible to swallowed saliva and has a higher pH than the liquid contents at the bottom (Merritt 2003). As long as a forage diet is eaten, this stomach pH gradient is maintained and there is less acid exposed to the margo plicatus and proximal nonglandular stomach. However, when a high grain, low roughage diet is fed, there is disruption of the stomach pH gradient, which increases pH content fluidity and mixing of gastric contents. This mixing and fluidity exposes acids from the lower portion of the stomach to the margo plicatus and nonglandular mucosa. In addition, volatile fatty acids are higher in the high grain diets and can act synergistically with stomach acid to affect nonglandular cellular metabolism. Disruption of the pH gradient and ulceration has been described in pigs fed finely ground high concentrate diets (Argenzio 1999), although studies have shown that the equine nonglandular mucosa is...
more resistant to VFA affects that pigs (Nadeau et al. 2003a, b; Andrews et al. 2006a,b).

The described technique of pH electrode placement in this issue of EVE might prove to be an excellent research tool to evaluate the effects of acid suppressive agents on gastric acid secretion in the fed state. However, the technique will probably not be used to assess horses presented to the equine hospital with EGUS. Therefore, more clinically relevant techniques should be developed in the future to assess gastric pH in the clinical patient.

A method for evaluating gastric juice pH in horses with EGUS presented to the equine hospital is accomplished by aspirating gastric juice during endoscopic examination. Several recent studies showed that aspiration of gastric juice and subsequent measurement of pH is valid in evaluating the effect of omeprazole (4 mg/kg bwt, per os, q. 24 h, 14 days) on acid suppression. In these studies, gastric juice was aspirated through the endoscope biopsy channel just prior to insufflation. In these studies gastric juice pH was significantly higher (pH >4.0) 17–19 h after the 14th daily dose of omeprazole (Andrews et al. 2006b, 2015; Videla et al. 2011; Huff et al. 2012; Loftin et al. 2012; Woodward et al. 2014). The collection of gastric juice during the gastroscopic examination is relatively simple, but daily fluctuations in pH, pH profile or pH status in the fed state cannot be evaluated.

In the future, other techniques for measuring stomach pH will be developed for use in horses. Recently, a wireless capsule system (SmartPill pHp)3 was used to measure gastric juice pH, temperature and pressure in a horse and ponies (Elliott et al. 2008; Stokes et al. 2012). This system is currently Food and Drug Administration-approved to measure gastric emptying and intestinal transit time in man. Unfortunately, the commercially available wireless receiver was modified for the horse studies to allow collection of adequate wireless data to determine pH profile. The lack of adequate transmission from the capsule was probably due to extensive gut fill in the GI tract and body wall thickness. Until better systems for measuring gastric pH are developed in the future, we are thankful to the authors for the development of the PEG tube method reported in this issue of EVE.

Author’s declaration of interests

No conflicts of interest have been declared.

Manufacturers’ addresses

1Merial Ltd, Duluth, Georgia, USA.
2MILA International, Erlanger, Kentucky, USA.
3SmartPill Corporation, Buffalo, New York, USA.

References


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from:


