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EFFECTS OF SODIUM BICARBONATE ON FLUID, ELECTROLYTE AND ACID–BASE BALANCE IN RACEHORSES

D. R. LLOYD and R. J. ROSE*

Department of Veterinary Clinical Sciences, University of Sydney, New South Wales 2006, Australia

SUMMARY

Sodium bicarbonate given by nasogastric tube has been used by some trainers as the key ingredient in a 'milkshake'. It has been suggested that such treatment given 3–5 h prior to racing may enhance a horse's racing performance by increasing the blood buffering capacity and enhancing lactate clearance from skeletal muscle, thereby delaying the onset of fatigue. Several experiments were conducted to examine the effects on fluid, electrolyte and acid–base values of 0.5 g kg^{-1} dose of sodium bicarbonate, were examined. The effects of fasting, the simultaneous administration of glucose (0.5 g kg^{-1}) or the withholding of water were also examined to determine whether they influenced the uptake and elimination of sodium bicarbonate. Six Thoroughbred horses were used, each wearing a urine and faecal collection harness. Prior to sodium bicarbonate administration, venous blood, urine and faecal samples were collected for 24 h to establish control values. After administration of sodium bicarbonate (0.5 g kg^{-1}) in 2 l of water, samples were collected at various times for up to 46 h. There were significant increases in water consumption, from 0.5–2.3 l h^{-1} at 2 h post-administration. Urine output increased by approximately three fold and did not return to control levels until 18 h post-administration. Urinary sodium concentration increased from 95 ± 16 mmol l^{-1} (mean ± SEM) to peak values of 349 ± 12 mmol l^{-1} at 12 h. In the 24 h after sodium bicarbonate administration, approximately 80% of the sodium intake ($NaHCO_3$+feed) was excreted in the urine. There was no significant change in the total urinary potassium and chloride excretion. Faecal water content did not change following sodium bicarbonate administration, but there was an increase in faecal sodium content. The mean increase in venous blood bicarbonate concentration was 7.6 ± 0.4 mmol l^{-1} after the 0.5 kg^{-1} dose. Water deprivation for 6 h after

*To whom correspondence should be addressed.

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sodium bicarbonate administration, fasting or the co-administration of glucose did not affect the peak blood bicarbonate concentration or the time to peak concentration. However, the withholding of water did result in a faster rate of decrease in blood bicarbonate concentration when water was resupplied.

KEYWORDS: Sodium bicarbonate; milkshake; horse; electrolyte; acid–base.

INTRODUCTION

Sodium bicarbonate has been administered to racehorses, as the main ingredient in a 'milkshake', prior to racing with the expectation that it can improve performance by delaying the onset of fatigue (Rose & Lloyd, 1992). There is no clearly defined formula for a 'milkshake' and there have been reports of a number of other ingredients, apart from sodium bicarbonate, being included. Some of the common constituents are glucose, sodium chloride, potassium chloride, vitamin E, sugar (sucrose), glycopyrraline, and beta-agonists such as clenbuterol and salbutamol (Swann, 1990; Roelofson, 1992; Rose & Lloyd, 1992). These ingredients are generally mixed together in approximately 2–3 l of water and administered to a racehorse via a nasogastric tube.

The changes in acid–base status that are caused by the administration of sodium bicarbonate at doses of 0.3–1.0 g kg^{-1} in horses have been investigated in several studies (Kelso *et al.*, 1987; Lawrence *et al.*, 1987a, b; Greenhaff *et al.*, 1990, 1991a, b; Roberts *et al.*, 1991; Harkins & Kamerling, 1992; Kline *et al.*, 1992; Hanson *et al.*, 1993; Lloyd *et al.*, 1993). Most of these studies have examined the effects of sodium bicarbonate administration over a 3–6 h period, while one study monitored changes in acid–base status up to 24 h (Greenhaff *et al.*, 1990). However, the effects of sodium bicarbonate administration on the overall fluid and electrolyte balance in the racehorse have not been investigated. The administration of large doses of sodium bicarbonate have been shown to cause fluid shifts, reflected by changes in the plasma total protein concentration (Roberts *et al.*, 1991; Greenhaff *et al.*, 1991a), as well as alterations in serum sodium (Na^+), potassium (K^+) and chloride (Cl^-) concentrations (Greenhaff *et al.*, 1991a; Hanson *et al.*, 1993). It is likely that there will be alterations in the concentration of urinary electrolytes as well.

While venous blood bicarbonate (HCO_3^-) or total carbon dioxide (TCO_2) concentration can provide a reliable indication of sodium administration (Irvine, 1992; Roelofson, 1992; Auer *et al.*, 1993), it may be possible to use urinary measurements as a screening test to determine whether an alkalinizing agent has been administered. This would avoid the need for venepuncture. The measurement of urinary pH or urine Na^+ concentration could provide an indication of the administration of sodium bicarbonate.

The effects on the fluid, electrolyte and acid–base balance of 0.5 g kg^{-1} dose of sodium bicarbonate in the racehorse were examined in experiment 1. The dose rate of 0.5 g kg^{-1} was used as it was reported to be the dose most commonly given to horses prior to racing. The highest reported dose rate of sodium bicarbonate

that has been administered to horses is 1.0 g kg^{-1} (Hinchcliff *et al.*, 1991; Kline *et al.*, 1992; Hanson *et al.*, 1993; Lloyd & Rose, 1995), while other studies have used dose rates of 0.3 g kg^{-1} (Lawrence *et al.*, 1987a, 1990).

As part of the pre-race routine, some trainers deny their horse access to water for several hours prior to racing so the horses do not carry a large fluid load during a race. While withholding water from horses for 6 h has been demonstrated to have no significant effects on the horses' acid–base status (Hanson *et al.*, 1993), it is possible that denying horses access to water could act in conjunction with a dose of sodium bicarbonate to produce a more profound alkalosis. If a large dose of sodium bicarbonate was also administered then the lack of access to water may have an effect on the blood HCO_3^- concentration. In experiment 2 a dose of sodium bicarbonate equivalent to that used in experiment 1 was given to the horses while denying them water for a 6 h period. The effects on the fluid, electrolyte and acid–base balances were then monitored to examine how water restriction influenced the horses' response.

When sodium bicarbonate is administered to a racehorse as a 'milkshake' it is often given in conjunction with a number of other ingredients, such as glucose (Rose & Lloyd, 1992). The inclusion of glucose and other substances will increase the osmolality of the solution, which may then influence the rate at which the contents are absorbed. It is not known precisely how much glucose is administered, but from questioning of trainers it seems that approximately 200 g of glucose is often given. Another factor which may influence the rate at which sodium bicarbonate is absorbed is the presence of feed in the stomach. If sodium bicarbonate is administered to a horse that has been fasted then it is possible that sodium bicarbonate will be absorbed more rapidly than if food was present. In experiment 3, the effects of overnight fasting were compared with feeding in horses administered sodium bicarbonate. In addition, glucose was added to the sodium bicarbonate solution to determine whether absorption of sodium bicarbonate was affected.

These experiments indicated that sodium bicarbonate administration resulted in substantial changes in fluid, electrolyte and acid–base balance, reflected in altered plasma and urinary electrolyte concentrations. Many of these findings have important implications for regulatory authorities who are concerned with the regulation and detection of agents that can produce metabolic alkalosis in racehorses.

MATERIALS AND METHODS

1. Administration of 0.5 g kg^{-1} sodium bicarbonate

Six Thoroughbred horses, each wearing urine and faecal collection harnesses, were placed in crushes. The harnesses were designed with a reservoir to permit quantitative collection of urine and faeces for each sampling period. For control values, venous blood, urine and faecal samples were collected every 6 h over the next 24 h period, prior to the administration of sodium bicarbonate. On the second day, a catheter was inserted into the jugular vein and sodium bicarbonate (0.5 g kg^{-1}) was administered via nasogastric tube, in 2 l water. Venous blood and urine samples were collected at the following times (h) post-administration: 0.5, 1,

2, 3, 4, 6, 8, 10, 12, 18, 22, 24, 28, 34, 40 and 46. Faecal samples were collected at 4, 10, 18, 22, 28, 34, 40 and 46 h post-administration. Water was freely available at all times.

At each sampling time, venous blood was collected into 2 ml heparinized syringes, sealed and immediately placed in a crushed ice slurry for blood gas and acid–base analyses (ABL300, Radiometer, Copenhagen, Denmark). A further 10 ml sample of blood was collected into an evacuated tube containing lithium heparin. The plasma was separated, by centrifuging, and analysed for Na^+, K^+, Cl^-, creatinine, total protein and osmolality. Urine was collected from the reservoir attached to the urine collection harness, at the times indicated above when it was freely produced. Volume and pH were measured immediately after collection (PHM83 Autocal pH meter, Radiometer, Copenhagen, Denmark). Portions were stored at −80°C for measurements of Na^+, K^+, Cl^-, creatinine, specific gravity and osmolality. Plasma and urinary Na^+ and K^+ concentrations were determined using flame photometry (343 Digital Flame Photometer, Instrumentation Laboratory Inc., Lexington, Kentucky, USA); Cl^- concentration was determined with a chloride titrator (CMT10, Radiometer, Copenhagen, Denmark); osmolality was determined using a vapour pressure osmometer (5500, Wescor Inc., Utah, USA); creatinine concentration was measured on a TDx analyser (Abbott Laboratories Diagnostics Division, Texas, USA) and total plasma protein and urine-specific gravity were measured by refractometry (Reichert refractometer, Cambridge Instruments Inc., Buffalo, USA).

