Journal of Equine Veterinary Science 43 (2016) 32–38

Contents lists available at ScienceDirect

Journal of Equine Veterinary Science

journal homepage: www.j-evs.com

Original Research

The Effect of Serum-Based Bioactive Proteins for the Prevention of Squamous Gastric Ulcers in Horses

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ARTICLE INFO

Article history:
Received 25 January 2016
Received in revised form 6 May 2016
Accepted 6 May 2016
Available online 12 May 2016

Keywords:
Bioactive serum protein
Equine squamous gastric disease
Horse

ABSTRACT

The objective of this study was to determine the effects of serum-based bioactive proteins on the prevention of squamous gastric ulcer formation in horses in moderate exercise programs over a 21-day period. Horses without ulcers were identified and randomly assigned to treatment or control group. Horses were subjected to a training program which induced squamous gastric ulceration in control horses. In horses treated with 210-g bioactive proteins, the incidence of squamous ulcers was significantly reduced ($P = .0001$) compared to control horses. In horses treated with 80-g bioactive proteins, 66.67% (10/15) of the control horses developed squamous gastric ulceration compared to 33.55% (5/15) of those administered bioactive proteins. In conclusion, dosing horses with bioactive proteins derived from serum was effective for preventing gastric ulcers in horses experiencing stress from exercise or training.

1. Introduction

The high incidence of equine squamous gastric disease (ESGD) in performance horses of multiple disciplines has been identified in numerous publications [1–3]. The exposure of the squamous mucosa to volatile fatty acids and hydrochloric acid can result in cellular damage in a time-dependent manner [4]. The physical aspects of exercise increase abdominal pressure, pushing the acidic contents upward [5]. Exercise beyond a walk for prolonged periods of time such as is seen in race horses and endurance horses can lead to ulceration of the squamous mucosa due to acid exposure. Furthermore, the roughage in the diets of performance horses may be decreased along with sporadic feeding resulting in prolonged periods with less material in the stomach to buffer the continual acid secretion [6].

Mechanisms to prevent ESGD include omeprazole, which is a proton pump inhibitor, dietary and behavioral management, and supplements. Omeprazole has been shown to effectively prevent the formation of squamous gastric ulcers and prevent recurrence in race horses during training [7–9]. Continuous access to grass pasture, splitting the ration into multiple feedings, and decreasing sweet feeds that increase volatile fatty acids can all decrease squamous mucosal ulcers in the horse [10]. Decreasing exercise can also decrease the formation of gastric ulcers, but this is not often a viable option for horses in training.

A number of oral supplements for the prevention of ESGD have been evaluated. Antacids alone are of limited value due to the short duration of their effect [11]. Combinations of pectin-lecithin, antacid and *Saccharomycis cerevisa*, herbs, and coating agents have shown protective effects against ESGD [12–15]. When bovine colostrum containing immunoglobulins and growth factors were supplemented in the diet of race horses, their racing performance and postrace recovery improved [16]. It is well established that plasma-derived proteins from bovine, porcine, and other sources, when added to the diets of

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http://dx.doi.org/10.1016/j.jevs.2016.05.003

several species of animals, lead to improvements in appetite, weight gain, intestinal growth, and gut barrier function in a number of intestinal disorders [17–20]. Plasma proteins added to pig diets have been shown to reduce proinflammatory cytokines including tumor necrosis factor α and interleukin 8 in the intestinal tract [21–22]. In horses, improved gait kinematics were observed with the supplementation of serum-based bioactive proteins [23–24]. Bovine serum concentrate added to the drinking water of pigs reduced the morbidity associated with ulcers in growing pigs [25]. Based on the recognized effect of bioactive proteins from either bovine colostrum or plasma proteins in horses and the prevention of gastric ulcers in pigs, the value of bioactive proteins for prevention of ESGD should be considered. The objective of these studies was to evaluate the effect of orally administered bioactive proteins on the prevention of ESGD in horses during a western performance training/showing environment.

