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Original Research

A Proton-Pump Inhibitor Modifies the Concentration of Digestion Biomarkers in Healthy Horses

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ABSTRACT

To determine the concentration of various blood biomarkers associated with digestion in healthy horses treated with different doses of omeprazole (OMPZ), four Arabian horses without gastric ulcers were selected and distributed in one factorial with four oral treatments (Control; $OMPZ^{BOLUS}$; $OMPZ^{4mg/kg}$; $OMPZ^{1mg/kg}$). Control did not receive any treatment. $OMPZ^{BOLUS}$ were given 4 mg/kg of omeprazole in a single dose on the day before blood sampling. In the $OMPZ^{4mg/kg}$ and $OMPZ^{1mg/kg}$ treatments, horses were treated over 11 days. All treatments were performed 16 hours before morning feeding. The "washout" period was 21 days between rounds. After an overnight fasting period, blood samples were collected from all animals (T1), after which the animals received supplementation, and blood samples were collected after 30 minutes (T2), 1.0 hours (T3), 1.5 hours (T4), 2.0 hours (T5), 3.0 hours (T6), 4.0 hours (T7), 5.0 hours (T8), 6.0 hours (T9), and 7.0 hours (T10). Blood samples were analyzed for total plasma protein (TPP), glucose, urea, creatinine, uric acid, cholesterol, triglycerides, calcium, phosphorus, and magnesium. The results showed differences between treatments for urea, cholesterol, uric acid; between phases for glucose; and between phase and treatment for creatinine, triglycerides, phosphorus, and magnesium; however, there was no difference for TPP and calcium between treatment and between phases. Oral administration of OMPZ in healthy equines interfered with the metabolism of digestion biomarkers of lipid, mineral, and protein metabolism, although the animals were treated for a maximum of 11 days. Horses treated with a proton-pump inhibitor need to be evaluated regularly to avoid significant modification in their metabolic parameters.

1. Introduction

Gastric ulcer syndrome in equines is an important factor that compromises the performance of equine athletes. It occurs with high frequency in these animals, varying between 60% and 90% [1,2]. This elevated morbidity has motivated the adoption of preventative treatments to reduce the occurrence of gastric ulcers among equine athletes. Several medication regimens can be used as preventative treatments.

Management strategies are based mainly on decreasing gastric acidity, maintaining the pH above 4, covering the ulcers with an agent that is resistant to acid, and stimulating the release of protective factors in the gastric mucosa [2]. Proton-pump inhibitors (PPIs) have been primarily used for ulcer treatment, relieving the symptoms and creating a favorable environment for wound healing [3,4].

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However, several researchers have demonstrated that PPI treatment is not without side effects, most likely because the reduction of gastric pH can modify digestion and the absorption of nutrients throughout the digestive tract, changing the concentration of some biomarkers in the blood [5–9].

Omeprazole (OMPZ), which has been widely used in athletic horses, acts by lowering gastric pH by reducing production of the acid pentagastrin [10]. It is the only agent that is allowed for use in horses, which inhibits the proton pump, and several studies demonstrate the safety and efficacy of oral administration in foals and adult horses, healing more than 75% of the horses treated and kept in training [11,12]. Reduction of gastric pH after treatment lasts up to 16–18 hours after administration [13] and therefore might interfere with the digestion and absorption of nutrients regularly ingested by equines. Furthermore, because lower doses, approximately one quarter of the regular treatment dose, can prevent ulcers in equines, some veterinarians use OMPZ more often, sometimes for longer periods of time. However, there is no follow-up regarding the possible side effects of PPI on the digestive process in equines, as observed in human, because there are numerous reports of adverse effects of PPI after short and long periods of use [9,14,15].

The objective of the present study was to determine the concentration of different blood biomarkers associated with digestion in healthy horses treated with different doses of OMPZ. Changes in some biomarkers were expected because of the change in pH in the initial portions of the digestive tract of the treated animals, similar to such changes in other species.

