EFFECT OF ORALLY ADMINISTERED SODIUM BICARBONATE ON CAECAL PH

by

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B.S., University of Washington, June 2004
D.V.M., University of California, Davis, June 2010

A REPORT

submitted in partial fulfillment of the requirements for the degree

MASTER OF SCIENCE

Department of Biomedical Sciences
College of Veterinary Medicine

KANSAS STATE UNIVERSITY
Manhattan, Kansas

2014

Approved by:

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2014

Abstract

Effect of orally administered sodium bicarbonate on caecal pH

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Reasons for performing study: Caecal acidosis is a central event in the metabolic cascade that occurs following grain overload. Buffering the caecal acidosis by enterally administered sodium bicarbonate may be beneficial to affected horses.

Objectives: To determine the effect and duration of enterally administered sodium bicarbonate ($NaHCO_3$) on caecal pH in healthy horses.

Study design: Prospective controlled study using normal horses with caecal cannulas

Methods: 9 horses previously fitted with a caecal cannula. 6 horses received 1.0 g/kg bwt $NaHCO_3$ via nasogastric tube and 3 control horses were given 3 L of water via nasogastric tube. Clinical parameters, water consumption, venous blood gases, caecal pH, faecal pH and faecal water content were measured at 6 hour intervals over a 36 hour study period.

Results: Horses that received enterally administered $NaHCO_3$ had a significantly increased caecal pH that lasted the duration of the study. Treated horses increased their water intake, developed metabolic alcalemia, significantly increased sodium concentrations and significantly decreased potassium concentrations.

Conclusions and potential relevance: Enterally administered $NaHCO_3$ may be beneficial in buffering the caecal acidosis that occurs following an acute carbohydrate overload.

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Chapter 1- Introduction

Horses are hindgut fermenters, with complex carbohydrates metabolized by bacteria in the caecum. Sudden increases in rapidly fermentable carbohydrates cause a proliferation in bacterial species that produce lactate as a byproduct of fermentation, causing caecal and faecal pH to decrease significantly [1-3]. Additionally, following caecal acidosis, the mucosal barrier of the caecum is damaged, increasing its permeability. This results in the absorption of lactic acid and bacterial endotoxin or exotoxin into the systemic circulation [4; 5]. In 2000 the USDA Animal Health and Monitoring System published that over 50% of laminitis cases result from ingestion of an excessive amount of carbohydrate [6].

Carbohydrate overload has been used to reliably produce laminitis in several studies [3; 7; 8] .These studies were able to demonstrate the systemic effects of lactic acidaemia by measuring haematological and biochemical parameters, including caecal and faecal pH.

The current standard of treatment for the prevention of laminitis following acute grain overload is gastric lavage to remove the gastric contents if detected prior to gastric emptying and mineral oil administration in the hopes of speeding transit through the large intestine [9]. The authors are aware of no attempts to prevent caecal acidosis by buffering caecal contents.

Sodium bicarbonate ($NaHCO_3$) has long been used in horses for the correction of metabolic acidosis. It has been used safely in healthy horses up to a dose of 1.5g/kg bwt enterally. Administration at this dose resulted in a significant increase in blood pH and bicarbonate concentration within one hour after administration [10]. Using caecal infusions of sodium carbonate (Na_2CO_3), Willard et al (1977) [11] demonstrated that caecal pH increased, however to our knowledge, the effects of enterally administered $NaHCO_3$ on caecal pH have not been investigated. Thus, it is our objective to investigate the effect and duration of enterally administered sodium bicarbonate on caecal pH in healthy horses to be used as a potential treatment following ingestion of an acute carbohydrate overload.

Chapter 2- Materials and Methods

This project was approved by the Kansas State University Institutional Animal Care and Use Committee.

Nine healthy, mature, Quarter horses (4 mares and 5 geldings) previously fitted with caecal cannulas were used in this study [12]. Average body weight of the horses was 531 kg (range 429 to 628 kg). All horses were housed individually in stalls, fed hay ad libitum, and had free access to water. Six horses were randomly allocated to the treatment group (T) and 3 horses were used as controls (C). Treatment group horses received 1g/kg bwt $NaHCO_3$ [Arm & Hammer® baking soda][1] via a nasogastric tube in 3 L water and control horses received 3 L water via nasogastric tube. Water intake was measured every 6 hours for 24 hours before the start of the study and thereafter every 6 hours for a 36 hour study period. Heart rate, respiratory rate, and rectal temperature were recorded every six hours.

