Efficacy of omeprazole paste for prevention of gastric ulcers in horses in race training

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Objective—To determine the minimal effective dosage of omeprazole oral paste for the prevention of naturally occurring ulcers in horses starting race training. Design—Prospective study. Animals—175 horses. Procedure—Horses in the dose selection portion of the study were sham-dose treated or received 1 mg (0.45 mg/lb) or 2 mg (0.9 mg/lb) of omeprazole/kg, PO, every 24 hours for 28 days or 4 mg of omeprazole/kg (1.8 mg/lb; loading dose), PO, every 24 hours for 4 days, then 1 or 2 mg of omeprazole/kg, PO, every 24 hours for 24 days. Horses in the dose confirmation portion of the study were sham-dose treated or received 1 mg of omeprazole/kg, PO, every 24 hours for 28 days. Gastric ulcer scores at the beginning and end of the study were compared. Results—Sham-dose-treated horses had significantly higher ulcer scores than did horses treated with any of the omeprazole dosages evaluated. Among horses treated with omeprazole, there was no significant interaction of dose (1 or 2 mg/kg) and loading dose; therefore, the lowest effective dose (1 mg/kg) was evaluated in the dose confirmation portion of the study. In the dose confirmation study, 4 of 39 (10%) sham-dose treated horses remained ulcer free, which was significantly different from the proportion of horses (31/38 [82%]) receiving 1 mg of omeprazole/kg that remained ulcer free.

Conclusions and Clinical Relevance—Results indicated that omeprazole administered at a dosage of 1 mg/kg, PO, every 24 hours for 28 days was effective for prevention of gastric ulcers in horses starting race training. (J Am Vet Med Assoc 2005;226:1681–1684)

Results of studies concerning prevalence of gastric ulcers in horses in race training indicate that 90% of Thoroughbreds in training, 87% of Thoroughbreds that died during race training, and 81% of clinically normal Thoroughbreds in race training have gastric ulcers. Results of 1 study indicate that the prevalence of gastric ulcers in Standardbred racehorses is 87%. In that study, horses > 2 years old had more severe ulcer scores than horses < 2 years old. Gastric ulcers have been associated with signs of abdominal pain and colic, particularly in horses in training. Loss of appetite and poor coats have also been associated with gastric ulcers in horses. Gastric ulcers may affect the condition and performance of horses in race training. The subclinical effects of gastric ulcers are difficult to determine; however, gastric ulcers have been associated with decreased performance in horses with decreased hemoglobin concentrations. Results of 1 study indicate that horses with gastric ulcers had lower RBC counts and hemoglobin concentrations than those without gastric ulcers.

With the high prevalence of gastric ulcers in horses in race training, there is an obvious need for prevention. Management modifications including pasture feeding or continual access to hay can provide prolonged reduction of gastric acidity. Furthermore, the adverse effects of nonsteroidal anti-inflammatory drugs on the protective mechanisms of the stomach are well documented. Because most of these management factors are not feasible for horses in race training, a pharmacologic method of prevention is indicated.

Effective treatment of gastric ulcers depends on decreased gastric acid secretion to increase the pH within the stomach. Omeprazole is a potent inhibitor of gastric acid secretion. Omeprazole decreases gastric acid secretion by blocking the H⁺-K⁺-ATPase enzyme system at the secretory surface of the gastric parietal cell. Omeprazole paste was approved by the FDA in 1999 for the treatment of gastric ulcers in horses. The purpose of the study reported here was to determine the minimal effective dosage of omeprazole paste for the prevention of naturally occurring ulcers in horses starting race training.

Materials and Methods

Horses—A multicenter study was performed at private training facilities in Iowa, Oklahoma, California, and Kentucky in the United States and in Quebec, Canada. All horses were privately owned, under the guidance of a licensed trainer, and subjected to the routine training activity of the facility. Horses were housed in the same individual stalls in proximity to the other horses in the same replicate throughout the study period. Rations were typical for horses in race training. To be included in the study, horses had to be free of gastric ulcers and entering a training regimen that...
would be expected to result in gastric ulcer formation under the management conditions. Horses included in the study had not received medications for treatment of gastric ulcers within 2 weeks of the start of the study (day 0), and nonsteroidal anti-inflammatory medications were not administered during the study except in 5 horses. Physical examinations were completed from day 1 to 7 days (day 7) to 3 days (day 28) of the study. Body weights were obtained between day 7 and day 28. Horses were observed twice daily, and any clinical signs of illness were recorded. All observers were unaware of treatment group allocation. Horses were exercised and managed as typical for horses in race training from day 7 through day 28.

