

Effect of omeprazole paste on intragastric pH in clinically normal neonatal foals

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Objective—To evaluate the efficacy of omeprazole paste, a commonly used antiulcer drug, on intragastric pH in clinically normal neonatal foals.

Animals—6 clinically normal foals between 5 and 14 days of age.

Procedure—Intragastric pH was recorded in each foal by use of a disposable antimony pH electrode with internal reference. Values for intragastric pH were recorded every 4 seconds by use of an ambulatory pH monitor. There were two 24-hour recordings of intragastric pH for each foal, with 24 hours between recordings. Foals were not administered any drugs during the first recording. Foals were administered omeprazole paste (4 mg/kg, PO) 1 hour after the start of the second recording. Mean pH was calculated for each hour of each 24-hour recording session. Hourly mean values were compared between the first and second 24-hour recordings.

Results—Complete data were obtained from 4 of 6 foals during the first 24-hour recording and 6 of 6 foals during the second 24-hour recording. Foals had significantly higher mean hourly intragastric pH for hours 2 to 22 following omeprazole administration, compared with corresponding hourly pH values in foals during the first recording.

Conclusion and Clinical Relevance—Omeprazole paste can effectively increase intragastric pH in clinically normal neonatal foals within 2 hours after oral administration of the first dose and can be administered to neonatal foals at the rate of 4 mg/kg, PO, every 24 hours. (*Am J Vet Res* 2004;65:1039–1041).

Gastric ulcer syndrome in horses encompasses an array of conditions and affects foals and adult horses. Ulcers in the squamous and glandular portions of the gastric mucosa have been reported in foals of all ages, including neonatal foals.¹⁻³ Ranitidine, a histamine 2 receptor antagonist, can effectively increase intragastric pH in clinically normal equine neonates for up to 8 hours after oral administration (6.6 mg/kg) or 4 hours after IV administration (2 mg/kg).⁴ However, the same dosage of ranitidine administered IV to critically ill foals did not consistently result in a similar effect.⁵

Omeprazole is the only product approved by the FDA for the treatment of gastric ulcers in horses. It has a greater degree and duration of suppression of gastric acid and better clinical evidence of efficacy for healing of lesions, compared with results for histamine 2 receptor antagonists.⁶⁻¹¹ Omeprazole is recommended at a dosage of 4 mg/kg, PO, every 24 hours for the treatment of horses and foals 4 weeks of age and older that have gastric ulcers.¹² Omeprazole has been used in clinically affected neonatal foals; however, its pharmacodynamic effects in this group of horses have not been documented.^{13,14} Therefore, the specific objective of the study reported here was to evaluate the effect of omeprazole paste on intragastric pH in clinically normal neonatal foals.

Materials and Methods

Animals—Six clinically normal neonatal Quarter Horse foals (3 males and 3 females) were used in the study. Foals ranged from 5 to 11 days of age and weighed between 51.8 and 83.6 kg at the onset of the study. Selection criteria included normal parturition, normal results for a physical examination, adequate passive transfer of immunoglobulins as indicated by an IgG concentration \geq 800 mg/dL for a whole-blood test,⁴ and typical appearance of healthy gastric mucosa as determined by use of gastroscopy.

Foals and their mares were kept in pastures before the onset of the study. During each 24-hour recording session, each foal and its mare were housed in a box stall (3.67 \times 7.34 m) and observed frequently. Between the two 24-hour recording sessions, foals and mares were again allowed to commingle with other foals and mares in pastures. Specific variables monitored included attitude, appetite, size of each mare's udder, rectal temperature, and frequency and character of urination and defecation. All procedures were approved by the University of Florida Institutional Animal Care and Use Committee.

Study design—Intragastric pH was measured continuously during two 24-hour periods. For each foal, the first 24-hour recording session served as a control period; hence, no drugs were administered. Foals were allowed to rest for 24 hours, then there was a second 24-hour recording session. We did not believe it was necessary to have a prolonged washout period on the basis that there was no effect of age or prior recordings in another study⁴ conducted with similar instruments and procedures. During the second session, foals were administered omeprazole paste^b (4 mg/kg, PO) 1 hour after recording commenced. Omeprazole was administered to each foal by adjusting the dosing dial of the administration syringe to approximate as closely as possible the amount for that foal; we believed this would simulate administration in on-farm conditions.

Preparation for recordings—Intragastric pH was recorded by use of a disposable antimony pH electrode with internal reference.^c Electrodes were positioned by use of endoscopic guidance. Briefly, a 2.5-m videoendoscope was inserted nasogastrically to enable investigators to evaluate the gastric

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mucosa. Once the gastric mucosa was visually inspected and declared normal, the electrode and its attached lead wire were passed through the biopsy channel of the endoscope until the electrode tip was seen emerging from the tip of the endoscope. The endoscope was then advanced until the electrode tip was well below the fluid line of the gastric contents. A specially marked guide wire was advanced through the biopsy channel during concurrent withdrawal of the endoscope; the guide wire pushed the electrode out of the biopsy channel, leaving the electrode in position within the stomach of the foal. After the endoscope was fully removed, the electrode was connected to an ambulatory pH recording device.^{4c} When an appropriate pH (pH, < 4.0 [with fluctuation]) was obtained, the electrode was sutured to the nose of the foal by use of a Chinese finger-snare pattern. The electrode was also secured to the nose and neck of the foal by use of adhesive tape. The recording device was attached to the back of each foal by use of a harness. This arrangement allowed each foal to move freely around the stall and suckle the mare.

