Omeprazole Paste: Treatment and Prevention of Recurrence of Gastric Ulcers in Horses

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Omeprazole as a paste formulation at 4.0 mg/kg PO q 24 h is highly effective in healing gastric ulcers in horses, while 2.0 or 4.0 mg/kg PO q 24 h effectively prevents recurrence of gastric ulcers in Thoroughbred horses in race training. Omeprazole paste did not result in any adverse affects in the horses during the 58-d treatment period. Author’s address: College of Veterinary Medicine, The University of Tennessee, P.O. Box 1071, Knoxville, Tennessee, 37901-1071; Bradford Park Veterinary Hospital, 1255 E. Independence, Springfield, Missouri (Sifferman); Rood & Riddle Equine Hospital, 4901 Mt. Horeb, Lexington, Kentucky (Bernard); Peterson, Smith, Matthews, Hahn and Slone Equine Hospital, 4747 S.W. 60th Avenue, Ocala, Florida (Hughes); Merial Limited, 2100 Ronson Road, Iselin, New Jersey (Holste, Daurio, Alva, Cox). © 1999 AAEP.

1. Introduction

Omeprazole, a substituted benzimidazole, is a potent inhibitor of gastric acid secretion in horses.1,2 Omeprazole decreases gastric acid secretion by blocking the H+K+-adenosine triphosphatase (acid pump) in the secretory membrane of the parietal cell.3,4 This enzyme catalyzes the exchange of hydrogen ions for potassium ions in the final step of hydrochloric acid production by the parietal cell. Therefore, omeprazole is characterized as an acid-pump inhibitor and blocks gastric acid secretion irrespective of stimulus.5

Inhibition of gastric acid secretion has been the mainstay for gastric ulcer treatment in horses.6,7 Omeprazole has been shown to be effective in the treatment of gastric ulcers in horses. An oral gel formulation of omeprazole aided healing of flunixin meglumine-induced gastric ulcers in young horses.8 Furthermore, a “delayed release” formulation of omeprazole in capsules showed healing of endoscopically verified gastric ulcers in pleasure horses and Thoroughbred race horses.8,9

This study was designed to demonstrate the efficacy of an oral commercially formulated and packaged omeprazole paste in the treatment and prevention of recurrence of equine gastric ulcer syndrome.

2. Materials and Methods

This study was conducted as a multicenter clinical trial at commercial training centers in Texas, Florida, and Kentucky. Animals were managed with due regard for their well being and in compliance with the protocol approved by the Merck Research Laboratory Institutional Animal Care and Use Committee. One hundred Thoroughbred horses in race train-
ing (53 geldings, 5 stallions, and 42 mares) with endoscopically-verified naturally occurring gastric ulcers were used in this study. The horses were 2–11 years old and weighed 375–523 kg. All horses were appropriately acclimated to the facility before starting the treatment period. Horses were dewormed with ivermectin \( ^c \) 10–12 d before starting treatment. Before beginning treatment (days \(-3 \) to \(-1 \), the horses were randomly allocated to replicate groups of 4 horses based primarily on ulcer score and secondarily on sex. All horses in one replicate were exercised in the same order each day throughout the trial.

Horses were housed in approximately 3.0-m \( \times \) 3.0-m stalls inside well-ventilated barns. Stalls were bedded with wood shavings and the horses were fed grass hay and either a pelleted feed or sweet feed ration. Water was provided ad libitum.

Omeprazole as a commercially formulated paste \( ^b \) packaged in individual dose syringes was used in the study. An empty syringe (sham dosing) or omeprazole was administered orally once daily between 7 and 9 AM. Of the 100 horses entering the study, 25 were sham-dosed for the full 58 d of the study. The remaining 75 horses all received omeprazole paste, 4 mg/kg PO q 24 h, for 28 d (days \(0 \)–\(27 \)). At day 27 (after 28 daily doses), 25 of these horses treated with omeprazole continued on this dosing regimen (Group IIiii), while 25 received half-dose omeprazole (2 mg/kg PO q 24 h) (Group IIii), and 25 horses were sham-dosed with an empty syringe (Group IIi).

Endoscopic examination of the stomach was performed on each horse using a 3-m videoendoscope 1–3 d before the study and on days 13, 20, 27, and 57 of the study to confirm and score the presence of gastric ulcers. Feed was withheld for 6–12 h and water was withheld for 2–4 h before endoscopic examination. Horses were sedated and lightly restrained for endoscopic examination. The endoscopist was blinded to treatment group assignments. For each horse, a score for the stomach was given based on the worst gastric ulcer present. The following scoring system for equine gastric ulcers was used: 0, Intact mucosal epithelium (could have reddening and/or hyperkeratosis); 1, small single or small multifocal ulcers; 2, large single or large multifocal ulcers; and 3, extensive (often coalescing) ulcers with areas of apparent deep ulceration.