Faeces were collected, weighed and processed, for percentage water, Na^+ and K^+ content. The percentage water content was determined by drying a sample of faeces of known weight for several days in an incubator. The sample was then reweighed and the water content calculated. The Na^+ and K^+ content was determined by the following method. Dry faeces (0.5 g) were weighed into a 50 ml boiling tube and several glass beads were placed in each tube. Nitric acid (5 ml) was added and the tubes allowed to stand overnight. The following morning 5 ml of a 1:1 solution of nitric acid and perchloric acid was added and the tubes heated on a digestion rack. Initially the tubes were heated until boiling and then allowed to simmer for 2 h or until digestion was complete, leaving at least 1 ml of liquid. The remaining solution was made up to 25 ml in a volumetric flask with distilled water and then transferred to a 25 ml container. The samples were stored at room temperature and the Na^+ and K^+ concentration measured using an atomic absorption spectrometer (Spectra AA.20, Varian Technology Pty Ltd, Australia). The above method was also used to determine the Na^+ and K^+ content of the feed which was 1046 and 2002 mmol, respectively.

The results were analysed by analysis of variance with time as the repeated measures factor. Where the F values were significant ($P<0.05$), a post-hoc Tukey test was used. A paired t-test was used to compare the total quantities of electrolytes that were excreted in the urine. All results are reported as mean ± SEM.

2. Effect of water deprivation on the response to sodium bicarbonate administration

During a period of water deprivation, the effects of sodium bicarbonate administration were examined on fluid, electrolyte and acid–base status. The same six horses used in experiment 1 were also used in this study. The protocol was the

same as in experiment 1, except that the horses were denied access to water for 6 h after the administration of sodium bicarbonate (0.5 g kg^{-1}). Water was resupplied to the horses with their evening feed. Venous blood and urine samples were collected every half hour for 12 h after dosing.

The results were compared with experiment 1 using an analysis of co-variance with time as a repeated measures factor. The results from experiment 2 only were analysed by analysis of variance with time as the repeated measures factor. Where the *F* values were significant, a post-hoc Tukey test was used. It was not possible to perform statistical analysis on the urine data due to the infrequent urination. Results are reported as mean ± SEM. There was a 6 month period between experiments 1 and 2 and so the two experiments should be regarded as independent studies, despite the fact that the same horses were used.

3. The effects of fasting and the co-administration of glucose on the response to sodium bicarbonate administration

Six horses were used in a Latin Square design with three horse pairs and three treatments. On the day before the experiment, the horses' final meal was at 1600 h. Two horses were randomly assigned to each treatment on the first day. The first treatment consisted of feeding the horses at 0630 h and administering sodium bicarbonate (1.0 g kg^{-1}) at 0800 h. The second treatment group had their morning feed withheld and were given sodium bicarbonate (1.0 g kg^{-1}) at 0800 h. The third treatment group had their morning feed withheld and were given sodium bicarbonate (1.0 g kg^{-1}) and glucose (0.5 g kg^{-1}) at 0800 h. The horses were allowed free access to water at all times. Blood samples were collected, via a jugular vein catheter, prior to sodium bicarbonate administration, every half hour for the first 6 h post-administration and then every hour until 12 h. Samples were collected into 2 ml heparinized syringes, sealed and immediately placed in a crushed ice slurry for blood gas analyses within 1 h, as outlined in experiment 1.

The results were analysed using a Latin Square analysis of co-variance, with time as a repeated measures factor. The time to peak HCO_3^- concentration, and the maximum increase in HCO_3^- concentration were determined for each horse, and the effects of the three treatments were compared using an analysis of variance. Results are reported as mean ± SEM.

RESULTS

1. Administration of 0.5 g kg^{-1} sodium bicarbonate

There was little variation in the values obtained from the four sampling times during the 24 h prior to the administration of the treatment, as is evident by the small standard errors. The average of these values provided a good indication of the resting levels for each horse.

The administration of sodium bicarbonate caused a significant increase in water intake from a control level of 0.5 l h^{-1} to a maximum of 2.3 l h^{-1} at 2 h after administration (Fig. 1). There was also an increase in the urine output with the production of 0.8 l h^{-1}, between 3 and 4 h post-administration from a resting rate of 0.23 l h^{-1}. Output had returned to normal levels by 18 h (Fig. 1). It was not poss-

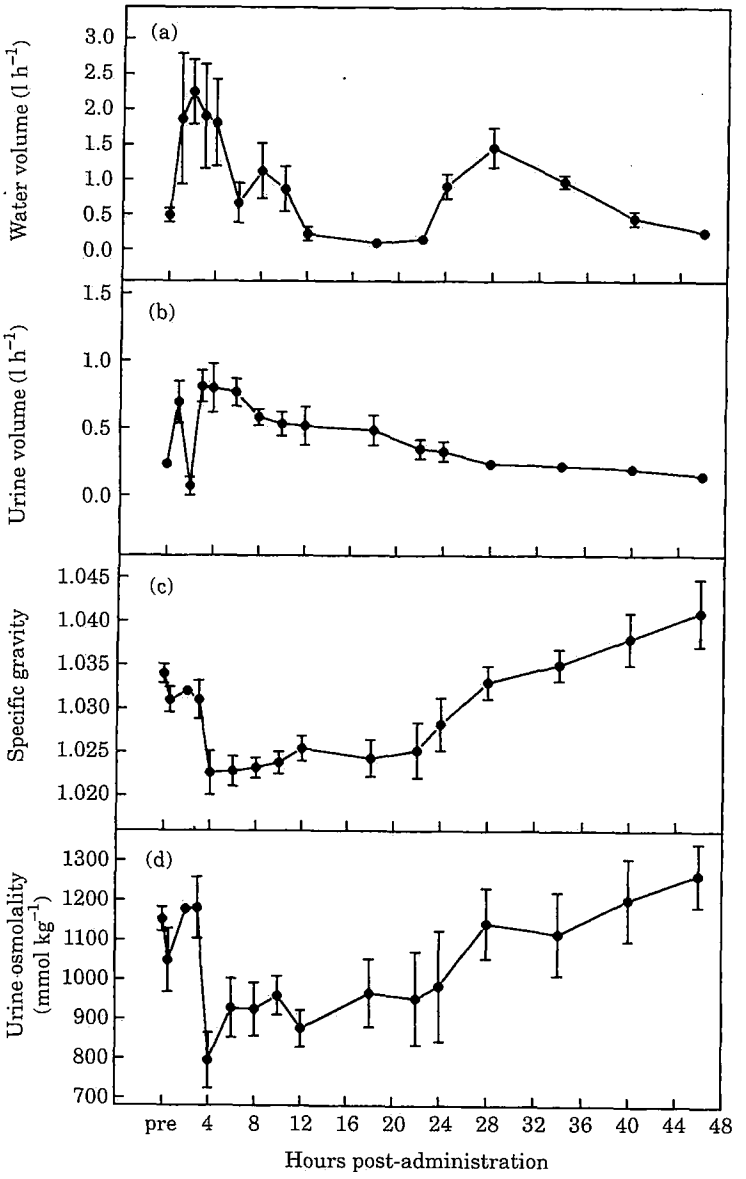

Fig. 1. Changes (mean ± SEM) in (a) water intake, (b) urine volume, (c) specific gravity and (d) urinary osmolality in six Thoroughbred horses after receiving sodium bicarbonate (0.5 g kg^{-1}). The 'pre' value represents the average of the samples collected in the 23 h prior to treatment.

ible to perform statistical analyses on the urinary values as the horses urinated infrequently and not enough urine was produced at each sample time for valid statistical comparisons to be made. The administration of sodium bicarbonate caused a more dilute urine to be produced, as can be seen from the decrease in

