Hyperglycemia, hypernatremia, and hyperosmolarity in 6 neonatal llamas and alpacas

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A 3-day-old 10-kg (22-lb) female llama cria was admitted to the Oregon State University Veterinary Teaching Hospital for evaluation of anorexia, weakness, hyperthermia (rectal temperature, 41.7°C [107.0°F]), and trembling. All signs had become progressively worse over a period of 6 hours. The dam had had dystocia, and the cria had never suckled the dam. Cow colostrum and llama plasma had been administered, and the cria had been fed 180 to 240 ml of goat milk replacer every 4 hours.

Initial examination confirmed the owner's findings and revealed tachycardia (132 beats/min), dehydration (dry mucus membranes and prolonged skin tent over the neck and eyelid), ataxia, and a base-wide stance of the hind limbs. Rectal temperature was 40°C (104°F), and respiratory rate was 24 breaths/min. The cria could not stand up or lie down without assistance. The trembling was further defined as a fine constant head tremor. Laboratory evaluation revealed high blood glucose (686 mg/dl; reference range for neonatal llamas, 94 to 170 mg/dl), sodium (161 mEq/L; reference range, 148 to 155 mEq/L), urea (47 mg/dl; reference range, 10 to 21 mg/dl), and creatinine (3.6 mg/dl; reference range, 1.1 to 2.9 mg/dl) concentrations. Calculated plasma osmolality was 387 mOsm/L, and although a reference range has not been established for llamas, plasma osmolality for most other domestic mammals typically ranges between 270 and 320 mOsm/L. Venous blood pH (7.23; reference range, 7.35 to 7.5) and bicarbonate concentration (17 mEq/L; reference range, 23 to 32 mEq/L) were low. Hematologic abnormalities included neutrophilia (41,360 WBC/µl; neutrophil fraction, 91%) with a left shift and lymphopenia. Serum immunoglobulin concentration was > 800 mg/dl.

The llama was able to urinate and defecate without straining, helping to rule out stranguria and tenesmus as causes for the base-wide stance and allowing treatment efforts to focus on possible infectious and metabolic diseases. To correct metabolic abnormalities and treat presumptive sepsis, the llama was given 1 L of lactated Ringer's solution by rapid IV infusion, followed by additional 100-ml boluses every 2 hours. Blood sodium concentration was 159 mEq/L after the initial fluid bolus. The llama was also treated with fluoxetine meglumine (0.25 mg/kg [0.11 mg/lb] of body weight, IV, q 6 h), cefotiofur sodium (5 mg/kg [2.3 mg/lb], IV, q 12 h), and potassium penicillin G (22,000 U/kg [10,000 U/lb, IV, q 6 h]. After 12 hours of treatment, blood sodium concentration had increased to 172 mEq/L, whereas blood glucose concentration had decreased to 504 mg/dl, and azotemia had lessened. Plasma osmolarity had increased to 400 mOsm/L. Cerebrospinal fluid had high sodium (175 mEq/L; reference range, 151 to 157 mEq/L), glucose (390 mg/dl; reference range, 66 to 73 mEq/L), and protein (140 mg/dl; reference range, 39 to 48 mg/dl) concentrations without cytologic evidence of infection of the CNS (2 WBC/µl; reference range, 0.3 to 1.5 WBC/µl). Urine glucose concentration was 1,000 mg/dl, and urinary fractional clearance of sodium was calculated to be 1.8% (reference range, < 1.5%). Serum cortisol concentration was 3.2 µg/dl (reference range, 1.0 ± 0.13 µg/dl), and serum insulin concentration was < 5.0 µU/ml (reference range, 5.6 ± 0.1 µU/ml), yielding an insulin-to-cortisol ratio of 156 µU/µg (reference range, 768 ± 34 µU/µg). Serum concentrations of triglycerides (265 mg/dl; reference range, 8.3 to 55.8 mg/dl), nonesterified fatty acids (1.02 mEq/L; reference range, 0.91 ± 0.17 mEq/L), and β-hydroxybutyrate (12.65 mg/dl; reference range, 0.12 to 0.75 mg/dl) were high. Bacterial culture of blood samples did not yield any organisms.

