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Original Research

Effect of Chronic Furosemide on Salt and Water Intake of Ponies

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ABSTRACT

Furosemide is used acutely in racehorses and chronically for treatment of edema and congestive heart failure, but the behavioral effects on horses of chronic administration of this drug have not been studied. The objectives of this study were to measure salt and water intake as well as sodium and water losses in ponies treated chronically with furosemide. The salt and water intake of ponies was measured daily for 3 weeks before and 3 weeks during treatment with furosemide at a dose of 0.5 mg/kg/d. Fecal dry matter was measured for 9 days before and during furosemide treatment by collecting a fecal sample from each pony's stall and drying it overnight in a 100°C oven. Urine volume and urine sodium content were measured daily for three consecutive days during pretreatment, treatment, and post-treatment periods so that sodium and water status could be calculated. Sodium chloride intake increased in ponies treated daily with furosemide from 7.9 ± 2.2 (standard error of the mean) to 20.3 ± 2.4 g/d and was significantly higher than control for all weeks of treatment ($P < .03$). Water intake was also significantly increased from 8.9 ± 1 during the control period to 11 ± 0.7 kg/d during furosemide treatment ($P < .001$), and the ponies drank more water than they lost. Urine volume and urine sodium concentrations increased significantly during treatment with the diuretic, whereas urinary potassium and calcium concentrations decreased.

1. Introduction

Diuretics are administered to horses for therapeutic reasons to decrease the incidence and severity of exercise-induced pulmonary hemorrhage [1,2], for congestive heart failure, edema, and acute renal failure [3]. The mode of action of furosemide is the inhibition of the active reabsorption of electrolytes, including sodium, in the thick ascending limb of the loop of Henle [4].

Furosemide causes an immediate loss of body weight that is indicative of a reduction in body water including blood volume.

Horses administered furosemide acutely demonstrate an increase in water and salt intake [5,6]. The acute effects of the drug on the horse's physiology and behavior have been investigated, but the chronic effects have not. Our interest is in the chronic effects on the ingestive behavior of the horse, particularly on its salt and water intake.

The aims of this study were to determine whether salt intake and water intake would increase over time with daily furosemide treatment, whether changes in plasma protein and fecal water content occurred, and whether sodium and water needs could be maintained behaviorally, that is, by changes in ingestive behavior. Potassium and calcium losses were also measured.

2. Methods

This study was approved by the Cornell University Institutional Animal Care and Use Committee.

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2.1. Subjects and Procedures

Six Shetland-type pony geldings, ranging in age from 8 to 13 years, mean weight of 250.9 ± 11.3 kg, were used. They were housed in 2.5 × 1.3-m tie stalls and released into a grassless paddock for 1 hour during the day. They were fed grass hay except when outside or during salt presentation. The hay contained 2.42% potassium and 0.01% sodium [7]. Water was available in buckets and salt blocks in small pans. Water buckets were large so that the level was low and were tied in place in the mangers. The buckets were weighed twice daily to determine water intake, and spillage was minimal. The salt was available to the ponies for an hour per day when no other food or water was available. Salt blocks were dried in an oven at 100°C overnight and then weighed (kg) to calculate daily NaCl consumption. A fecal sample from each pony was collected daily in the afternoon for 9 days during the control period and for 9 days during the furosemide treatment and dried to constant weight.

The experiment was divided into two 21-day periods: pre-furosemide treatment (CON) and furosemide treatment (FUR) plus a 3-day post-treatment period (POST). Weekly periods were used to test for and increase with time in response to sodium depletion. Furosemide (National Laboratories, Somerville, NJ) was administered at a dose of 0.5 mg/kg IM daily. CON injections were an equal volume of 0.9% NaCl IM daily.

2.2. Sodium, Other Electrolytes, and Water Intakes and Excretion

During each treatment period (CON, FUR, and POST), each pony was placed for three consecutive days in raised 1.82 × 0.8-m metabolism stalls that allowed collection of urine in a pan beneath the center of the stall. There were only four metabolism stalls, so four ponies were placed in them for 3 days and, the following week, the remaining two ponies were placed in the metabolism stalls for the following 3 days. The collection occurred midway through the CON period during the first week and second week of FUR treatment and during the first week POST. The urine was strained through a metal screen and cheesecloth to eliminate any hay or other debris. Urine volume was determined and the urine analyzed for sodium and potassium using a flame photometer (Model 443, Instrumentation Laboratory). Samples were analyzed in duplicate and the standards checked during each day's analysis. Calcium was measured by flame atomic absorption spectrometry on two dilutions of each sample. Salt and water intake were measured during the 3-day periods in the metabolism stalls so that CON, FUR, and POST sodium, potassium, calcium, and water changes could be measured.

2.3. Plasma Protein

During one of the 3 days in the metabolism stall, a sterile polyethylene catheter was placed in the jugular vein for blood sampling of each pony. Blood samples were taken before CON or FUR (0.5 mg/kg) injections and at 30 minutes, 1, 2, 3, 4, 14, and 24 hours after injection. Blood samples were drawn into preheparinized sterile tubes and immediately refrigerated. Plasma protein concentration was estimated to within 0.1 g/dL with a handheld refractometer (Veterinary Refractometer; AO Veterinary Instruments).

2.4. Statistical Analysis

2.4.1. Salt and Water Intake

Descriptive statistics are given for daily salt and water intake for each treatment group (CON and FUR) across Days 1 to 21. Water intake data were Gaussian, whereas salt intake data were not; therefore, a square root transformation was applied to salt intake data to achieve normality and homogeneity of the variances. Data for daily salt and water intake were grouped into weeks 1, 2, and 3 (corresponding to Days 1–7, 8–14, and 15–21, respectively). Differences in weekly salt intake and in weekly water intake between treatment groups (CON vs. FUR) were evaluated using paired *t*-tests.

2.4.2. Fecal Dry Matter

A Wilcoxon rank sign test for paired data was used to compare mean fecal dry mater in the CON and FUR conditions.

2.4.3. Sodium and Water Intake and Excretion

For sodium intake and excretion data (determined during 3 days in metabolism stalls), a square root transformation was applied to sodium intake, and a natural logarithmic transformation was applied to urine sodium concentrations to achieve normality of the variables and homogeneity of the variances. Paired *t*-tests were used to compare sodium intake and urine sodium loss between treatment conditions (CON vs. FUR) during the 3-day urine collection period. Water intake and excretion data (collected during 3 days in metabolism stalls) were normally distributed, so paired *t*-tests were used to compare water intake and urine volume between treatment groups (CON vs. FUR) during the 3-day urine collection period.

2.4.4. Potassium and Calcium Excretion

Potassium data were normally distributed; so paired *t*-tests were used to compare potassium concentrations between treatment periods. For calcium data, a natural logarithmic transformation was applied to achieve normality of the variables and homogeneity of the variances. Paired *t*-tests were then used to compare calcium concentrations between treatment periods (CON vs. FUR).

2.4.5. Plasma Protein

Because of small sample sizes in each treatment group, a nonparametric Wilcoxon signed-rank test was used to compare plasma protein concentrations between treatment groups (CON vs. FUR) at each pre- and post-injection sampling time (0, 0.5, 1, 2, 3, 4, 14, and 24 hours).

Statistical significance was set at $P < .05$, and all tests were two tailed. All statistical analyses were performed using JMP 10.0 (SAS Institute, Cary, NC). To facilitate the reader's interpretation, continuous data are presented as means ± standard error of the mean.