Exercise-associated hyponatremia in Alaskan sled dogs: urinary and hormonal responses

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Hinchliff, K. W., G. A. Reinhart, J. R. Burr, and R. A. Swenson. Exercise-associated hyponatremia in Alaskan sled dogs: urinary and hormonal responses. J. Appl. Physiol. 83(3): 824–829, 1997.—Exercise-associated hyponatremia occurs in horses and humans, both species that sweat, and in sled dogs, which do not sweat. To investigate the mechanism of exercise-associated hyponatremia in sled dogs, we measured water turnover, serum electrolyte concentrations and osmolality, plasma renal hormone concentrations, and urine composition of 12 fit Alaskan sled dogs before, during, and after a 490-km sled dog race (Ex group). Water turnover and serum electrolyte concentrations were measured in six similarly fit dogs that did not run (Sed group). Water turnover was significantly larger ($P<0.001$) in Ex [190 ± 19 (SD) ml·kg$^{-1}$·day$^{-1}$] than in Sed dogs (51 ± 13 ml·kg$^{-1}$·day$^{-1}$). There were significant ($P<0.001$) decreases in serum sodium concentration (from 148.6 ± 2.8 to 139.7 ± 1.9 mmol/l) and osmolality (from 306 ± 9 to 296 ± 5 mosmol/kgH$_2$O) of Ex, but not Sed, dogs during the race. Plasma concentrations of arginine vasopressin decreased, whereas aldosterone and plasma renin activity increased significantly ($P<0.01$) during the race. Urine osmolality was unchanged, whereas urine sodium, potassium, and chloride concentrations decreased significantly ($P<0.05$) and urine urea concentration increased ($P=0.06$). These results demonstrate increased water turnover associated with hyponatremia and renal sodium conservation with maintained high urine osmolality in exercising Alaskan sled dogs.

deuterium; arginine vasopressin; aldosterone; osmolality; renin; atrial natriuretic peptide

HYponatREMIA, a reduction in serum sodium concentration to abnormally low levels (25), occurs during or after prolonged exercise in humans, horses, and sled dogs (2, 4, 9, 10, 12, 22, 23, 27). Symptomatic hyponatremia of human athletes is associated with very low serum sodium concentrations ($<130$ mmol/l), whereas lesser reductions in serum sodium concentration in humans, horses, and dogs are not associated with clinical signs (10–12, 14, 23). Symptomatic and asymptomatic hyponatremia in human athletes is typically associated with participation in races of $>4$-h duration (11, 27), whereas in horses symptomatic and asymptomatic hyponatremia occurs during or immediately after endurance racing (50–100 miles) or after participation in a 3-day event (4, 22, 23). Hyponatremia without associated clinical signs is reported in dogs competing in the 1,100-mile Iditarod Trail sled dog race and in dogs competing in shorter races (2, 14).

The pathogenesis of symptomatic exercise-associated hyponatremia in human athletes is debated (11, 16, 21). Symptomatic exercise-associated hyponatremia in humans is attributed to either water intoxication secondary to ingestion of large quantities of hypotonic fluids (10, 16) or to a disproportionately large loss of sodium, compared with net losses of body water, during running (11). Symptomatic hyponatremia of human runners is associated with increased total body water (TBW) (16). In contrast, hyponatremia after exercise in clinically normal horses is believed to be attributable to large losses of sodium with a lesser reduction in TBW (4, 22). Regardless of the role of each of these mechanisms, exercise by humans and horses is associated with a reduction in body sodium content, both of individuals that develop hyponatremia and those that do not, because of losses of large quantities of sodium in sweat (e.g., 155 mmol sodium and 4.1 liters sweat during a 4-h treadmill run by humans and 5.90 mol sodium and 37 liters sweat during a 7-h run by horses) (5, 16, 19, 25). Exercise-associated hyponatremia is unexpected in dogs because they do not sweat appreciably and, therefore, loss of significant quantities of sodium by this route is unlikely.

To our knowledge, apart from our previous reports (2, 14), the development of exercise-associated hyponatremia has not been reported in species that thermoregulate during exercise by mechanisms other than evaporation of sweat or in species that exercise in frigid conditions. Here we document the development of hyponatremia (a serum sodium concentration $<140$ mmol/l; see Ref. 6) with renal sodium and potassium conservation and maintenance of high urine osmolality in Alaskan sled dogs during prolonged exercise. We speculate that exercise-associated hyponatremia in these dogs is attributable to solute diuresis and urine sodium loss mandated by the large solute (urea) intake related to the high metabolizable energy intake of racing Alaskan sled dogs (13), although an increase in TBW cannot be excluded as a factor contributing to the hyponatremia.