Blood Collection and Analysis

Prior to the start of the study each horse had a 14 gauge intravenous catheter [Abbocath®-T][2] placed in the left jugular vein for serial collection. Blood samples were collected preceding the administration of sodium bicarbonate and thereafter at 6 hour intervals for a 36 hour study period. A 3 ml blood sample was collected in plastic lithium heparin tubes for measuring of packed cell volume (PCV) and plasma protein (PP) concentrations. A 2 ml blood sample was collected anaerobically into a heparinized [Heparin Sodium Injection, USP][3] syringe, which was capped and kept on ice until blood gas analysis was performed within 20 min of collection. Blood pH, PCO_2, PO_2, bicarbonate and electrolyte concentrations were measured by a blood gas analyzer [NOVA Stat Profile Critical Care Xpress][4]. Packed cell volume (PCV) was determined using a microhematocrit centrifuge and plasma protein (PP) was measured using a refractometer. Each sample was run in duplicate.

Faecal pH and faecal water content

Fresh faeces were collected at 6 hour intervals to measure faecal pH and faecal water content. Two grams of faeces were placed into a small plastic container with equal weight deionized water, vortexed for 20 seconds and pH was measured using a pH meter [Thermo Scientific Orion Star™ Series pH Meter][5]. Faeces were frozen at -20° C until analyses were performed, at which time they were thawed to room temperature. Twenty grams of faeces were

weighed, dried in an incubator at 90 to 100° C for 30 hours and weighed again. Faecal water content was calculated using the following formula:

Water content = 100 x (wet weight – dry weight)/wet weight

Caecal pH

Caecal fluid pH readings were taken at 6 hour intervals with a pH electrode [Thermo Scientific Orion Star™ Series pH Meter][4]. Approximately 0.5 L of caecal contents were manually removed from the caecum and the calibrated pH electrode was placed directly into contents for accurate measurement.

Statistical analysis

Generalized linear models were used to evaluate potential associations between the outcome of interest with treatment groups, C and T, time (every 6 hours for 36 hours), and the interaction between time and treatment group, with a significance set at $P < 0.05$. Outcomes of interest included caecal pH, faecal pH, water consumption, faecal water content and concentrations of blood constituents. An effect was included in all models to account for repeated measures on individual horses. Where interactions were deemed significant ($P < 0.05$), a Tukey's comparison was used to evaluate potential differences between treatment groups at specific hours ($P < 0.01$). All values are reported as mean ± standard error (s.e).

Chapter 3- Results

All horses had normal clinical parameters upon entry into the study and the vital parameters remained within normal limits throughout the duration of the study.

Water intake

The effect of treatment on water intake was modified by time relative to treatment. Water intake was not significantly different between the horses in the control and treatment groups for the 24 hours preceding the administration of $NaHCO_3$. There was an interaction between treatment group and water intake ($P < 0.01$). At 6 and 12 hours post administration, T horses consumed significantly more water than C horses. After 6 hours post-treatment, T horses consumed 22.3 ± 1.5 L and C horses consumed 11.3 ± 2 L. Between 6 hours and 12 hours T horses consumed 17.1 ± 1.5 L and C horses consumed 5 ± 2 L ($P < 0.01$) (Figure 3.1).

Venous Blood Gas Analysis

Administration of $NaHCO_3$ induced a metabolic alcalemia ($P < 0.01$) (Figures 3.2 and 3.3) by 6 hours following treatment. The increase in pH (7.51 ± 0.0) and bicarbonate (35.7 ± 0.7) peaked at 6 hours after $NaHCO_3$ administration and was significantly elevated compared to C horses for 18 and 24 hours ($P < 0.01$).