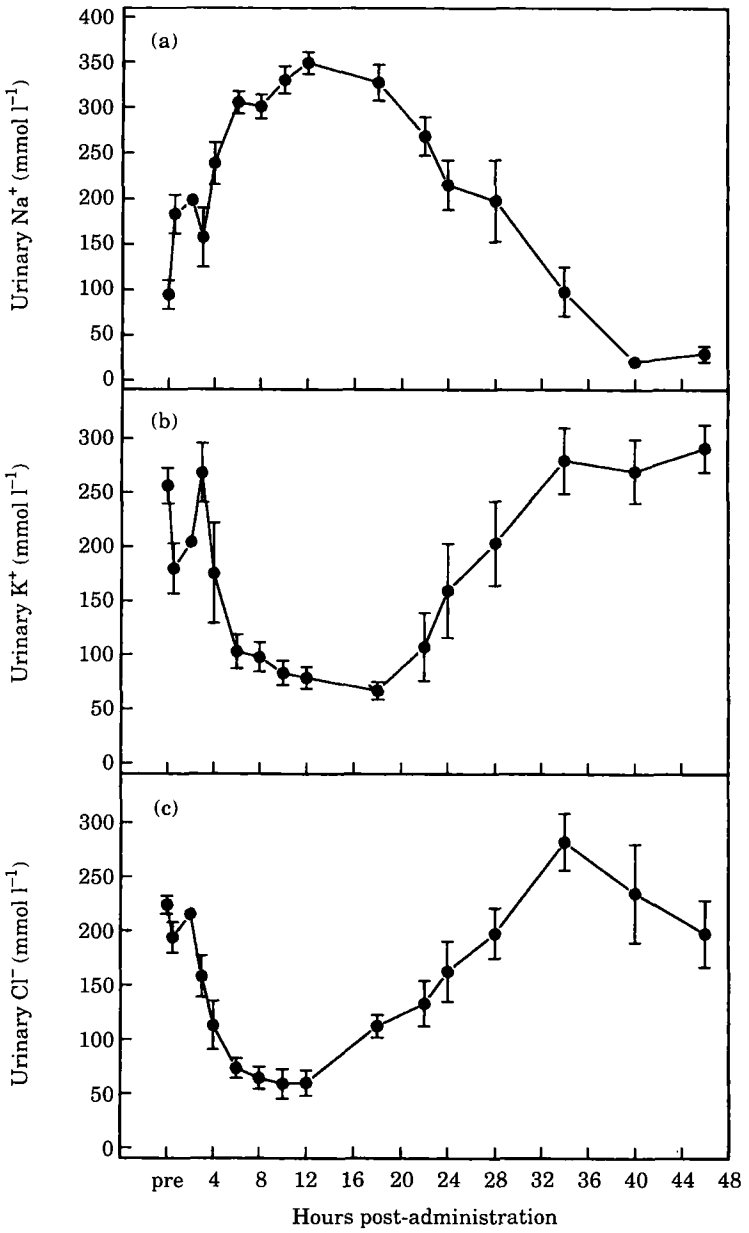

Fig. 2. Changes (mean ± SEM) in (a) urinary sodium (Na^+), (b) potassium (K^+) and (c) chloride (Cl^-) concentrations in six Thoroughbred horses after receiving sodium bicarbonate (0.5 g kg^{-1}). The 'pre' value represents the average of the samples collected in the 24 h prior to treatment.

the specific gravity, and also resulted in a decreased urinary osmolality (Fig. 1). The peak decrease in specific gravity and urinary osmolality occurred at 4 h post-administration, which coincided with the increased urine volume. The specific

gravity and urinary osmolality had returned to control levels at 28 h post-administration, when the rate of urine production had also returned to normal.

There was an increase in the urine Na^+ concentration from 94.9 ± 16.0 mmol l^{-1} to a maximum of 349.3 ± 12.1 mmol l^{-1} at 12 h (Fig. 2), decreasing to control levels by 34 h. Changes in urinary K^+ followed a similar time-course except that a decrease was observed (Fig. 2) from control values of 256.2 ± 16.6 mmol l^{-1} to a minimum value of 66.3 ± 8.1 mmol l^{-1} at 18 h post-administration. The urinary Cl^- concentration also decreased, from the resting concentration of 223.9 ± 8.4 mmol l^{-1} to reach the lowest concentration of 59.2 ± 13.7 mmol l^{-1} at 10 h, returning to the control levels by 28 h (Fig. 2). The total amount of Na^+ excreted in the urine over the 24 h period after sodium bicarbonate administration was 3381 ± 179 mmol. This was significantly higher than the amount excreted during the 24 h prior to administration where only 598 ± 87 mmol were excreted in the urine. The amount of Na^+ excreted in the urine in the 24 h after treatment represented approximately 80% of the total Na^+ intake ($NaHCO_3$+feed). The amount of Cl^- in the urine for 24 h after sodium bicarbonate administration was 1276 ± 97 mmol, which was not significantly different to that in the previous 24 h (1249 ± 99 mmol). The total quantity of K^+ excreted in the urine over the 24 h prior to treatment was 1372 ± 86 mmol, which was also not significantly different from the 1290 ± 71 mmol excreted in the urine over the 24 h following treatment. The fractional Na^+ excretion increased from a control value of 0.41 ± 0.09% to a peak at 3.27 ± 0.52% 6 h post-treatment. This was higher than the range usually encountered in adult horses of 0.2–1.0% (Rose & Hodgson, 1993). The K^+ and Cl^- fractional excretion values were within the normal ranges for horses of 15–65% and 0.04–1.6%, respectively (Rose & Hodgson, 1993) throughout the experimental period.

Sodium bicarbonate administration produced a metabolic alkalosis that was reflected by a significant increase in venous blood pH which rose from an initial level of 7.356 ± 0.005 to a peak of 7.491 ± 0.007 at 4 h post-administration (Fig. 3). The level remained stable for 2 h and then declined and was not significantly different from the resting level at 24 h. As a result of the metabolic alkalosis, the urine became more alkaline and its pH increased from 7.6 ± 0.1 by 0.9 pH units, to 8.5 ± 0.1, over 4 h. The urine pH remained elevated for approximately 20 h when it started to decline and had returned to the control values by 34 h (Fig. 3).

Venous blood carbon dioxide tension (PCO_2) was raised by sodium bicarbonate treatment, changing by approximately 3 torr by 2 h and remaining elevated for the next 10 h, when it started to decrease and was not significantly different from the initial value by 24 h (Fig. 4). The changes in the venous HCO_3^- concentration followed a similar trend to blood pH. Sodium bicarbonate (0.5 g kg^{-1}) caused a mean increase in HCO_3^- concentration of 7.6 ± 0.4 mmol l^{-1}, with an average time to peak concentration of 5.5 ± 0.7 h (Fig. 4). The peak mean concentration was 36.7 ± 0.7 mmol l^{-1}. By 2 h, the HCO_3^- concentration significantly increased from the pre-administration concentration of 30.0 ± 0.3 mmol l^{-1}, and had returned to control levels by 22 h. The time-course for changes in standard bicarbonate (SBC) was similar to those for blood pH and HCO_3^- concentration, with the mean peak level of 33.4 ± 0.6 mmol l^{-1} occurring at 6 h post-administration (Fig. 4).

There was a 4.5 mmol l^{-1} increase in plasma Na^+ concentration over the 4 h

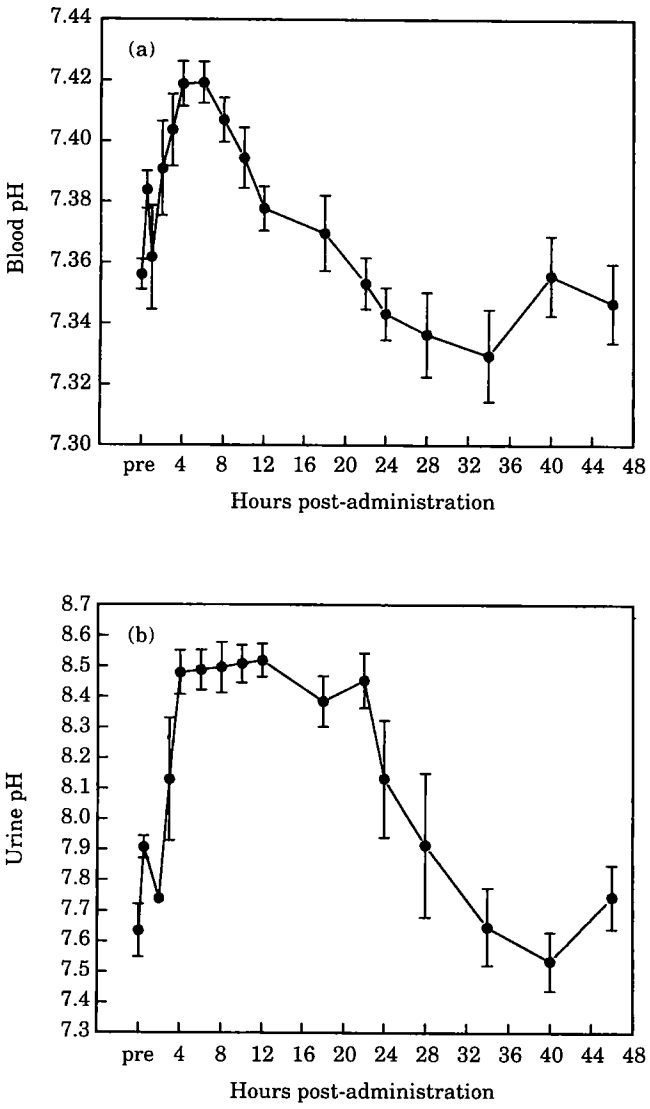

Fig. 3. Changes (mean ± SEM) in (a) venous blood and (b) urine pH in six Thoroughbred horses after receiving sodium bicarbonate (0.5 g kg^{-1}). The 'pre' value represents the average of the samples collected in the 24 h prior to treatment.

following sodium bicarbonate administration, however this increase was not significant (Fig. 5). There were significant decreases in plasma K^+ and Cl^- concentrations (Fig. 5). Plasma K^+ significantly decreased from a control value of 4.0 ± 0.1 mmol l^{-1} to 3.2 ± 0.1 mmol l^{-1} at 6 h but was not significantly different from the control value by 12 h. Plasma Cl^- concentration decreased by a maximum of 2.9 mmol l^{-1} between 4 and 8 h after administration and was not significantly different from the resting value by 12 h.