The llama's condition did not improve during the first 12 hours, except that the hyperthermia resolved, and the llama would eat a little. Treatment was continued as before; in addition, 200 ml of milk replacer was offered every 2 hours by bottle. Appetite, including suckling of the dam and intake of milk replacer, frequency of urination, and clinical condition improved steadily during the next 48 hours, and IV fluid administration was discontinued in step-wise fashion during that period. Serum sodium concentration decreased from 165 mEq/L 36 hours after admission to 150 mEq/L 6 days after admission. Serum glucose concentration...
Ruminants/Camelids

The volume of urine produced.

no more than 0.5 mEq/h. Clinical recovery coincided
mOsm/h, but blood sodium concentration decreased

ed with regular insulin to aid in glucose clearance.

with distant history of exogenous glucocorticoid admin-

hyperglycemia, hypercholesterolemia, azotemia, and meta-
bolic acidosis. Calculated plasma osmolarity was

of hyperglycemia and hyperosmolarity, and most had

impaired glucose clearance because of diabetes melli-
tus develop hyperosmolar coma after events (eg, severe
infectious disease, ingestion of fluids with a high car-
brbohydrate content, and accidental or intentional omis-
these inciting events often also decrease water intake,
leading to inadequate volume replacement during
diuresis. Most crias described in the present report also
had a history of a stressful event (eg, sepsis, trauma,
premature birth, or death of the dam) prior to the onset
of hyperglycemia and hyperosmolarity, and most had
direct (eg, history of exogenous glucocorticoid admin-
istration or oral administration of a glucose-containing
electrolyte solution) or indirect (eg, stress leukogram,
hyperlipidemia, or hypercortisolemia) evidence that
the hyperglycemia was stimulated by glucogenic fac-
tors. Affected crias apparently did not have diabetes
mellitus, as glucose homeostasis returned to normal in
the 3 crias that recovered, but it is likely that they had
a diabetes-like inability to clear excess glucose. Adult
camelids have a minimal insulin response and pro-
longed hyperglycemia following administration of
exogenous glucose. If the same is true for crias, then
they would seem to be predisposed to develop hyper-
glycemia and hyperosmolarity in response to gluco-
genic stimuli. In contrast, calves, which frequently are
confronted by stressful events, have a much more vig-
orous pancreatic response to hyperglycemia and rarely
or never develop pathologic hyperglycemic hyperos-
molarity. If this line of reasoning is correct, it is
important to recognize that this degree of pancreatic
function is normal in camels; it is the glucogenic
stimulus that is abnormal and stimulates development
of hyperglycemia and hyperosmolarity.

Insufficient water intake probably played an
important role in the development of hypernatremia in these crias. Persistent hyperglycemia leads to a redistribution of body water from the intracellular to the extracellular space, which may initially result in a decrease in blood sodium concentration secondary to dilution, as was seen in 1 cria described in the present report. Hypernatremia subsequently develops as extracellular water is lost during glucose diuresis and is not replaced through an increase in intake. Hypernatremia is an uncommon finding in people with hyperosmolar coma but was a consistent finding in these crias. Most of these crias had little opportunity to increase their fluid intake because of intermittent bottle feeding, the effort required to nurse the dam, or the lack of availability of water. Renal conservation of sodium to combat hypovolemia (as represented by the inappropriate low urinary fractional clearance),4 mineralocorticoid effects of glucocorticoids, and administration of sodium-containing electrolyte solutions may also have contributed to the hypernatremia. Because increases in sodium concentration typically have a greater effect on plasma osmolarity than increases in glucose concentration, measuring blood sodium concentration may be the best way to assess the severity of the abnormalities in affected crias. Similar to people with hyperosmolar coma, severe hypernatremia (> 175 mEq/L) was associated with a grave prognosis.