MATERIALS AND METHODS

Experimental design. Blood and urine samples were collected from dogs before, at the midpoint, and at the finish of a 490-km sled dog race. Water turnover during the race was measured by using deuterium oxide. Another group of dogs did not participate in the race but had blood collected and water turnover measured coincident with that of dogs participating in the race.

Dogs. Seventeen fit Alaskan sled dogs were studied (12 males, 5 females, weighing 26.7 ± 2.9 kg, 2–7 yr old) that were competing in the 1994 Copper Basin 300. The dogs were all from the same kennel and had completed ~1,200 miles of training during the previous 4 mo. Twelve dogs (Ex group) were administered deuterium oxide (0.25 mg/kg, 99.9%,...
Merck) orally between 4 and 6 h before the start of the race (labeled dogs). The remaining five dogs (unlabeled) were used to monitor changes in background enrichment of deuterium oxide during the race.

Another group of six similarly trained dogs (5 females, 1 male, weighing 22.3 ± 3.6 kg, 2–7 yr old) from the same kennel served as a sedentary control group (Sed); the dogs were housed in unheated kennels (their usual housing) and were fed and given water three times per day.

Diet. Dogs were fed to appetite a diet providing 52, 29, and 20% of calories from fat, protein, and carbohydrate, respectively. An attempt was made to determine the average daily food intake of each dog during the race by having the dog drivers feed a “phantom dog.” At every feeding stop, the drivers were asked to place into a container food of the same quantity and composition, including snacks, as that fed a dog in the team. These food samples were then analyzed for sodium, potassium, and protein content by proximate analysis, and the estimated intake of dogs in the team was calculated. Dogs were fed approximately every 6 h.

No attempt was made to measure water consumption of the dogs because of the constant availability of snow and ice. However, the dogs are trained not to eat snow or ice while running, and we assume that most of their water was supplied with feed. The dogs were fed the above diet as a watery gruel, and were offered water flavored with a small amount of feed. The dogs completed the 490-km race in 65 h at an average speed of 7.5 km/h. Two labeled dogs were eliminated from the study because of lameness after completing ~300 km of the race.

Water turnover. TBW of the Ex dogs was 18.7 ± 2.2 liters (0.69 ± 0.04 ml/kg), which was not significantly different (P > 0.05) from that of the Sed dogs (15.6 ± 4.7 liters, 0.68 ± 0.1 ml/kg). Water turnover was significantly different (P < 0.001) between Ex (5.0 ± 1.8 l/day, 190 ± 19 ml·kg⁻¹·day⁻¹) and Sed (1.13 ± 0.3 l/day, 51 ± 13 ml·kg⁻¹·day⁻¹) groups.

Serum constituents. There were significant (P < 0.001) decreases during the race in serum sodium (6%), potassium (20%), calcium (8%), and total protein (14%) concentrations and osmolality (3.4%) of Ex dogs (Fig. 1, Table 1). There were no significant (P > 0.05) changes in these variables in Sed dogs. Serum creatinine and chloride concentrations did not change significantly (P > 0.05) in either Ex or Sed dogs. Serum urea nitrogen concentrations increased (30%, P < 0.05) during the race in Ex but not in Sed dogs (Table 1).

Plasma concentrations of AVP decreased significantly (48%, P < 0.001), Aldo and plasma renin activity increased significantly (190 and 220%, respectively,
P < 0.01), and ANP was unchanged (P = 0.08) during the race (Figs. 1–2, Table 2).

Urine. Urine osmolality was unchanged during the race (P = 0.5), whereas decreases in urine sodium (73%), potassium (57%), and chloride (79%) concentrations of Ex dogs were significant (P < 0.05) (Table 3). There was a trend for urine urea nitrogen concentration to increase during the race (22%, P = 0.06). Fractional clearance of sodium and chloride decreased significantly (P < 0.05) during the race (Fig. 1, Table 2).

DISCUSSION

This study confirms the development of hyponatremia during prolonged exercise by sled dogs and demonstrates that this phenomenon is associated with large water turnover, renal sodium conservation, and high urine osmolality. Urine osmolality was maintained during the race at its initial high concentration, despite a marked reduction in urine sodium and potassium concentrations, by an increase in urine urea concentration. The increase in urine urea concentration likely reflected the increased protein intake and, hence, renal solute load mandated by the dogs' large energy requirements while racing (13).