Initially, the plasma total protein concentration rose by 5 g l^{-1} over the first half

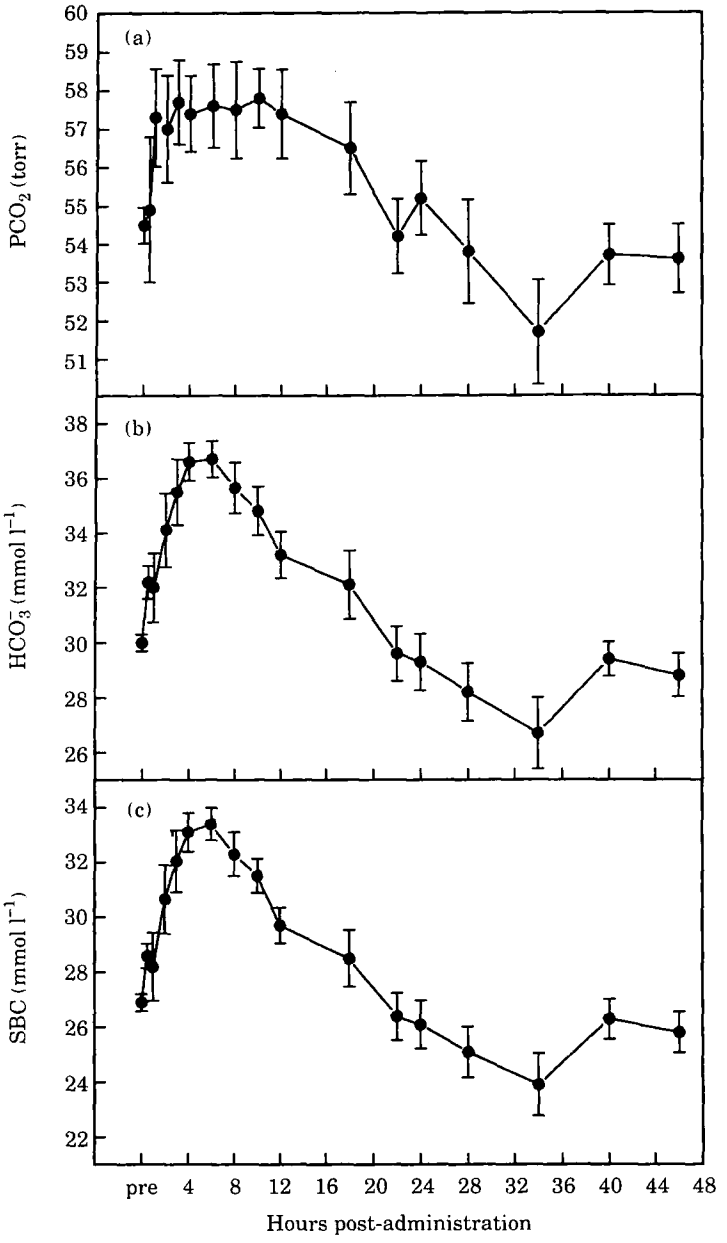

Fig. 4. Change (mean ± SEM) in (a) venous blood carbon dioxide tension (PCO_2), (b) bicarbonate (HCO_3^-) and (c) standard bicarbonate (SBC) concentrations in six Thoroughbred horses after receiving sodium bicarbonate (0.5 g kg^{-1}). The 'pre' value represents the average of the samples collected in the 24 h prior to treatment.

hour and then significantly decreased below the initial value by an average of 4 g l^{-1} between 4 and 6 h. After 6 h it gradually rose until, by 10 h, it was significantly different from the control value (Fig. 6). There was an increase in the

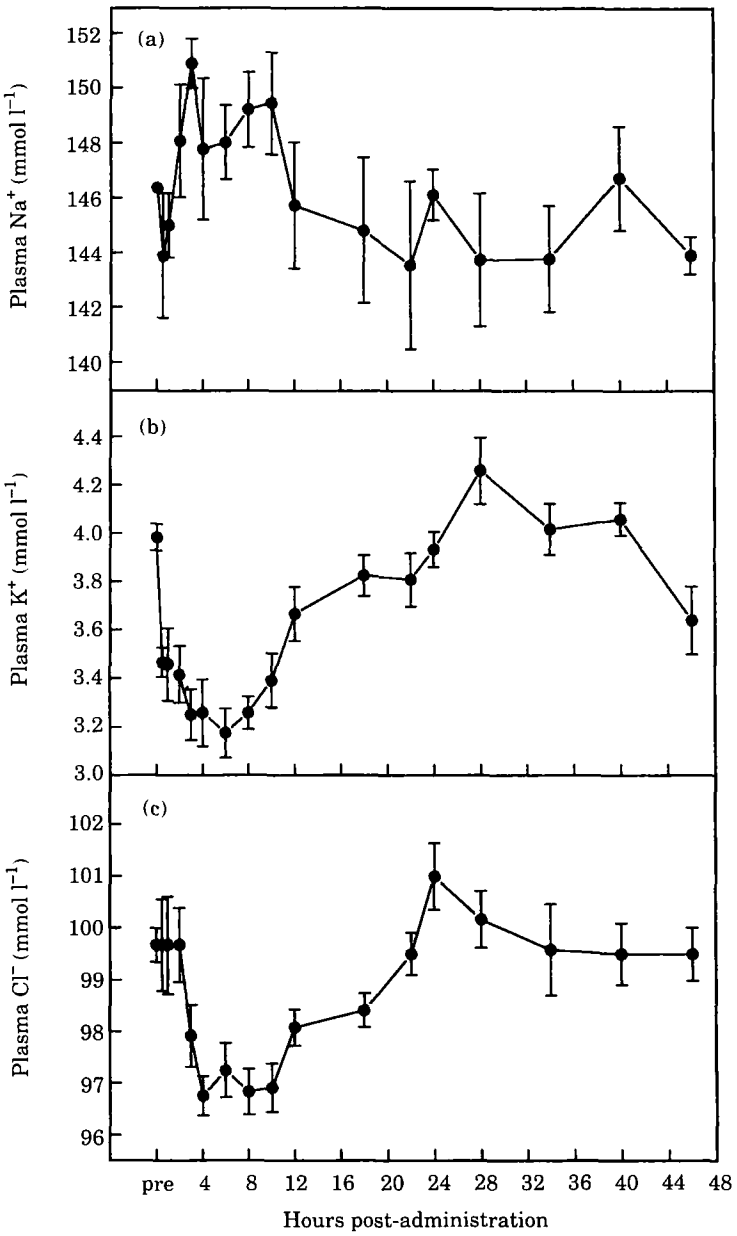

Fig. 5. Changes (mean ± SEM) in (a) venous plasma sodium (Na^+), (b) potassium (K^+) and (c) chloride (Cl^-) concentrations in six Thoroughbred horses after receiving sodium bicarbonate (0.5 g kg^{-1}). The 'pre' value represents the average of the samples collected in the 24 h prior to treatment.

plasma osmolality between 1 and 6 h, from an initial value of 277.9 ± 0.9 mmol kg^{-1} with a mean peak plasma osmolality of 285.8 ± 2.9 mmol kg^{-1} occurring at 1 h (Fig. 6).

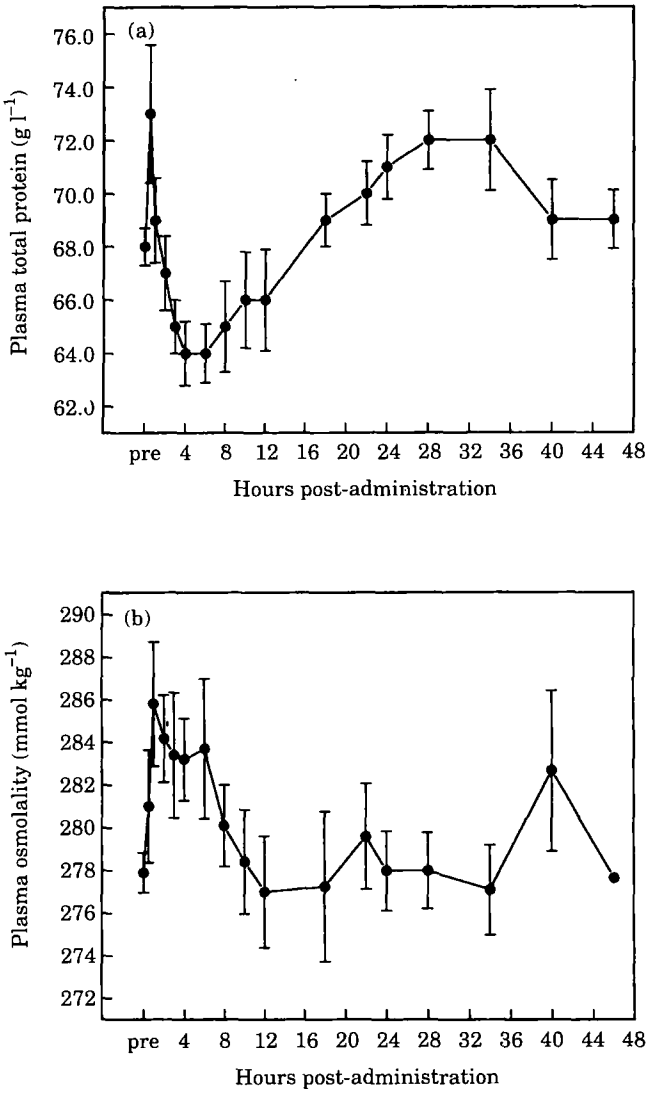

Fig. 6. Changes (mean ± SEM) in (a) venous plasma total protein concentration and (b) osmolality in six Thoroughbred horses after receiving sodium bicarbonate (0.5 g kg^{-1}). The 'pre' value represents the average of the samples collected in the 24 h prior to treatment.