The pooled data from all four trials were analyzed. Change in ulcer score from baseline to days 13, 20, and 27 was analyzed nonparametrically using a modified Friedman's test (Cochran-Mantel-Haenszel procedure) to assess differences between omeprazole and the sham-dosed control. \(^{10}\) The blocking factor used for these analyses was the trial. The modified Friedman's test statistic is equivalent to weighted sum Wilcoxon rank-sum statistics calculated separately by trial, with the weight defined as the reciprocal of the standard deviation of the ranks for that trial.

Change in ulcer score from day 27 to day 57 was analyzed nonparametrically as above using a modified Friedman's test, with contrasts tested using Dunn's procedure to assess differences among omeprazole maintenance regimens (i.e., group IIi versus IIiii, IIiii, and group IIiii versus IIIii). A value of \( p < 0.05 \) was considered significant.

3. Results

There was significant \(( p < 0.01)\) improvement in gastric ulcer scores by days 13, 20, and 27 in horses treated with omeprazole compared with sham-dosed controls. Gastric ulcer scores were improved \(( p < 0.01)\) in 65 of 75 (86.7%), 67 of 75 (89.3%), and 69 of 75 (92%) omeprazole-treated horses at these days, respectively. Gastric ulcers were healed in 43 of 75 (57.3%), 50 of 75 (66.7%), and 58 of 75 (77.3%) omeprazole-treated horses at days 13, 20, and 27, respectively, whereas gastric ulcers were healed in only 1 of 25 (4.0%), 2 of 25 (8.0%), and 1 of 25 (4.0%) sham-dosed controls at these days, respectively.

Gastric ulcer scores were significantly \(( p < 0.01)\) worse by day 57 in horses where omeprazole treatment was discontinued on day 27 compared with those horses continuing on omeprazole treatment. There were no significant differences in the change in gastric ulcer scores from day 27 to day 57 between horses treated with omeprazole at either 2 or 4 mg/kg body wt/d. Furthermore, only 6 of 38 (16%) of omeprazole-treated horses had recurrence of gastric ulcers by day 57, whereas 18 of 20 (90%) of nontreated horses had recurrence of gastric ulcers by day 57.

4. Discussion

Omeprazole, given orally as a commercially formulated packaged paste at 4 mg/kg body wt/d, produced significant healing of naturally occurring gastric ulcers in Thoroughbred race horses in training. By day 27 (after 28 daily doses), 77.3% of horses with gastric ulcers were healed. Healing rates observed in this study were higher than those previously reported when omeprazole was given at 1 mg/kg body wt/d\(^b\) and similar to those reported when omeprazole was given at 4 mg/kg body wt/d.\(^d\) In the later dose-titration study with horses with nonsteroidal anti-inflammatory drug–induced gastric ulcers, omeprazole treatment resulted in a time- and dose-dependent positive effect on gastric ulcer healing.

Healing and time-to-healing rates seen in this present study with omeprazole treatment were similar to previous reports using histamine type 2 receptor antagonists.\(^{11}\) In that previous study, 84% of treated horses healed when treated with ranitidine (6.6 mg/kg body wt q 8 h) for 4 weeks. However, the healing and time-to-healing rates in the present study were achieved at an omeprazole dose of 4.0 mg/kg body wt/d, whereas similar healing rates using ranitidine were achieved at a dose of 6.6 mg/kg body wt q 8 h or 19.8 mg/kg body wt/d.\(^{11}\) From these data, omeprazole appears to be five times more

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potent, on an equimolar basis, than ranitidine in healing gastric ulcers in horses. Furthermore, omeprazole requires once daily administration to effect this healing rate, whereas ranitidine requires three time daily dosing.

The results of this present study show that after initial healing of gastric ulcers with omeprazole paste at 4 mg/kg body wt/d, 2 and 4 mg/kg body wt/d prevented recurrence during the subsequent 30-day treatment period. Furthermore, only 6 of 38 (6%) of omeprazole-treated horses had recurrence of gastric ulcers by day 57, whereas 18 of 20 (90%) nontreated horses had recurrence of gastric ulcers by day 57. Gastric-ulcer recurrence rate in the horses in this study was 90%, which is similar to previously reported prevalence rates in horses.12,13 Gastric-ulcer recurrence rates in people vary from 20% to 70% following a 6-week course of antiulcer treatment.14 Since management and the stress of training have been shown to be a factor in causing and maintaining gastric ulcer disease in horses12, high recurrence rates are not unexpected once horses are taken off treatment while in training. Thus, maintenance therapy may be necessary to prevent recurrence of gastric ulcer disease in horses. Omeprazole at either 2 or 4 mg/kg body wt/d appeared to be effective as a maintenance therapy for gastric ulcers in horses in race training, since only 16% of horses at these doses had recurrence gastric ulcers.

It can be concluded from this study that omeprazole paste (4.0 mg/kg body wt PO q 24 h), is effective in healing gastric ulcers in horses, while maintenance therapy of either 2 or 4 mg/kg body wt/d effectively prevents gastric ulcer recurrence.

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References and Footnotes


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