Venous PCO_2 was increased at 6 hours after treatment administration in horses receiving $NaHCO_3$ (44.4 ± 1.2 mmHg) compared to horses receiving water alone (38 ± 1.6 mmHg).

Packed Cell Volume and Plasma Protein

Administration of $NaHCO_3$ had no effect on PCV and PP.

Serum electrolytes

Administration of $NaHCO_3$ induced a significant and persistent increase in sodium concentration and decrease in potassium concentration in serum ($P < 0.05$). Compared to C horses these changes remained for 30 hours after administration of $NaHCO_3$ in T horses (Figures 3.4 and 3.5). There were no significant changes in the serum concentrations of chloride, calcium and magnesium between the treatment and control groups.

Faecal pH and faecal water content

There was no significant difference between the faecal pH or faecal water content of horses administered water and those administered $NaHCO_3$. Although there was a trend for horses given $NaHCO_3$ to have a higher faecal pH, this was not statistically significant ($P = 0.07$).

Caecal pH

Administration of $NaHCO_3$ resulted in an increase in the caecal pH of T horses that lasted the entirety of the study ($P < 0.05$) (Figure 3.6). In the control horses there was a decrease in cecal pH at time 6 hours (6.3 ± 0.07) and again at time 24 hours (6.3 ± 0.07).
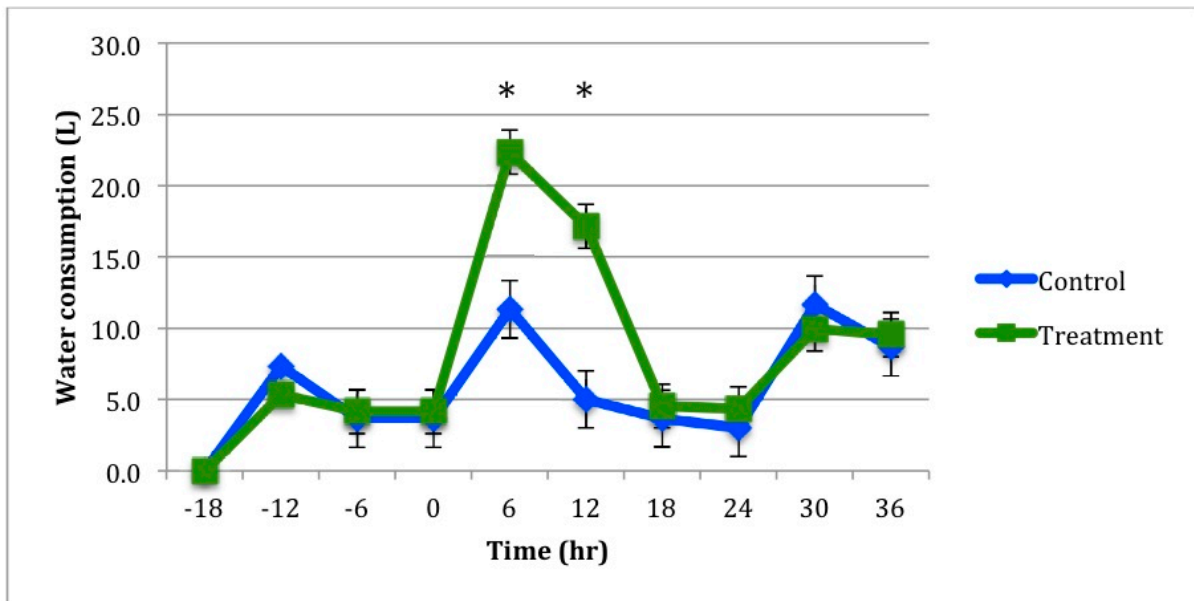
Water Consumption

Figure 3.1: Water consumption (L) of horses 18 hours prior to administration of enteral $NaHCO_3$

and 36 hours following administration. Time 0 indicates when $NaHCO_3$ was administered.