It was not possible to perform statistical analyses on the data derived from the collection of faeces due to the different sample collection times. However it was noted that the percentage water content of the faeces ranged from mean values of 72–78% after the administration of sodium bicarbonate, and did not appear to be different from the control period where the percentage faecal water content was 76.1 ± 0.5%. Over the control period of 24 h, the mean hourly rate of faecal Na^+ elimination was 15.6 mmol h^{-1}, and appeared to increase in the 22 h following sodium bicarbonate administration to mean values of 21.7 mmol h^{-1}. In contrast,

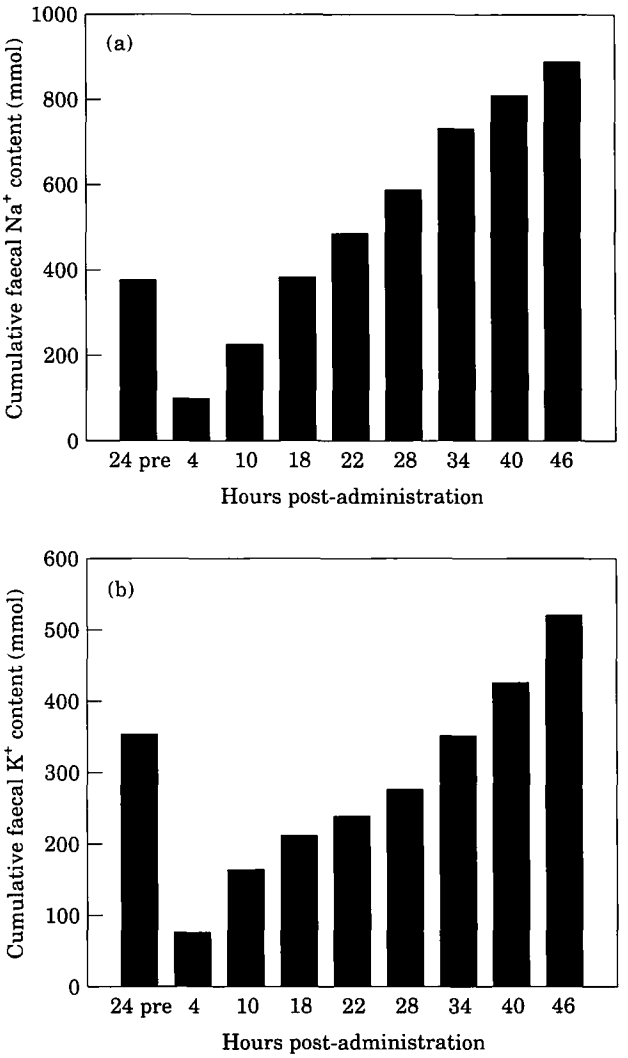

Fig. 7. Cumulative faecal sodium (Na^+) and potassium (K^+) content from six Thoroughbred horses prior to treatment, and for 46 h after administration of sodium bicarbonate (0.5 g kg^{-1}). Values represent the mean output from the six horses at each time. The 'pre' value represents the total output in the 24 h prior to treatment.

faecal K^+ elimination was found to decrease slightly following bicarbonate, from control values of 14.9 to 10.9 mmol h^{-1} in the 22 h after sodium bicarbonate (Fig. 7).

2. Effect of water deprivation on the response to sodium bicarbonate administration

When water was resupplied to the horses 6 h after sodium bicarbonate administration, a large amount of water, 7.5 ± 1.6 l, was consumed within half an hour of availability. When the horses were allowed free access to water they produced over

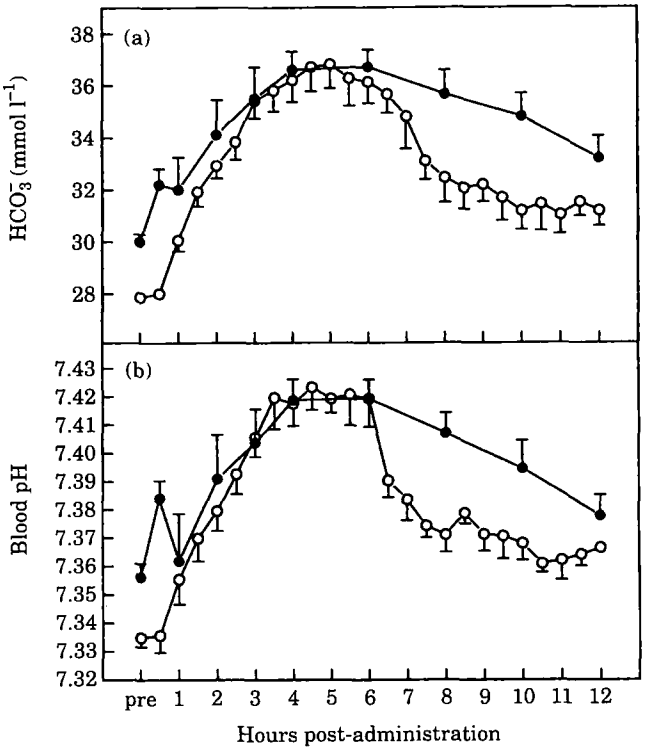

Fig. 8. Changes (mean ± SEM) in (a) venous blood pH and (b) bicarbonate (HCO_3^-) concentration in six Thoroughbred horses after receiving sodium bicarbonate (0.5 g kg^{-1}). Horses were allowed free access to water (●) or were denied access to water for 6 h after treatment (○). The 'pre' value represents the average of the samples collected in the 24 h prior to treatment.

a 12 h period a total of 4.86 l of urine more than those horses that were denied access to water. Changes in specific gravity, urinary osmolality, and urinary Na^+, K^+ and Cl^- concentrations were also similar to those observed when water was freely available. In both experiments there was an increase in urine pH of approximately 1 pH unit, which persisted for 12 h post-administration.

There was significant difference in the shifts in venous blood pH compared with experiment 1, with a peak increase in blood pH of 0.088 pH units when water was withheld compared with an increase of 0.063 pH units when water was freely available (Fig. 8). Blood pH was significantly higher than the control value for the 12 h period after administration. There was a difference in the rate of decline in blood pH between the treatments, with the blood pH decreasing more rapidly in this experiment after water was made available at 6 h. The changes in venous blood HCO_3^- concentration (Fig. 8) were not significantly different to values when water was freely available. However, a similar trend was observed in the HCO_3^- concentrations to blood pH where the levels decreased more rapidly after water was available at 6 h administration, compared with when water was freely available (experiment 1).

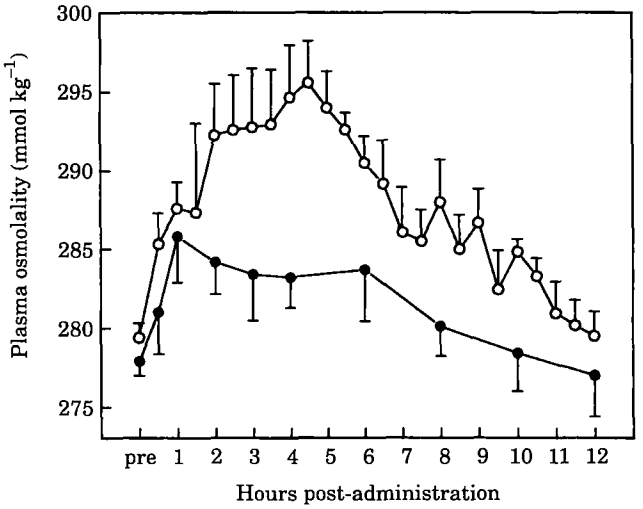

Fig. 9. Changes (mean ± SEM) in venous plasma osmolality in six Thoroughbred horses after receiving sodium bicarbonate (0.5 g kg^{-1}). Horses were allowed free access to water (●) or were denied access to water for 6 h after treatment (○). The 'pre' value represents the average of the samples collected in the 24 h prior to treatment.

Plasma Na^+, K^+ and total protein concentrations were not significantly affected by denying the horses access to water after sodium bicarbonate administration compared with when it was freely available. The plasma Cl^- concentration affected by the availability of water, being slightly higher over the course of the experiment when water was not available after sodium bicarbonate administration. There was a significant difference in plasma osmolality when water was unavailable (Fig. 9). The plasma osmolality continued to rise from a control value of 279.4 ± 0.9 mmol kg^{-1} until it reached a mean peak level of 295.6 ± 2.6 mmol kg^{-1} at post-administration; in experiment 1, peak plasma osmolality was 285.8 ± 2.9 mmol kg^{-1}, 1 h after administration with a decline in values from this point.