The study protocol was approved by the Merrel Animal Care and Use Committee. The study was performed in 2 parts: dose selection for prevention of gastric ulcers (prevention phase) and dose confirmation for the prevention of gastric ulcers.

Gastroscopy — Gastroscopy was performed once between day 7 and 1 day and again on day 28 by use of a 3-m video endoscope. Food was withheld from horses for 6 to 8 hours, and water was withheld for approximately 2 hours prior to gastroscopy. Horses were sedated with xylazine hydrochloride (1 mg/kg [0.45 mg/lb], IV) with or without butorphanol tartrate (0.02 mg/kg [0.009 mg/lb], IV), and a twitch was applied as needed. The entire squamous and glandular mucosa of the stomach had to be seen gastroscopically for a valid examination.

For each horse, the gastroscopist, who was unaware of treatment group allocation, recorded an ulcer score. The ulcer scoring system has been used in previous studies.11-13 Lesions in the gastric mucosa were scored as follows: 0, intact mucosal epithelium (can have reddening with or without hyperkeratosis); 1, small single or small multifocal lesions; 2, large single or large multifocal lesions; and 3, extensive (often coalescing) lesions with areas of deep ulceration.

The incidence of health observations made during the treatment phase of both parts of the study was compared by category of health observation (abscess, gastrointestinal abnormality, musculoskeletal abnormality, respiratory abnormality, skin abnormality, soft tissue injury, fever, or inappetence) for horses that were sham dose treated and treated with omeprazole by use of the Cochran-Mantel-Haenszel row analysis of results from the 3 study sites that provided data was evaluated by the modified Friedman test. Additional comparisons were performed for sham-dose-treated versus pooled results from treatment groups (group 1 vs groups 2, 3, 4, and 5); dose effect (groups 2 and 4 vs groups 3 and 5); and loading effect (groups 2 and 3 vs groups 4 and 5), and the interaction of dose and loading dose. Values of P ≤ 0.05 were considered significant. Statistical analysis was performed with commercial software.

Results

For the dose selection portion of the study, 3 test sites provided data for 95 horses that were allocated to 19 replicates, including 60 Quarter Horses that were 2 years old and 33 Standardbreds from 2 to 6 years of age (13 were 2 years old, 19 were 3 years old, and 1 each was 4, 5, and 6 years old). There were 55 females, 20 males, and 20 geldings with a mean body weight of 442 kg (972 lb).

Two Quarter Horses and 1 Standardbred were removed from the study at the owners’ request. This resulted in 92 horses in 5 groups; there were 17 horses in group 1 and 18 horses in group 3. Groups 2, 4, and 5 each had 19 horses.

The frequency of each gastric ulcer score after 28 days of treatment was determined for each treatment group (Figure 1). Because all horses had ulcer scores of 0 at the start of treatment, an ulcer score of 0 at the end of the prevention phase indicated that ulcer severity did not increase during this phase and a score > 0 indicated that ulcer severity increased. Four of 17 (24%) horses in group 1, 16 of 19 (84%) horses in group 2, and 16 of 18 (89%) horses in group 3 remained ulcer free. When omeprazole was administered as a loading dose of 4 mg/kg for 4 days before it was administered at a dose of 1 mg/kg, 15 of 19 (79%) horses did not develop ulcers. Similarly, when omeprazole was administered as a loading dose of 4 mg/kg for 4 days before it was administered at a dose of 2 mg/kg, 15 of 19 (79%) horses remained ulcer free. The ulcer scores increased significantly (P < 0.001) in the sham–dose-treated horses (group 1), compared with the pooled results from treated horses (groups 2, 3, 4, and 5).

Among horses treated with omeprazole, there was no significant interaction of dose (1 or 2 mg/kg) and
loading dose (yes or no; \( P = 0.856 \)). Therefore, the 2 main factors, presence or absence of the loading dose of 4 mg of omeprazole/kg and the dose of 1 or 2 mg of omeprazole/kg, were evaluated without concern for the other factor. The protection provided by administration of 1 mg of omeprazole/kg (groups 2 and 4) and 2 mg of omeprazole/kg (groups 3 and 5) was not significantly different (\( P = 0.842 \)). At 1 mg of omeprazole/kg, 31 of 38 (82%) horses remained ulcer free, whereas at 2 mg of omeprazole/kg, 31 of 37 (84%) horses remained ulcer free. The loading dose had no effect on the prevention of ulcer development (\( P = 0.394 \)). Thirty-two of 37 (86%) horses that did not receive a loading dose remained ulcer free, whereas 30 of 38 (79%) horses receiving a loading dose remained ulcer free.