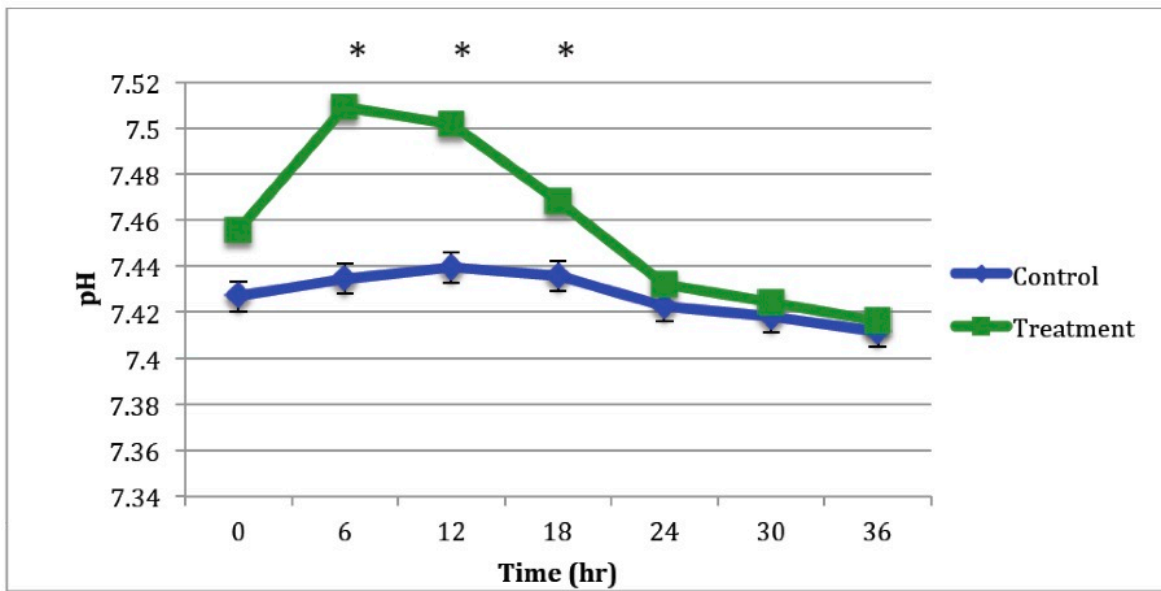*Significant difference ($P < 0.01$).

Blood pH

Figure 3.2: Blood pH values for horses administered $NaHCO_3$ and control horses. Time 0 indicates when $NaHCO_3$ was administered. *Significant difference ($P < 0.01$).
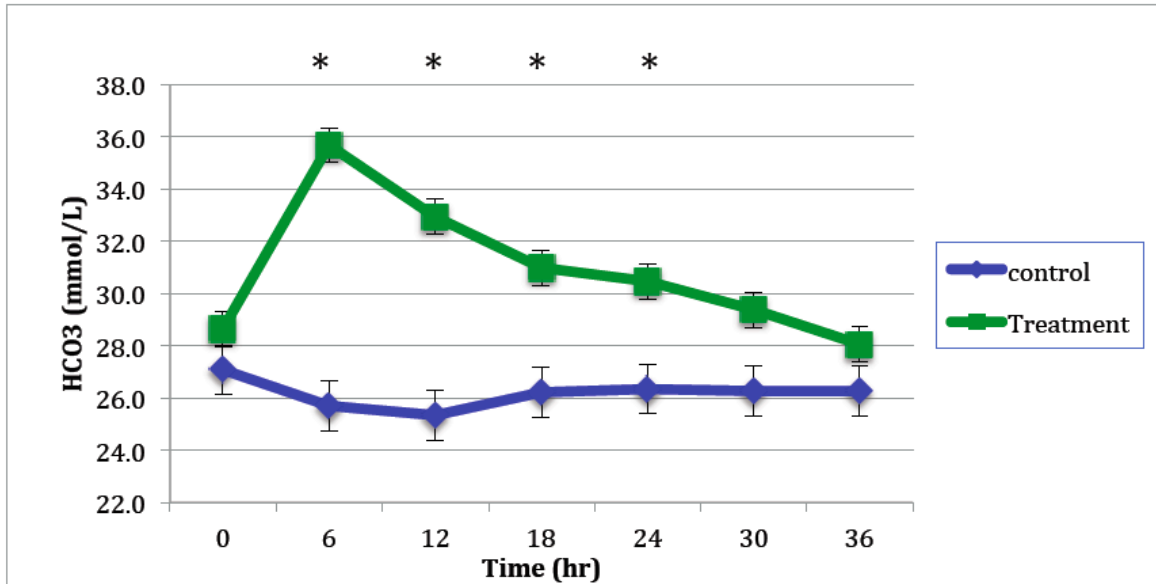
Plasma Bicarbonate