3. The effects of fasting and the co-administration of glucose on the response to sodium bicarbonate administration

There were no significant effects of fasting, or the combination of fasting and the co-administration of glucose with sodium bicarbonate, on the venous blood pH, PCO_2, HCO_3^- and SBC concentrations in the 12 h after sodium bicarbonate administration. The changes in each of these measurements were very similar between all three treatments (Fig. 10). When the increase in venous blood HCO_3^- concentration and the time taken to reach the peak HCO_3^- concentration for each horse and for each treatment were compared, no significant differences in either of these measurements were found between the treatment groups.

DISCUSSION

While there have been a number of studies conducted to examine the effects of sodium bicarbonate on performance and acid–base balance (Kelso *et al.*, 1987;

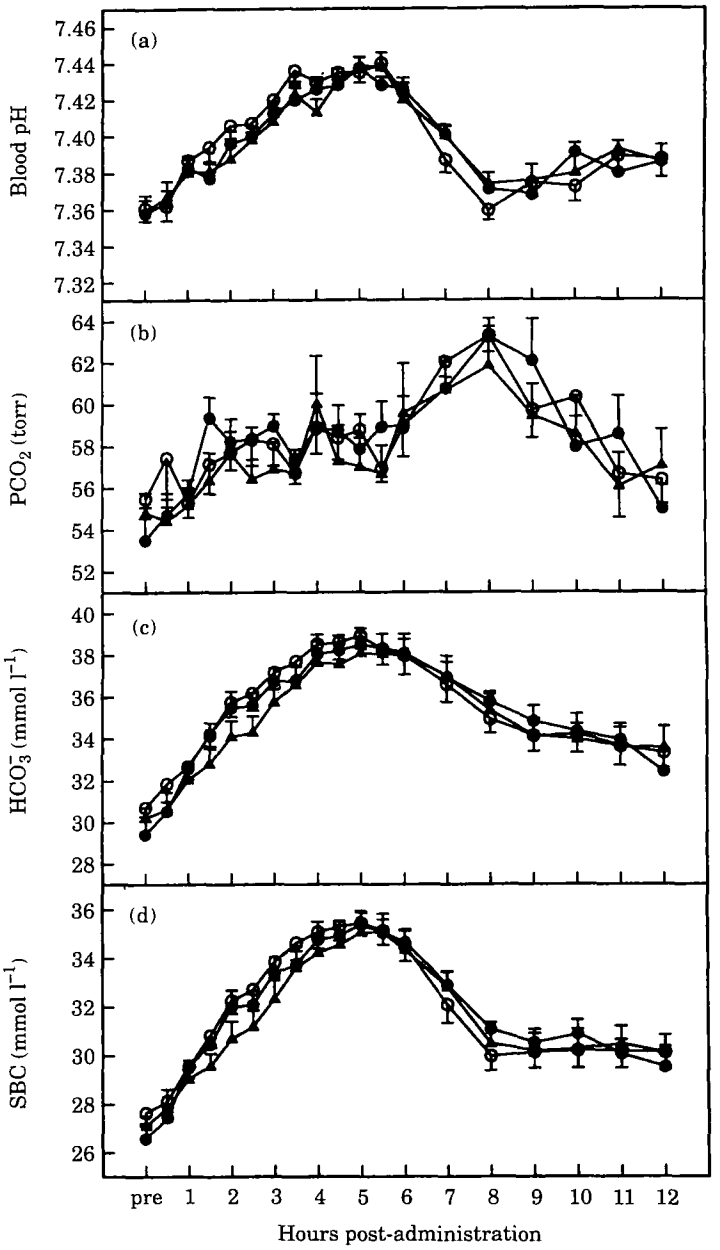

Fig. 10. Changes (mean ± SEM) in (a) venous blood pH, (b) carbon dioxide tension (PCO_2), (c) bicarbonate (HCO_3^-) and (d) standard bicarbonate (SBC) concentrations in six Thoroughbred horses after receiving sodium bicarbonate (1.0 g kg^{-1}). Horses were either given their morning feed (●), had their morning feed withheld (○), or had their morning feed withheld and given glucose (0.5 g kg^{-1}) with the sodium bicarbonate solution (▲).

Lawrence *et al.*, 1987a, b; Greenhaff *et al.*, 1991a, b; Roberts *et al.*, 1991; Harkins & Kamerling, 1992; Lloyd *et al.*, 1993; Lloyd & Rose, 1995), there have been no

reports of the effects of sodium bicarbonate on the overall fluid, electrolyte and acid–base status. The studies reported here examined the effects of a single dose of sodium bicarbonate and also investigated other factors that could play roles in altering the horses' response to sodium bicarbonate.

1. Administration of 0.5 g kg^{-1} sodium bicarbonate

The administration of a hypertonic solution of sodium bicarbonate (0.5 k kg^{-1}) is likely to have resulted in fluid moving into the gastrointestinal tract from other fluid compartments, causing the initial increase in the plasma total protein concentration. However, as sodium bicarbonate was absorbed into the circulation and the plasma Na^+ and HCO_3^- concentrations are increased, the tonicity of the plasma is also increased, indicated by the increased plasma osmolality. Fluid then moved into the plasma to decrease plasma osmolality, increasing the plasma volume, and causing a decrease in total protein concentration. This effect has been reported by other researchers (Greenhaff *et al.*, 1991a; Jahn *et al.*, 1991; Roberts *et al.*, 1991). An increased plasma tonicity may induce a thirst sensation (Willatts, 1987), resulting in an increase in water consumption. The increase in water consumption also may have added to the decrease in the plasma protein concentration.

While the urinary Na^+ concentration increased due to the large Na^+ load, the excretion of the other major electrolytes in the urine was relatively constant. The total amount of K^+ and Cl^- were relatively unchanged after sodium bicarbonate administration compared with the total amounts excreted in the previous 24 h. Studies in humans have also noted no significant changes in the total amounts of K^+ and Cl^- excreted in the urine in a 24 h period after sodium bicarbonate administration (Oster *et al.*, 1988). The reduced urinary concentrations of K^+ and Cl^- were therefore a dilutional effect resulting from the increased urinary volume. The dilution of the urinary electrolytes is the likely cause of the decrease in the urinary osmolality. Interestingly, sodium bicarbonate ingestion has been shown to cause a significant increase in urinary osmolality in humans (Oster *et al.*, 1988). However, in the latter study, the treatment was not given as a single dose but was given in several doses over a 24 h period. During an acute increase in the plasma HCO_3^- concentration, the renal tubules continue to reabsorb the normal amount of HCO_3^- (24–28 mEq l^{-1} of filtrate), and excess HCO_3^- is excreted in the urine (Roberts *et al.*, 1956), causing an increase in urinary pH. While the anion that is normally excreted with Na^+ in the urine is Cl^-, there was no change in the total amount of Cl^- excreted in the 24 h period after sodium bicarbonate, indicating that it is another anion, such as HCO_3^-, that is accompanying the increased urinary Na^+ output. Increased urinary HCO_3^- and Na^+ outputs and urinary pH were found in human subjects after the administration of sodium bicarbonate (Oster *et al.*, 1988).

During metabolic alkalosis, there is an influx of K^+ intracellularly and an efflux of H^+ extracellularly, maintaining intracellular electrical neutrality (Willatts, 1987). The H^+ efflux into the blood then buffers the increased HCO_3^- concentration. This was reflected in the current study where a decrease in the plasma K^+ concentration was found while the blood pH was increased. In addition, it is likely that the increased plasma osmolality caused fluid to move into the extracellular

fluid, diluting plasma K^+. There were relatively small decreases in plasma Cl^- concentration (2.9 mmol l^{-1}) compared with mean increase in the other anion HCO_3^- of 7.6 mmol l^{-1}. The decreased plasma Cl^- observed after sodium bicarbonate administration has been attributed to an increase in the urinary Cl^- excretion with Na^+ (Heigenhauser & Jones, 1991). However, in the current study there was no significant increase in the amount of Cl^- excreted in the urine. This is consistent with the findings by Oster *et al.* (1988) who also found no significant increase in urinary Cl^- output over 24 h in humans who had received several doses of sodium bicarbonate.

It was not possible to make direct comparisons between the pre- and post-treatment Na^+ and K^+ faecal contents due to the different collection times. However, over a similar time period there was an increase in the faecal Na^+ content after administration of sodium bicarbonate which could be directly attributed to the ingestion of the large Na^+ load. The decreased faecal K^+ content was likely due to the decreased intake of K^+ following denial of hay during the day.

The sodium bicarbonate induced alkalosis may act to depress respiration, which will result in a retention of CO_2 as the body attempts to reduce the alkalotic state by increasing carbonic acid formation (Greenhaff *et al.*, 1990) thereby contributing to the increased venous PCO_2. An increased arterial PCO_2 has also been observed following sodium bicarbonate administration (Lloyd *et al.*, 1993). The peak increases in venous blood pH and HCO_3^- were similar to the responses noted after the administration of 0.6 g kg^{-1} of sodium bicarbonate (Greenhaff *et al.*, 1990). However, in that study, the peak pH was found at 8 h after administration, while in the current study the peak was observed between 4 and 6 h. Another study found that the peak blood pH occurred between 2.5 and 3 h after administering sodium bicarbonate (0.4 g kg^{-1}) (Harkins & Kamerling, 1992). The increase in venous blood HCO_3^- concentration can be significantly influenced by the dose of sodium bicarbonate administered. The mean peak increases in the HCO_3^- concentration after a dose of 0.5 g kg^{-1} was 7.6 ± 0.4 mmol l^{-1} compared with an increase of 10.1 ± 0.3 mmol l^{-1} after a 1.0 g kg^{-1} dose (Lloyd & Rose, 1995).