2. Materials and Methods

2.1. Animals and Production System

Four Arabian adult nonpregnant mares were selected, with a mean age of 13 years and weight of 370 kg. They were housed at the Equine Research Nucleus at Federal Rural University of Pernambuco and were all in maintenance and free of gastric ulcers as confirmed by endoscopy. The horses were kept at pasture with mixed grass types (cultivated and native), with access to water and mineralized salt ad libitum, and received commercial concentrate (crude protein, 19%; fat, 8.0%; acid detergent fiber, 6.2%; neutral detergent fiber, 6.4%; and digestive energy, 4.1 Mcal/kg), twice daily, so that 50% of the necessary energy for animals in maintenance could be obtained from the concentrate, according to National Research Council [16] guidelines. All procedures were in accordance with the guidelines for the use of animals in experimentation of the Federal Rural University of Pernambuco (#62/2007-CTA/DZ).

2.2. Experimental Design

Horses were distributed randomly into a factorial design with four animals and four treatments. The treatments were control—5.0 mL of drinking water orally in a single dose, simulating the treatment with the PPI; $OMPZ^{BOLUS}$—omeprazole at 4.0 mg/kg orally in a single dose; $OMPZ^{4mg/kg}$—omeprazole at 4.0 mg/kg, orally every 24 hours, for 11 days; and $OMPZ^{1mg/kg}$—omeprazole at 1.0 mg/kg, orally every 24 hours, for 11 days. All experimental groups were treated 16 hours before receiving their morning concentrate (8 AM). Between treatment rounds, horses went through a washout period of 21 days, where they remained free in the pasture, without supplementation with concentrate and without administration of OMPZ.

2.3. Blood Collection and Analysis of Digestive Biomarkers and Other Metabolites

Blood samples were collected in vacuum tubes containing sodium heparin in the following experimental phases: after 12 hours of fasting and 16 hours after administration of treatment (T1), and then 0.5 hours (T2), 1.0 hour (T3), 1.5 hours (T4), 2.0 hours (T5), 3.0 hours (T6), 4.0 hours (T7), 5.0 hours (T8), and 6.0 hours (T9) after supplying the concentrate. The horses received an amount of concentrate equivalent to 3.5 Mcal/digestive energy in their morning meal. During blood collection periods, horses had free access to water but were given no food and were allowed to remain free in the stall.

Blood samples were immediately centrifuged, and the plasma samples obtained were divided into two aliquots. One was immediately used to determine glucose and total plasma protein (TPP), and the other was frozen to determine the concentrations of urea ([URE]), creatinine ([CREAT]), uric acid ([UrAc]), total cholesterol ([COLE-T]), triglyceride ([TRIG]), calcium ([Ca]), phosphorus ([P]), and magnesium ([Mg]) at a later time.

Plasma glucose concentration ([GLUC]) was measured using a portable glucometer (Accu11 Check Advantage II, Roche, Germany), which had been validated for use in equines [17]. The concentration of TPP ([TPP]) was obtained with a refractometer. Concentrations of the other biomarkers (URE, CREAT, UrAc, COLE-T, TRIG, calcium, phosphorus, and magnesium) were obtained with the use of commercial kits (Doles Reagent) and semiautomatic biochemistry equipment (Doles D 250; Doles). The area under the curve (AUC) for glucose was calculated according to the method described in the literature [18,19]. The analysts had no knowledge of the experimental group to which the animals had been allocated.

2.4. Statistical Analysis

Results were analyzed by two-way analysis of variance for repeated measures. Post hoc tests were performed using Tukey test. The significance level was set at $P < .05$ for all tests. SigmaStat 3.0 (SPCC Inc, Jandel Scientific, San Rafael, CA) for Windows 7 was used for all analyses. The results were expressed as the means ± standard error of the mean.

3. Results and Discussion

The results of this experiment demonstrated that different doses of omeprazole (OMPZ), interfered with the concentration of some blood biomarkers in healthy animals, even when administered 16 hours before concentrate