For the dose confirmation portion of the study, 3 test sites provided 80 horses that were allocated to 40 replicates, including 56 Thoroughbreds and 24 Quarter Horses. Sixteen Thoroughbreds were 1 year old, 32 were 2 years old, 2 were 3 years old, 4 were 4 years old, and 1 each was 6 and 7 years old. All Quarter Horses were long yearlings that would be 2 years old within 3 months of study completion. There were 40 females, 20 males, and 20 geldings with a mean body weight of 437 kg (961 lb). Three horses were removed from the study at the owners' request; therefore, 77 horses completed the study. Thirty-nine horses were sham dose treated, and 38 horses were treated with omeprazole (1 mg/kg, PO, q 24 h) for 28 days.

The frequency of each gastric ulcer score was determined for treatment group (Figure 2). Again, all horses had ulcer scores of 0 at the start of treatment; therefore, an ulcer score of 0 at the end of the prevention phase indicated that ulcer severity did not increase. Four of 39 (10%) horses in group 1 remained ulcer free, which was significantly (\( P = 0.001 \)) different from group 2 in which 31 of 38 (82%) horses were ulcer free.

When the 57 horses treated with 1 mg of omeprazole/kg (group 2) from the dose selection portion of the study and the dose confirmation portion of the study were combined and compared with the 56 sham–dose-treated horses (group 1), 47 of 57 (82%) group 2 horses remained ulcer free and 8 of 56 (14%) group 1 horses were ulcer free. Ulcer scores in group 2 horses were significantly (\( P = 0.001 \)) different from ulcer scores in group 1 horses (Figure 3).

Fifteen separate health-related conditions were reported in study horses, including respiratory infections (\( n = 5 \)), brief lever of unknown origin (3), laceration (2), abscess (2), urticaria (1), proximal sesamoid bone fracture (1), and incomplete feed consumption on 1 occasion (1). All health-related conditions that were reported would have been expected to develop in horses in race training. The only health-related condition that was significantly (\( P = 0.046 \)) different between horses treated with omeprazole and sham–dose-treated horses was the proximal sesamoid bone fracture in the musculoskeletal abnormality group, which occurred in 1 of 59 (1.7%) sham–dose-treated horses. This health-related condition was not clinically relevant in respect to the omeprazole treatment.
Discussion

When horses from both portions of the study were combined, 47 of 57 (82%) horses treated with omeprazole at a dosage of 1 mg/kg, PO, every 24 hours for 28 days were free of ulcers, whereas only 8 of 56 (14%) sham–dose–treated horses remained ulcer free. These results indicated that omeprazole administered at a dosage of 1 mg/kg was effective in preventing the development of gastric ulcers in horses starting race training, and horses in this study were subjected to an adequate ulcerogenic stimulus during the initial training period, which provided a good method for evaluating the preventative dose of omeprazole. The initiation of race training in multiple breeds of horses and by numerous trainers consistently induced gastric ulcers. Results of a study15 evaluating race training as a mechanism to induce and maintain gastric ulcers indicated that all horses developed gastric ulcers within 2 weeks of entering training.

Results of 1 study12 indicate the effectiveness of omeprazole paste for the treatment of gastric ulcers when administered at a dose of 4 mg/kg. Results of a subsequent study16 support use of this dose for treatment of gastric ulcers. In that study, 94% of 403 horses had fewer ulcers and ulcers in 63% of horses had completely healed. Results of another study17 in horses with ulcers that resolved after treatment with omeprazole administered at a dose of 4 mg/kg indicate that decreasing the dose of omeprazole to 2 mg/kg prevented recurrence of ulcers while the ulcerogenic stimulus was maintained. Results of the study reported here indicated that omeprazole administered at a dose of 4 mg/kg, PO, every 24 hours for 28 days prevented development of gastric ulcerations in horses starting race training and that a loading dose of omeprazole was not required.

Omeprazole paste has been administered long-term at a dosage of 20 mg/kg (9.1 mg/lb), PO, once daily for 91 days to mature Thoroughbred horses without any adverse effects.17 Similarly, adverse effects were not detected when omeprazole was administered at a dosage of 40 mg/kg (18.2 mg/lb), PO, once daily for 21 days to mature Thoroughbred horses.18 Omeprazole administered orally is readily accepted by horses. In the study reported here, adverse effects were not associated with omeprazole treatment in horses.

One consideration regarding the use of omeprazole in racehorses in training is the regulatory issues concerning use of medications in racehorses. Results of 1 study19 indicate that administration of omeprazole is not associated with a direct enhancement in performance as determined by short-term incremental treadmill testing. However, because of the reported13 effects of chronic ulceration on feed intake, performance, and hematologic values, it is reasonable to expect that horses without gastric ulcers would be more competitive than those with chronic severe gastric ulceration.

References