The strong ion difference (SID) can be calculated using the formula given by Stewart (1983) where: SID=(sum of all the strong cations)−(sum of all the strong anion concentrations). During the time of peak blood pH at 6 h post-administration the SID can be calculated on the following basis:

$$SID=(148 \text{ mmol } l^{-1} + 3.2 \text{ mmol } l^{-1})-(97.3 \text{ mmol } l^{-1})=53.9 \text{ mmol } l^{-1}$$

By comparison, the SID prior to administration of sodium bicarbonate was 49.8 mmol l^{-1}, indicating that the SID increased by 4.1 mmol l^{-1}. This was slightly less than the expected increase, which was predicted to be approximately 7 mmol l^{-1}, corresponding to the increase in HCO_3^- concentration. The difference in values may be attributed to an increased PCO_2.

2. Effect of water deprivation on the response to sodium bicarbonate administration

As part of the pre-race routine of some trainers, horses are denied access to water for several hours prior to racing. Therefore, if a trainer was to give a horse sodium bicarbonate and then deny it access to water for several hours, it is poss-

ible that there would be differences in the fluid shifts and acid–base balance compared with when water was freely available. As a result of the restricted access to water, the horses were forced to conserve fluid, resulting in a slightly decreased urine output over the 12 h period, compared with experiment 1. This occurred despite the necessity for excretion of the increased electrolyte load. While the formation of a more concentrated urine would permit the excretion of increased quantities of Na^+ and HCO_3^- and therefore conservation of water, the urinary concentration of Na^+, K^+ and Cl^- did not appear to be affected by water restriction. However, there appeared to be substantial fluid shifts between body fluid compartments as the plasma osmolality increased substantially following water restriction, suggesting fluid movement out of the extracellular fluid.

The denial of access to water caused the plasma osmolality to be significantly increased above that found in experiment 1. After water was resupplied at 6 h and large amounts of water were consumed, the plasma osmolality decreased rapidly (Fig. 9). The large intake of water at 6 h also had obvious effects on the venous pH, and HCO_3^- concentrations. The increased water intake probably diluted the blood HCO_3^- concentration, causing a more rapid decline after 6 h, and as a result the blood pH also decreased more rapidly compared with when water was freely available. A similar effect was noted with the plasma Na^+ concentration which declined rapidly once water was ingested. Plasma K^+ and Cl^- concentrations did decrease slightly after 6 h but the effect was not as obvious compared with the Na^+ and HCO_3^- concentrations.

Compared with experiment 1, the horses' venous blood HCO_3^- concentrations after the administration of sodium bicarbonate and denial of water for 6 h showed there was a higher average peak increase in HCO_3^- concentration of approximately 2 mmol l^{-1} following water restriction. This is despite the fact that the peak HCO_3^- concentrations were similar in both groups (Fig. 8). It is possible that a cross-over experimental design may have shown a statistically significant effect of water restriction.

3. The effects of fasting and the co-administration of glucose on the response to sodium bicarbonate administration

The presence of feed in horses' stomach may influence the rate at which sodium bicarbonate is absorbed. In addition, the presence of other substances in the 'milkshake' mixture, such as glucose, may also have an effect on the rate of absorption of sodium bicarbonate. The conditions in which sodium bicarbonate is administered to racehorses prior to racing could not be standardized as the routine varies between trainers. However, when the effects of fasting and the inclusion of glucose in the sodium bicarbonate solution were examined, no large effects on the changes in venous blood pH, PCO_2, HCO_3^- or SBC concentrations were observed (Fig. 10). While the inclusion of glucose has been shown to increase the rate of absorption of oral fluids in humans (Gisolfi *et al.*, 1991), the extremely hypertonic nature of the solution used in the current study, probably tempered any demonstrable effects on fluid and electrolyte absorption.

Implications for the detection of sodium bicarbonate administration

Currently the administration of sodium bicarbonate is detected by the measure-

ment of venous blood HCO_3^- concentrations in New Zealand (Irvine, 1992) and total carbon dioxide (TCO_2) concentrations in Australia (Lloyd & Rose, 1992; Auer *et al.*, 1993). In Ontario, Canada, venous blood pH, HCO_3^- and Na^+ concentrations are measured to determine whether sodium bicarbonate has been administered (Roelofson, 1992). A similar testing method is also used in other parts of North America. While the measurement of three different values provides an extremely high degree of protection for trainers who have not given their horses any sodium bicarbonate, it is possible that some treated horses will escape detection because all three measurements have not exceeded the threshold values. Further, the administration of substances such as potassium bicarbonate, potassium citrate, calcium lactate and *tris* (hydroxymethyl) aminomethane which can cause alkalosis may go undetected if the threshold for sodium is not exceeded. Based on this study, there are several measurements which could be used as screening tests to provide an indication of the administration of sodium bicarbonate. Urinary Na^+ concentration could provide a good indication between 8 and 20 h after sodium bicarbonate administration, because there was a large increase in concentration. However, it would not be possible to distinguish the changes that occur due to sodium bicarbonate administration from the changes that could occur due to the administration of a large dose of some other sodium salt. In addition, the peak Na^+ concentration occurred 12 h after administration, which would make this impractical for testing at the racetrack as it would require horses to be detained for several hours after racing.

While an increased urinary pH was found to be an indicator of sodium bicarbonate administration in humans (McKenzie, 1988), it is not a good indicator in the racehorse. Urine pH was significantly elevated by sodium bicarbonate administration, but the rise was not sufficient for pH measurements to be used as a screening test, given that there is considerable variation in the urine pH of untreated horses. Coffman (1981) reported a normal range for urine pH of 7–9, whereas in this study the mean peak urine pH found after sodium bicarbonate was 8.52 ± 0.05. Clearly the rise is not sufficient for it to be used as an indicator, and it would not be possible to distinguish between treated and untreated horses with any certainty.

The plasma Na^+ concentration is another possible means for detecting sodium bicarbonate administration and has been used in conjunction with other measurements in Canada (Roelofson, 1992). There was a significant rise in the plasma Na^+ concentration after the administration of the 0.5 g kg^{-1} dose of sodium bicarbonate, with the peak value of 150.9 ± 0.9 mmol l^{-1}. An increase in plasma Na^+ concentration to this level would exceed the threshold established in Canada of 147 mmol l^{-1}, but alone it does not differentiate between sodium bicarbonate administration and the administration of other sodium salts. Furthermore, an increase in the measured plasma Na^+ concentration does not necessarily reflect increases in plasma Na^+ in the extracellular fluid, but may also indicate water movement out of the extracellular fluid and/or changes in the body K^+ content (Edelman *et al.*, 1958).

Blood pH could be used for the detection of sodium bicarbonate administration. However, using the threshold level of 7.430 set for venous blood pH in Canada, the mean peak pH from the current experiment in horses given 0.5 g kg^{-1}

dose of sodium bicarbonate would not have exceeded this threshold. A disadvantage associated with the measurement of blood pH using blood gas machines is that it is necessary to correct for the horse's body temperature to allow an accurate measurement to be made. In pre-race testing, such a requirement may cause difficulties when time is limited.

The determination of venous blood HCO_3^- or TCO_2 concentrations are simple measurements that can provide an indication of sodium bicarbonate administration. The mean increase in venous HCO_3^- concentration of 7 mmol l^{-1} after the dose of sodium bicarbonate (0.5 g kg^{-1}) was sufficient to allow a distinction to be made between the treated and untreated states. However, the mean peak concentration of 36.7 mmol l^{-1} was not sufficient to exceed the 38 mmol l^{-1} threshold set in Canada, or the 37.5 mmol l^{-1} threshold in New Zealand, indicating that these threshold levels are established with a considerable margin of safety and give a high degree of protection to innocent trainers. However, this dose would cause some horses to exceed the lower TCO_2 concentration thresholds of 35 and 37 mmol l^{-1} that have been set in Australia. Due to the fact that any thresholds must be set with a large margin of safety, it must be accepted that a 0.5 g kg^{-1} dose of sodium bicarbonate may go undetected. However, larger doses are likely to cause the threshold to be breached.

Based on the blood HCO_3^- concentration, it is not possible to determine precisely the dose of sodium bicarbonate given to a horse prior to racing, as several factors can influence the horse's response. However, from examining the blood HCO_3^- concentrations in Standardbred horses sampled at the racetrack prior to the ban on the use of alkalinizing agents (Lloyd *et al.*, 1992), it is likely that the trainers were administering dose rates that were considerably greater than the dose rate of 0.5 g kg^{-1} used in experiment 1. Because many horses had pre-race blood HCO_3^- concentrations in excess of 40 mmol l^{-1}, it is probable that the dose of sodium bicarbonate administered was close to 1.0 g kg^{-1} or even higher. It is not possible to give advice as to what could be considered a 'safe' dose of sodium bicarbonate. Individual horses may be affected by sodium bicarbonate in different ways and the same dose of sodium bicarbonate may produce variable increases in venous blood HCO_3^- or TCO_2 concentrations every time it is given. As a result, sodium bicarbonate should not be given to a horse within 48 h of racing.