Clinical signs in the crias described in the present report were related to the loss of intra- and extracellular water, with resultant circulatory failure and cellular dysfunction. The most common clinical signs were lethargy, anorexia, weakness, hyperthermia, base-wide stance of the hind limbs, head tremor, and eventually coma, with more severe signs seen in crias with the highest glucose and sodium concentrations. Because of osmotic extraction of water from the brain, CNS abnormalities were more common than would be expected for animals that were dehydrated but did not have hyperosmolarity. Important differential diagnoses for crias with similar signs include prematurity, sepsis, meningitis, peritonitis, congenital nervous system lesions, meconium impaction, and other congenital or acquired large-intestine obstructions.11-13 Laboratory analysis was necessary to establish the diagnosis. Severe hyperglycemia, glucosuria, hypernatremia, metabolic acidosis, and azotemia were the most frequent abnormalities.

The goal of treatment of these crias was to restore normal blood osmolality without causing cerebral edema. Treatment, therefore, consisted mainly of IV administration of isotonic fluids, followed by oral administration of hypotonic fluids. When treating crias with these signs, it is logical to avoid using fluids containing glucose or supraphysiologic concentrations of sodium and to avoid using glucocorticoids. The choice between isotonic and hypotonic fluids in people with hyperosmolar coma is less important than giving a sufficient volume of fluids to restore renal function while avoiding rapid changes in osmolarity.14 Slow administration of hypotonic fluids is advocated to treat hypernatremia in calves,15 because calves often have had the condition long enough to generate osmotic molecules (idiogenic osmolytes) in their brains to protect the CNS against dehydration. Also, affected calves typically do not have renal sodium retention and free water loss. Thus, slow restoration of normal systemic and CNS osmolarity is preferred. In contrast, abnormalities appeared to develop quickly in the crias described in the present report, giving them less time to produce idiogenic osmolytes in their brains. Because these crias were continuing to lose water secondary to glucose diuresis, slow administration of fluids may have restored renal output without correcting the hyperosmolarity, and even though isotonic, rather than hypertonic, fluids were used, hypernatremia worsened in 3 crias, 2 of which received only small volumes of fluid and died. Even with administration of relatively high volumes of isotonic fluids, hypernatremia resolved at a slower rate (up to 0.5 mEq/h) than has been recommended for neonatal calves (< 1.7 mEq/h)16 and other species; however, changes in plasma osmolality were similar. The slower correction rate was selected on the basis of concerns that rapid unforeseen changes in glucose concentration associated with a loss of glucogenic stimulation could have caused unanticipated changes in plasma osmolality. The inability to reduce blood sodium concentration to a value < 160 mEq/L while blood glucose concentration was > 500 mg/dl further highlighted the importance of correcting hyperglycemia in these crias.

Although all 6 of these crias had severe hyperglycemia, only 1 was treated with insulin. At the time, it was thought that hyperglycemia in camelids was attributable to the stress response and concurrent insulin resistance and that hyperglycemia would resolve spontaneously with time and treatment of the primary disorder. In addition, the detrimental effects of hyperglycemia in camelids had not been reported. It is now known that camelids have low baseline insulin concentrations and a poor pancreatic response to hyperglycemia.3 Insulin is used routinely to treat hyperglycemic hyperosmolarity in people, and there appears to be less concern about the rate at which blood glucose concentration is returned to reference limits with this disorder than in people with diabetic ketoacidosis.4 Therefore, it is likely that insulin administration would have been helpful in the treatment of these crias. It is recommended that fluid deficits be replaced prior to insulin administration, otherwise hypernatremia and the extracellular fluid deficit may worsen as water follows glucose into cells. Also, the blood glucose concentration should be monitored to avoid hypoglycemia. Frequent monitoring of sodium and glucose concentrations will help prevent rapid shifts of water into the CNS.

An additional goal of treatment of the crias described in the present report was to prevent or manage sepsis, which was presumed to be a contributory stressor in several of these animals. Infectious diseases are also considered an important risk factor for hyperosmolar coma in people6 and are known to induce hyperglycemia in llamas.17-18 Sepsis could contribute to hyperosmolarity by stimulating cortisol release, decreasing fluid intake, and affecting renal function. For these reasons and because of the poor prognosis for crias with sepsis and hyperosmolarity, veterinarians
should exercise care when treating sick crias with sodium- or glucose-containing fluids or with glucocorticoids and should monitor sick crias for hyperglycemia, hyperosmolarity, and hypernatremia.

References