Figure 3.3: Plasma bicarbonate values (mmol/L) for horses administered $NaHCO_3$ and control

horses. Time 0 indicates when $NaHCO_3$ was administered. *Significant difference ($P < 0.01$).
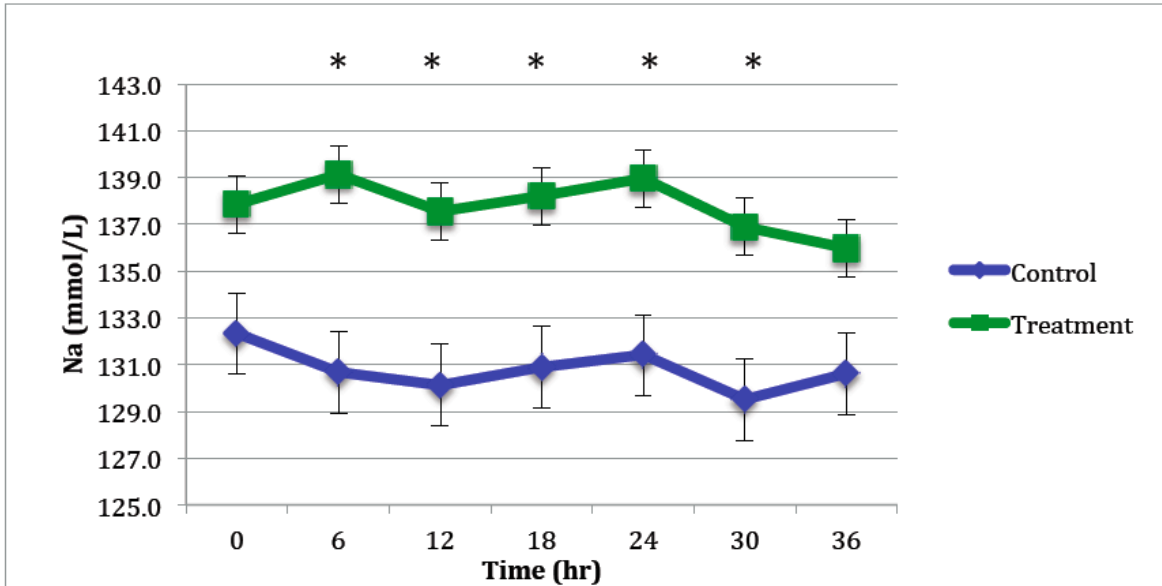
Plasma Sodium

Figure 3.4: Plasma concentrations of sodium (mmol/L) for horses administered $NaHCO_3$ and control horses. Time 0 indicates when $NaHCO_3$ was administered. *Significant difference ($P < 0.01$).