The administration of large doses of sodium bicarbonate has been shown to produce a number of significant effects on the fluid, electrolyte and acid–base balance. While the induced metabolic alkalosis resulting from the administration of sodium bicarbonate may be beneficial to performance, it is also possible that some of the other changes it causes may have other potentially adverse effects. The ingestion of the large sodium load produced significant fluid shifts which should be taken into account when interpreting any effects from performance studies. The venous blood HCO_3^- concentration provided a good indication of the administration of sodium bicarbonate and was not significantly affected by fasting, the co-administration of glucose, or water restriction. It is likely that the HCO_3^- concentration would also be elevated after the ingestion of other agents capable of producing metabolic alkalosis and could also be used as an indicator of their administration.

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REFERENCES

AUER, D. E., SKELTON, K. V., TAY, S. & BALDCOCK, F. C. (1993). Detection of bicarbonate administration (milkshake) in Standardbred horses. *Australian Veterinary Journal* **70**, 336–40.

COFFMAN, J. R. (1981). *Equine Clincial Chemistry and Pathophysiology*. pp. 266–7. Bonner Springs, Kansas: Veterinary Medicine Publishing Company.

EDELMAN, I. S., LEIBMAN, J., O'MEARA, M. P. & BIRKENFELD, L. W. (1958). Interrelationships between serum sodium concentration, serum osmolality and total exchangeable sodium, total exchangeable potassium and total body water. *Journal of Clinical Investigation* **37**, 1236–56.

GISOLFI, C. V., SPRANGER, K. J., SUMMERS, R. W., SCHEDL, H. P. & BLEILER, T. L. (1991). Effects of cycle exercise on intestinal absorption in humans. *Journal of Applied Physiology* **71**, 2518–27.

GREENHAFF, P. L., SNOW, D. H., HARRIS, R. C. & ROBERTS, C. A. (1990). Bicarbonate loading in the Thoroughbred: dose, method of administration and acid–base changes. *Equine Veterinary Journal* **9** (Suppl), 83–85.

GREENHAFF, P. L., HANAK, J., HARRIS, R. C. *et al.* (1991a). Metabolic alkalosis and exercise performance in the Thoroughbred horse. In *Equine Exercise Physiology 3*, eds. S. G. B. Persson, A. Lindholm, L. B. Jeffcott, pp. 353–60. Davis, California: ICEEP Publications.

GREENHAFF, P. L., HARRIS, R. C., SNOW, D. H., SEWELL, D. A. & DUNNETT, M. (1991b). The influence of metabolic alkalosis upon exercise metabolism in the Thoroughbred horse. *European Journal of Applied Physiology* **63**, 129–34.

HANSON, C. M., KLINE, K. H., FOREMAN, J. H. & FREY, L. P. (1993). The effects of sodium bicarbonate administered nasogastrically on plasma volume, electrolytes and blood gases in resting quarter horses. *Journal of Equine Veterinary Science* **13**, 593–6.

HARKINS, J. D. & KAMERLING, S. G. (1992). Effects of induced alkalosis on performance in Thoroughbreds during a 1,600-m race. *Equine Veterinary Journal* **24**, 94–8.

HEIGENHAUSER, G. J. F. & JONES, N. L. (1992). Bicarbonate loading. In *Perspectives in Exercise Science and Sports Medicine. Ergogenics-Enhancement of Performance in Exercise and Sport IV*, eds D. R. Lamb & M. H. Williams, pp. 183–212. Ann Arbor, Michigan: Brown & Benchmark.

HINCHCLIFF, K. W., MCKEEVER, K. H. & MUIR, W. W. (1991). Effect of oral sodium bicarbonate on indices of athletic performance in horses. In *Proceedings of the 72nd Conference of Research Workers in Animal Disease*, pp. 30.

IRVINE, C. H. G. (1992). Control of administration of sodium bicarbonate and other alkalis: The New Zealand experience. In *Proceedings of the 9th International Conference of Racing Analysts and Veterinarians 2*, ed. C. R. Short, pp. 139–43. Baton Rouge, Louisiana: International Conference of Racing Analysts and Veterinarians.

JAHN, P., LISKA, I., HANAK, J. *et al.* (1991). Effects of exercise and metabolic alkalosis on selected plasma amino acid concentrations in Thoroughbred racehorses. In *Equine Exercise Physiology 3*, eds S. G. B. Persson, A. Lindholm, L. B. Jeffcott, pp. 380–4. Davis, California: ICEEP Publications.

KELSO, T. B., HODGSON, D. R., WITT, E. H., BAYLY, W. M. GRANT, B. D. & GOLLNICK, P. D. (1987). Bicarbonate administration and muscle metabolism during high-intensity exer-

cise. In *Equine Exercise Physiology 2*, eds J. R. Gillespie, N. E. Robinson, pp. 438–47. Davis, California: ICEEP Publications.

KLINE, K. H., FOREMAN, J. H., HANSON, C. M. & FREY, L. P. (1992). Changes in blood gases and electrolytes of horses given varying doses of sodium bicarbonate. In *Proceedings of the 13th Equine Nutrition and Physiology Symposium*, pp. 113–4.

LAWRENCE, L., KLINE, K., MILLER, P. *et al.* (1987a). Effect of sodium bicarbonate on racing Standardbreds. In *Proceedings of the 10th Equine Nutrition and Physiology Symposium*, pp. 499–503.

LAWRENCE, L. M., MILLER, P. A., BECHTEL, P. J., KANE, R. A., KURCZ, E. V. & SMITH, J. S. (1987b). The effect of sodium bicarbonate ingestion on blood parameters in exercising horses. In *Equine Exercise Physiology 2*, eds J. R. Gillespie, N. E., Robinson, pp. 448–55. Davis, California: ICEEP Publications.

LAWRENCE, L., KLINE, K., MILLER-GRABER *et al.* (1990). Effect of sodium bicarbonate on racing standardbreds. *Journal of Animal Science* **68**, 673–7.

LLOYD, D. R. & ROSE, R. J. (1992). Issues relating to agents capable of producing metabolic alkalosis. *Australian Equine Veterinarian* **10**, 27–28.

LLOYD, D. R. & ROSE, R. J. (1995). Effects of $NaHCO_3$ on acid base status and exercise capacity. *Equine Veterinary Journal* **18** (Suppl) (in press).

LLOYD, D. R., REILLY, P. & ROSE, R. J. (1992). The detection and performance effects of sodium bicarbonate administration in the racehorse. In *Proceedings of the 9th International Conference of Racing Analysts and Veterinarians 2*, ed. S. R. Short, pp. 131–8. Baton Rouge, Louisiana: International Conference of Racing Analysts and Veterinarians.

LLOYD, D. R., EVANS, D. L., HODGSON, D. R., SUANN, C. J. & ROSE, R. J. (1993). Effects of sodium bicarbonate on cardiorespiratory measurements and exercise capacity in Thoroughbred horses. *Equine Veterinary Journal* **25**, 125–9.

MCKENZIE, D. C. (1988). Changes in urinary pH following bicarbonate loading. *Canadian Journal of Sports Science* **13**, 254–5.

OSTER, J. R., STEMMER, C. L., PEREZ, G. O. & VAAMONDE, C. A. (1988). Comparison of the effects of sodium bicarbonate versus sodium citrate on renal acid excretion. *Mineral and Electrolyte Metabolism* **14**, 97–102.

ROBERTS, K. E., RANDALL, H. T., VANAMEE, P. & POPPELL, J. W. (1956). Renal mechanisms involved in bicarbonate absorption. *Metabolism* **5**, 404–18.

ROBERTS, A., LAWRENCE, L., WILLIAMS, J., SODERHOLM, V. & HINTZ, H. (1991). Metabolic changes during exercise in horses given sodium bicarbonate. In *Proceedings of the 12th Equine Nutrition and Physiology Symposium*, pp. 159–64.

ROELOFSON, R. (1992). Sucrose and bicarbonate overloading of Standardbred horses in Ontario. In *Proceedings of the 9th International Conference of Racing Analysts and Veterinarians 2*, ed. C. R. Short, pp. 145–6. Baton Rouge, Louisiana: International Conference of Racing Analysts and Veterinarins.

ROSE, R. J.& HODGSON, D. R. (1993). *Manual of Equine Practice.* Philadelphia: W. B. Saunders, 297 pp.

ROSE, R. J. & LLOYD, D. R. (1992). Sodium bicarbonate: more than just a 'milkshake'? *Equine Veterinary Journal* **24**, 75–6.

STEWART, P. A. (1983). Modern quantitative acid-base chemistry. *Canadian Journal of Physiology and Pharmacology* **61**, 1444–61.

SWANN, P. (1990). *Performance Drugs in Sport.* pp. 83–5. Victoria, Australia: Forty-First Yeneb Pty Ltd.

WILLATTS, S. M. (1987). *Lecture Notes on Fluid and Electrolyte Balance*, 2nd Edn. pp. 3–65. Melbourne: Blackwell Scientific Publications.

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