2. Material and Methods

The study was completed in two phases. In phase 1, a dose of 210 g of bioactive proteins (contained in 382 g of supplement) was administered to 15 horses and compared to a control supplement (382 g) administered to 15 horses. In phase 2, a dose of 80 g of bioactive proteins (contained in 230 g of supplement) was administered to 15 horses and compared to a control supplement (230 g) administered to 15 horses. The two phases were conducted during separate periods with different horses.

2.1. Horses

From a pool of horses at a private training facility that had been similarly managed for at least the previous 3 weeks, the first 30 qualifying horses with a gastric score of zero (i.e., no squamous or glandular ulcer disease as determined by endoscopic examination) were selected for participation in each phase. Horses included in the studies had never received medications for treatment of gastric ulcers and had not received any nonsteroidal anti-inflammatories within 2 weeks of the start of the study (day 0). Each horse was uniquely identified by registered name, color, unique markings, and identified with a tag attached to the halter. Horses were individually kept in approximately 3.6 $\times$ 3.6 m stalls throughout the study period when not being exercised or trained. All horses were maintained following standard animal use and care guidelines and in accordance with applicable local regulations and informed consent of the owner. The study was approved by the Iowa State University Animal Care and Use Committee.

Physical examinations were completed, and body weights were obtained 1 day (day 0) before administration of treatment or placebo and again on day 21 of the study. Blood was obtained on days 0 and 21 for complete blood count and serum chemistries. Horses were observed at least twice daily, and any clinical signs of illness and consumption of study material were recorded. Horses were maintained at the same level of activity that they were doing for 1 week (days 1–7) before initiation of stress to allow for consistent consumption of the test supplements. Then, from days 7 to 21, horses were subjected to a 2-week period of physiologic stress induced by a training regimen applicable for each horse. Young horses were broke for being handled and to lead and lunge. They were also trained to load on and off trailers and were taken on short trips around town. The horses from 2 years up were being worked under tack and various levels of training for a finished saddle horse. This includes walk, trot, and canter in each direction in the correct leads and stopping on cue. A 15- to 30-minute session under tack 5 days a week is routine. Horses are also put on a mechanical walker for 30 to 60 minutes daily. Both horses in a replicate were treated similarly.

2.2. Gastroscopy

Gastroscopy was performed on each horse on day 0 to verify the absence of squamous gastric ulcers and glandular erosions (i.e., gastric lesion score, 0) and conducted again on all horses on day 21 at the conclusion of the trial. Horses were sedated with 20 μg/kg of detomidine (Dormosedan; Pfizer Animal Health, Kalamazoo, MI) and lightly restrained with a twitch for the endoscopic examinations. Food was removed from the stalls approximately 8 hours before endoscopy, and all horses were tied 2 hours before endoscopy to prevent intake of any bedding or water. The entire squamous mucosa and most of the glandular portions of the stomach including the pyloric antrum were viewed in all horses with a 3-meter gastroscope (Tele-View USB Video Gastroscope; Advanced Monitors Corporation, San Diego, CA). One endoscopist performed all gastroscopies was blinded to the identification of the horse groups. Gastric lesion severity was a score of 0 which indicated no erosion or ulcer but could include reddening or hyperkeratosis, and scores of 1 to 3 indicated the presence of erosions and ulcers of increasing severity. Reddening and hyperkeratosis and glandular ulcers were scored as present or absent.

2.3. Experimental Protocol

The studies used a randomized complete block design. Replicates of two horses were formed on the basis of similarity of sex, age, and weight, respectively. Age as a blocking factor assured both horses in a replicate were subjected to a similar training program in a model used previously to induce gastric ulcers [26,27]. All horses were the same breed. Within replicates, horses were randomly allocated to one of two study groups, which were randomly assigned as group A (placebo) and group B (treatment). All investigators and participants were blinded to treatment and control groups until completion of the study. The treatments for phase 1 were 382 g/d of pellets containing either 210 g of soybean meal (control; A) or 210 g of bioactive proteins derived from bovine serum isolate (Biothrive, APC Inc, Ankeny, IA; treatment; B). The total 382 g volume was split into two doses per day in individual plastic bags marked only as A or B. For phase 2, 230 g of pellets containing either 80 g of soybean meal (control; A) or 80 g of bioactive proteins (treatment; B) was split into