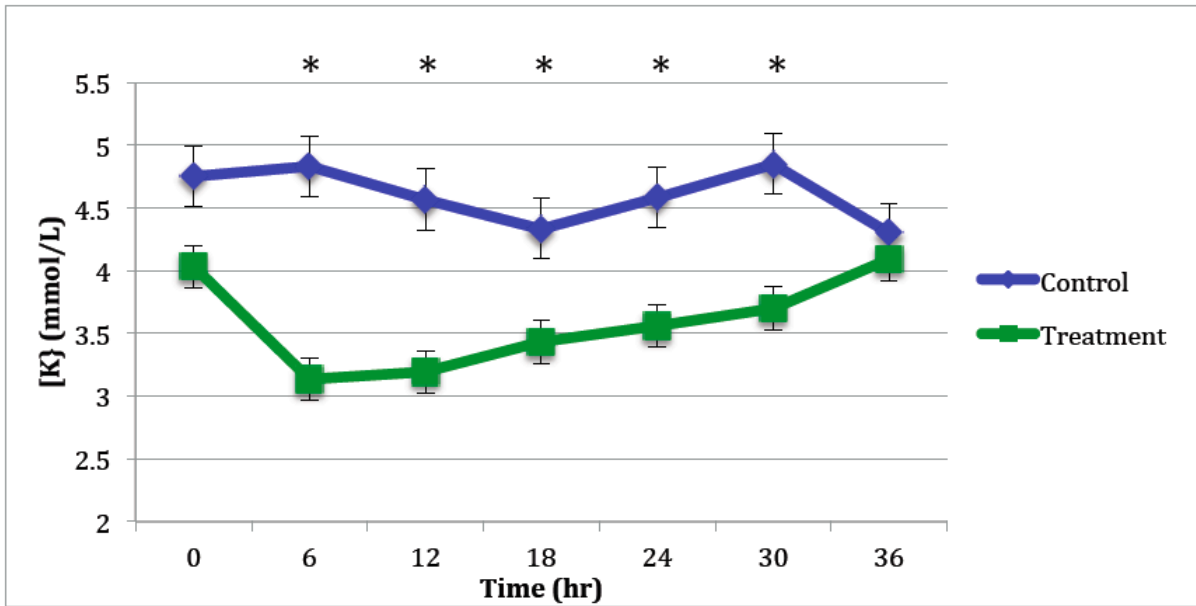## Plasma Potassium

Figure 3.5: Plasma concentrations of potassium (mmol/L) for horses administered $NaHCO_3$ and control horses. Time 0 indicates when $NaHCO_3$ was administered. *Significant difference (P < 0.01).
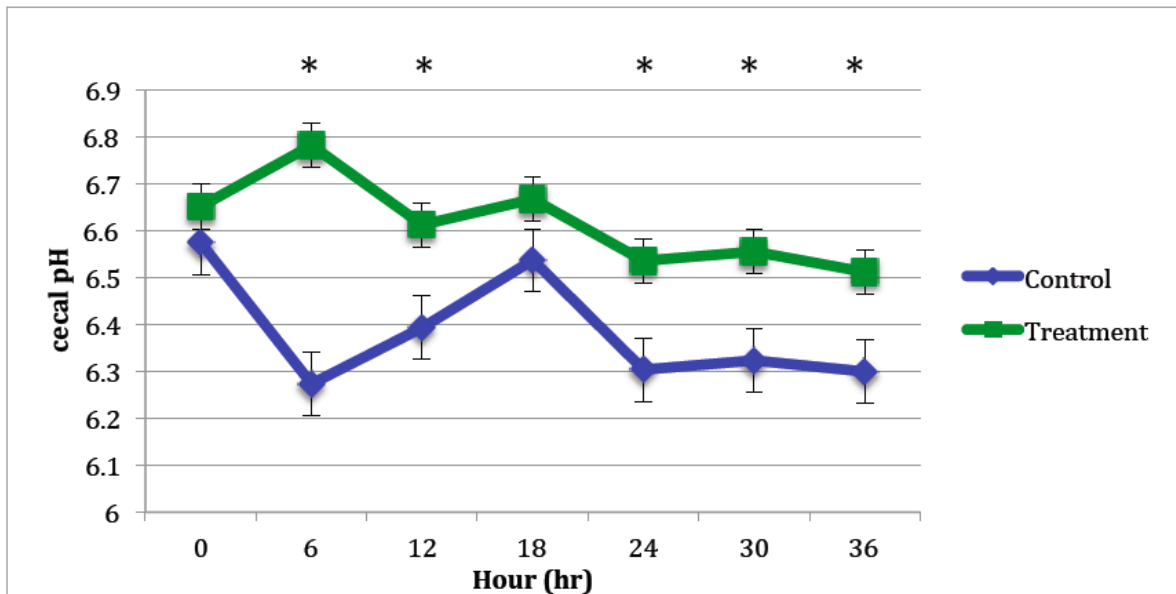
Caecal pH

Figure 3.6: Caecal pH values for horses administered $NaHCO_3$ and control horses. Time 0 indicates when $NaHCO_3$ was administered. *Significant difference ($P < 0.01$).