Exercise-induced hyponatremia can be attributed to one or more of several mechanisms including (21, 27) 1) a reduction in total body exchangeable cation content, 2) an increase in TBW, or 3) a permutation of these changes (for instance, a reduction in total exchangeable cation content with a lesser reduction in TBW). It is assumed that the empirical relationship between serum sodium concentration ([Na]s), total body contents of exchangeable sodium and potassium (Na and Ke, respectively), and TBW (7), i.e.

\[ [\text{Na}]_s = (\text{Na}_e + \text{Ke})/\text{TBW} \]

...demonstrated for humans applies to dogs as well (18). Human athletes with symptomatic hyponatremia have an increased TBW (estimated from excess fluid excretion) at the time that hyponatremia is diagnosed (16). Thus hyponatremia in these symptomatic individuals with serum sodium concentrations <130 mmol/l is likely in large part dilutional and attributable to the intake of large volumes of sodium-poor fluid while running (21). We cannot exclude a relative water excess as a cause of the hyponatremia observed in these dogs, as a small (~800-ml) increase in TBW could account for the observed decrease in serum sodium concentration if....

Table 1. Serum constituents of 12 Alaskan sled dogs before, during, and after a 490-km sled dog race and of 6 dogs that did not run.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Prerace</th>
<th>Midrace</th>
<th>Postrace</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ex</td>
<td>Sed</td>
<td>Ext</td>
</tr>
<tr>
<td>Sodium concn, mmol/l</td>
<td>148.6 ± 2.8</td>
<td>146.8 ± 2.7</td>
<td>144.9 ± 2.7 *</td>
</tr>
<tr>
<td>Potassium concn, mmol/l</td>
<td>4.8 ± 0.2</td>
<td>4.4 ± 0.3</td>
<td>4.7 ± 0.2</td>
</tr>
<tr>
<td>Chloride concn, mmol/l</td>
<td>115.7 ± 2.2</td>
<td>115.3 ± 2.8</td>
<td>114.7 ± 3.2</td>
</tr>
<tr>
<td>Calcium concn, mmol/l</td>
<td>2.4 ± 0.0</td>
<td>2.4 ± 0.1</td>
<td>2.2 ± 0.1 *</td>
</tr>
<tr>
<td>Total protein concn, g/l</td>
<td>63 ± 3</td>
<td>63 ± 4</td>
<td>58 ± 4 *</td>
</tr>
<tr>
<td>Urea nitrogen, mmol/l</td>
<td>8.7 ± 3.0</td>
<td>5.4 ± 7.3</td>
<td>11.6 ± 3.1 *</td>
</tr>
<tr>
<td>Creatinine concn, µmol/l</td>
<td>61.9 ± 17.7</td>
<td>55.7 ± 13.7</td>
<td>61.9 ± 17.7</td>
</tr>
<tr>
<td>Osmolality, mosmol/kgH2O</td>
<td>306.2 ± 9.3</td>
<td>305.8 ± 7.6</td>
<td>303.4 ± 9.5</td>
</tr>
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</table>

Values are means ± SD. Ex, dogs that participated in the race (n = 12 except n = 10); Sed, sedentary fit dogs (n = 6). Prerace, Midrace, Postrace: values measured before, during, and after the race, respectively. *P < 0.05 vs. Prerace value for that group.
Hormone | Prerace | Midrace | Postrace
--- | --- | --- | ---
Aldo, ng/l | 28 ± 26 | 104 ± 63* | 82 ± 46*
ANP, ng/l | 67 ± 19 | 71 ± 45 | 93 ± 39
PRA, µg·l⁻¹·h⁻¹ | 2.1 ± 1.5 | 4.1 ± 1.8 | 6.8 ± 5.2*
AVP, ng/l | 2.3 ± 0.5 | 2.0 ± 0.5 | 1.2 ± 0.3*

Values are means ± SD. Aldo, aldosterone; ANP, atrial natriuretic peptide; PRA, plasma renin activity; AVP, arginine vasopressin. *P < 0.05 vs. prerace value.

Regardless of changes in TBW, a reduction in serum sodium concentration indicates a relative excess of water in the body and may be viewed as a failure in free water excretion. Ingestion of inappropriately large quantities of water or impaired renal function have been suggested as causes of exercise-associated hyponatremia. However, given our previous observation that total exchangeable cation content of Alaskan sled dogs decreases during racing without a measureable decrease in TBW (14), the question arises as to what is the reason for the apparent lack of a decrease in extracellular fluid volume.