Intragastric pH was recorded every 4 seconds by the recording device. A new electrode was used for each recording session, and each electrode was calibrated by use of buffer solutions (pH, 1 and 7, respectively) before insertion.

Data analysis—At the conclusion of each recording session, data were downloaded to a personal computer via specialized software.^{4g} Mean pH was calculated for each hour of each recording session. Hourly mean values were compared between control and omeprazole sessions by use of a Mann Whitney *U* test.^h Significance was set at $P < 0.05$.

Results

Gastric squamous and glandular mucosa of all foals were considered normal at the start of each recording session. We did not detect adverse effects of the monitoring procedure or omeprazole administration in any of the foals.

Complete data were obtained for 4 of 6 foals for the baseline (ie, first) 24-hour recording; the indwelling electrode became disconnected in 1 foal at 4 hours and in another foal at 7 hours after the onset of recording. Complete data were obtained for 6 of 6 foals for the second 24-hour recording. Thus, group sizes were uneven for hours 5 to 24 of the study.

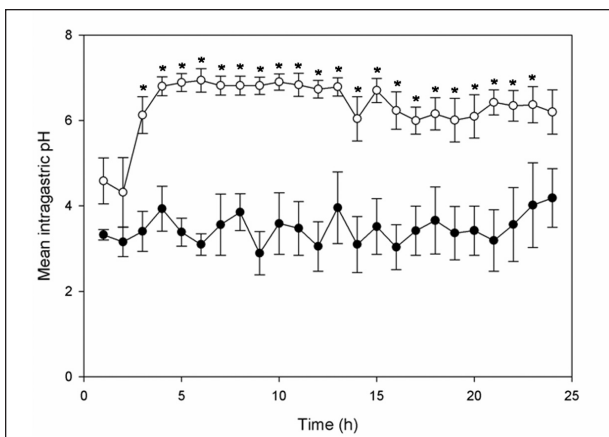


Figure 1—Mean \pm SEM hourly intragastric pH for 6 foals during a baseline 24-hour recording (ie, foals were not administered any drugs; black circles) and a second 24-hour recording when foals were administered omeprazole (4 mg/kg, PO) 1 hour after the onset of recording (white circles). Onset of each 24-hour recording was designated as time 0. *Within each time point, values differ significantly ($P < 0.05$) between groups.

Mean hourly pH for all foals ranged from 2.89 to 4.18 during the baseline recording and from 4.32 to 6.94 during the second recording (Figure 1). Mean intragastric pH was not significantly different between groups for the first 2 hours of recording. When administered omeprazole, foals had a significantly higher mean hourly intragastric pH for hours 3 to 23 of the study (ie, 2 to 22 hours after omeprazole administration). For hour 24 of the study (23 hours after omeprazole administration), foals had a higher but not significantly ($P = 0.88$) different intragastric pH after administration of omeprazole.

Discussion

Mean intragastric pH values in clinically normal untreated foals in the study reported here closely resemble those reported for slightly younger foals.¹ Placement of an indwelling pH electrode was adapted slightly from a technique reported elsewhere⁵ to enable us to combine the process with gastroscopy, which resulted in more efficient placement of the pH electrode without impairing accuracy.

Omeprazole, a substituted benzimidazole, is efficacious for reducing acid output in horses and healing ulcers in the gastric squamous and glandular mucosa.^{10,11,13,15,16} Although omeprazole has been recommended for use in foals¹⁷ and evaluated in a population of foals¹⁸ older than the foals we used in this study, its effects in a neonatal population had not yet been determined. In the study reported here, oral administration of omeprazole at the recommended treatment dosage¹² resulted in a significant increase in intragastric pH within 2 hours after the initial administration. In other studies^{4,5} conducted by our laboratory group, we have reported differences in intragastric pH patterns after administration of ranitidine and the response to ranitidine in critically ill neonatal foals, compared with the response in clinically normal foals. Although the differences in pH patterns between critically ill and clinically normal foals may be correlated with entero-gastric reflux in the critically ill foals, an explanation for the alteration in response to IV administration of ranitidine remains elusive. Thus, results of the study reported here for omeprazole may not be applicable to a population of critically ill foals.

The rapid onset of action documented in the foals reported here differs from results in adult horses that were administered omeprazole in enteric-coated granules.⁶ In that study, secretion of gastric acid was stimulated by infusion of pentagastrin and gastric acid output and pH were measured on days 1, 5, and 7 during daily administration of omeprazole (1.4 mg/kg, PO). The maximal antisecretory effect of orally administered omeprazole was not achieved after the first dose and was apparent only after the fifth daily dose. Another study⁸ in which investigators administered omeprazole, an FDA-approved product, at the rate of 4 mg/kg/d to fed adult horses revealed an effective increase in intragastric pH following the second daily dose. The quick increase in gastric pH following 1 dose of omeprazole paste in our foals may reflect more rapid and complete absorption of the drug in neonatal foals, compared with absorption in adult horses. In addition, the 22-hour duration of effect evident in this study is

consistent with the once-daily dosing interval recommended for older foals and adult horses.

^aSNAP foal IgG, IDEXX Laboratories Inc, Westbrook, Me.

^bGastroGard, Merial Ltd, Duluth, Ga.

^cZinetics 24, Medtronic Inc, Shoreview, Minn.

^dDigitrapper MD, Medtronic Inc, Shoreview, Minn.

^eDigitrapper Mark III, Medtronic Inc, Shoreview, Minn.

^fEsopHagram, Medtronic Inc, Shoreview, Minn.

^gPolygram 98, Medtronic Inc, Shoreview, Minn.

^hSPSS 11.0 for Windows, SPSS Inc, Chicago, Ill.

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