Chapter 4- Discussion

The results of this study suggest that enteral administration of $NaHCO_3$ to healthy horses causes significant changes in caecal pH, water consumption and certain blood parameters. The effects of orally administered $NaHCO_3$ on blood constituents in resting horses have been previously outlined [10; 13-15]. Although experimental designs differ among these studies, the conclusions were similar and in accordance with our results. With an oral dose of 1.0 g/kg bwt $NaHCO_3$, we were able to induce a metabolic alcalemia. Similar to Corn et al (1993), Kline et al (1995), Llyod et al (1995) and Rivas et al (1997), our results showed a significant and persistent increase in serum concentrations of sodium and significant and persistent decrease in serum concentrations of potassium in the $NaHCO_3$ treated horses.

During the induction of experimentally induced laminitis, caecal and faecal pH consistently and rapidly drop to values as low as 4.0 as early as 8 hours after carbohydrate administration [1-3; 16]. This decrease, following the rapid proliferation of Gram-positive bacteria [2; 17] has been hypothesized to cause a massive die off of bacteria which potentially release toxic substances that are absorbed through a transiently permeable caecal wall [4; 5].

In 1977, Willard et al [11] measured caecal pH in cannulated horses fed hay only, concentrate only or concentrate plus hourly caecal infusions of Na_2CO_3. They reported that Na_2CO_3 administration significantly increased caecal pH in horses being fed a concentrate diet. Although they did not use $NaHCO_3$ as we did, they were able to demonstrate that caecal pH can be manipulated.

In our study, we were able to significantly increase caecal pH in healthy horses following oral administration of $NaHCO_3$. This increase was present as early as 6 hours and lasted the duration of the 36 hour study period. This demonstrates that $NaHCO_3$ effectively reaches the caecum and has the ability to buffer its contents. There was a decrease in caecal pH at 6 and 24 hrs in the control horses. This decrease coincides with the once daily feeding of grain that these horses were receiving and we believe the cause of the decreased pH is likely the result of the ingested carbohydrate. Similarly, Willard et al (1977) [11] demonstrated the mean caecal pH in horses is at its lowest four to six hours after being fed grain. In contrast however, there was only a trend for faecal pH to be increased in treatment horses. A likely explanation for this to the ability of the large colon to absorb the bicarbonate ion, thus the pH returning to normal before reaching the rectum.

Lloyd et al and Kowalski et al [15; 18] measured water intake following the administration of $NaHCO_3$, and their results are similar to ours. As $NaHCO_3$ is absorbed into circulation, the concentration of Na^+ and HCO_3^- are increased, increasing the tonicity of the serum. This drives the thirst sensation and subsequent increase in water consumption [19]. Although water intake increased in our study, in accordance with what others have reported [15], faecal water content did not differ between treatment and control horses in our study. This can be attributed to the ability of the large colon to absorb great quantities of water [20].

Oral administration of 1 g/kg $NaHCO_3$ is safe to use in horses, with none of our treatment horses showing any adverse effects. Rivas et al (1997) noticed transient watery diarrhea in one horse following administration of 1.0 g/kg $NaHCO_3$, however, he also administered $NaHCO_3$ safely to horses at doses up to 1.5 g/kg [10]. Caecal pH was increased from 6.6 to 6.8 in healthy horses receiving 1 g/kg of $NaHCO_3$ by 6 hours following treatment and lasted throughout the duration of the study. This correlates with slightly less than two-fold decrease in the concentration of H^+ ions. Although we observed a significant increase in caecal pH in our study, it is difficult to determine if this would be sufficient to buffer the quantities of lactic acid produced in grain overload cases. To do so would require us to challenge these horses with oligofructose in models similar to what Pollitt and others have used to induce laminitis. This was not done because these horses are part of an ongoing series of nutritional studies and too valuable to take the risk of inducing laminitis. In conclusion, administration of $NaHCO_3$ has a rational basis following acute grain overload, however to what extent it will buffer the caecal acidosis has yet to be established and will require further investigation in an oligofructose-challenged population of horses.

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