Changes in serum total protein and potassium concentration during the race could be indicative of an expansion of the extracellular fluid volume. However, there are explanations other than a change in extracellular fluid volume for the decreases in serum potassium and protein concentration. A decrease in total body exchangeable cation content, as has been documented in sled dogs (14), would decrease serum potassium concentrations (7), and serum protein concentration could be reduced by a reduction in albumin and/or globulin content in the blood. The presence of an unmeasured solute in the plasma that may have increased extracellular volume was excluded by the correlation between the reduction in serum osmolality and sodium concentration.

Total body cation content of sled dogs decreases during a race (14). An explanation for the exercise-associated reduction in serum sodium concentration may, therefore, involve a reduction in total body exchangeable cation content. Before the race, dogs had low plasma Aldo concentrations and produced concentrated urine that contained substantial quantities of sodium (96 mmol/l) and potassium (157 mmol/l). Renal conservation of sodium during the race was indicated by the significant reductions in fractional clearance of sodium and urine sodium concentration and by an increase in plasma Aldo concentration (Fig. 1). The decrease in the sum of urine sodium and urine potassium concentrations from values greater than serum sodium concentration before the race to values below serum sodium concentration at the end of the race indicates marked renal cation conservation and could be interpreted as a change from negative free water clearance before the race to positive free water clearance at the end of the race, and would be appropriate for the observed decline in serum osmolality and AVP concentration (Fig. 2). In contrast to these dogs, renal sodium conservation and an increase in free water clearance are associated with a marked decrease in urine osmolality in humans during prolonged exercise (10, 17). Similarly, urine osmolality of horses decreases during prolonged running (25).
that act to reduce urinary sodium concentration. The large losses of sodium in the urine, if not offset by an increase in sodium intake or a decrease in TBW, may result in hyponatremia.

Urine osmolality of humans and horses decreases during prolonged exercise (10, 25), and in humans this is associated with an increase in free water clearance (10). There was no reduction in urine osmolality of dogs during the race despite the renal cation conservation. The reduction in osmolality attributable to the decreases in sodium and potassium urea levels was offset by an increase in urine urea concentration during the race; the sum of sodium and potassium urea declined by ~170 mmol/l, and urine urea nitrogen concentration increased by 200 mmol/l (Table 3). Thus urine osmolality was unchanged, in the face of a significant decline in plasma AVP concentration, because of an increase in urine urea nitrogen concentration. Had there been an increase in free water excretion due to ingestion of excess volumes of water, urine osmolality would have declined. The decline in plasma AVP concentration may have contributed to the increased urea concentration in urine-AVP increases tubular permeability to urea (1).

Water turnover in running Alaskan sled dogs substantially exceeds that of similarly trained and housed sedentary dogs (14). The greater water turnover of running dogs may be attributable to higher respiratory and renal water losses than occur in sedentary dogs. Respiratory losses likely account for only a fraction of the measured water turnover (8), and fecal losses are also likely to be minimal (20, 24). Estimated respiratory water loss was 800 ml/day (8), assuming a total daily CO₂ production of 90 mol (13), 5% CO₂ in expired air, minute ventilation of 271/min, inspired air temperature of 0°C, inspired humidity of 0 Torr, and a respiratory rate of 60 breaths/min. Together, fecal and respiratory losses were likely <1 l/day, indicating that water loss in the urine must have been substantial (4.5 l/day).

Urine volume is related to urine osmolality and the renal solute load of the diet; for a given urine osmolality, urine volume increases as intake of solutes that are excreted in the urine increases (18). Urine production can, therefore, be estimated from the renal solute load [principally urea, sodium, and potassium (18)] in the diet and urine osmolality. Racing Alaskan sled dogs consume over 45,000 kJ/day, of which ~900 g are contributed by protein (~13). An intake of 900 g/day of protein, equivalent to ~51 mol/day of urea, necessitates the excretion of 4.6 liters of urine with a urea concentration of 1,100 mosmol/kgH₂O. This estimate of urine volume, although approximate, is similar to the water turnover, less estimated respiratory water losses, measured in the dogs in the present study. Obviously, a smaller renal solute load or greater urine osmolality would result in a smaller obligatory volume of urine. The high water turnover of Alaskan sled dogs during a race appears to be related to their large metabolizable energy intake and, hence, large renal solute load.

Conclusions. This study documents the development of exercise-associated hyponatremia and hypoosmolar-


