Hypernatremia in Calves

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Hypernatremia (sodium chloride intoxication) is described in two calves due to presumed mixing errors of oral electrolyte solutions while undergoing therapy for neonatal diarrhea. The experimental induction of hypernatremia in two clinically normal calves is also reported. Physical findings in diarrheic calves included depression, weakness, dehydration, and diarrhea. Serum sodium concentrations were found to be 171.6 mEq/l and 208.0 mEq/l, respectively. Treatment with intravenous fluids was attempted in both cases, but one calf died after 6 hours and the other calf died after 2 days and exhibited periodic convulsions before death. Experimental induction with oral administration of 1 l of electrolyte concentrate, which contained approximately 2750 mEq sodium revealed that the normal calves would willingly consume the solution as mixed with milk and develop clinical signs of hypernatremia within 6 hours of administration. Serum sodium concentrations of 176.0 and 179.8 were found in the experimental calves and coincided with the onset of overt depression and weakness, at which time they were euthanatized. Cerebrospinal fluid electrolyte analysis paralleled the serum electrolyte alterations. (Journal of Veterinary Internal Medicine 1988; 2:66–70)

SALT (SODIUM CHLORIDE) poisoning has been reported occasionally in cattle associated with water deprivation combined with excess salt intake.[1–5] The condition has also been described in veal calves consuming excessive levels of salt in milk replacer.[6–8] Clinical signs are mainly referrable to digestive tract upset and central nervous system derangement.[2] Sodium is implicated as being the primary ion responsible for appearance of signs of salt toxicity in calves[7] and thus the condition is more appropriately termed hypernatremia. Central nervous system derangement due to elevated sodium levels occurs through inhibition of glycolysis in brain cells.[9]

Therapy for neonatal diarrhea with oral electrolyte solutions is presently a well-accepted and often lifesaving measure but has been reported to cause hypernatremia in children as a consequence of mixing errors of oral electrolyte solutions.[10,11] This paper describes hypernatremia presumed due to improper mixing of oral electrolyte solutions in calves undergoing therapy for neonatal diarrhea. Details of clinical and clinicopathologic alterations associated with experimental induction of hypernatremia due to an oral electrolyte solution in normal calves are also given and appropriate therapy discussed.

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Calf A

A 2-week-old female Holstein (calf A) weighing 40 kg was presented to the Veterinary Teaching Hospital, University of Guelph, with a history of diarrhea of 4 days' duration. Therapy at the farm included intramuscular chloramphenicol and oral electrolytes, both of undetermined quantities and duration. Upon admission, the calf was depressed and dehydrated (approximately 8% to 10%), and had pasty, yellow feces coating the perineal area. The heart rate was 132 beats/min, body temperature 38.3°C, and respirations 28/min. The clinical diagnosis was neonatal diarrhea with secondary dehydration and metabolic acidosis. The cause of the dehydration and depression was thought to be fluid and bicarbonate loss in the feces. Blood samples were obtained for blood gas analysis and serum electrolytes (sodium, potassium, and chloride). Feces were also collected and assessed for parasites, virus particles, and potential bacterial pathogens. Lactated Ringer's solution was administered intravenously (IV) at 800 ml/h for the first 4 hours for rehydration.

Results of serum electrolytes revealed hypernatremia (171.6 mEq/l), hyperchloremia (139.7 mEq/l), and hypokalemia (1.88 mEq/l) (Table 1), which changed our diagnostic considerations to include salt toxicity (hypernatremia). Intravenous fluid therapy was changed from lactated Ringer's solution to 5% dextrose at 40 ml/kg for 24 hours, and the calf was administered dexamethasone* at 1 mg/kg IV to counteract possible

* Dexamethasone, Austin, Joliette, Quebec.

TABLE 1. Diarrheic Calves' Serum Electrolytes, Concomitant Osmolality and Bicarbonate; CSF Electrolytes of Calf A

Time from Admission	Sodium (mEq/l)	Potassium (mEq/l)	Chloride (mEq/l)	HCO_3 (mmol/l)	Osmolality (mOsm/kg H_2O)
Calf A					
0 h	171.6	1.9	139.7	20.7	NA
2 h (CSF)	165.4	3.1	148.9		356
3 h	155.6	1.4	120.3	22	352
Calf B					
14 h*	148.4	2.9	123.3	17.3	NA
21 h	208.0	4.6	177.6	16.6	411
33 h	191.3	3.2	142.3	17.8	377
44 h	176.6	3.2	141.6	16.6	NA
49 h	164.7	3.1	127.4	20.8	NA
57 h	156.5	4.3	117.8	12.3	NA
61 h	Died				
Normal plasma value†	135–145	3.9–5.6	93–104	22–26	279–298

CSF: cerebrospinal fluid; NA: not available.
* Before feeding high-sodium electrolyte.
† Veterinary Teaching Hospital Manual, University of Guelph.

cerebral edema[12] and furosemide† at 2.2 mg/kg IV for its natriuretic action.

Two hours postadmission, after serum electrolyte values were known, a sample of cerebropsinal fluid (CSF) was obtained; electrolyte analysis showed parallelism with the initial serum sodium and chloride values (Table 1). Three hours postadmission, a repeat analysis of serum electrolytes showed reduction of sodium and chloride concentrations (Table 1).

Despite the above therapy, the calf died 6 hours postadmission. Fecal samples were positive for enterotoxigenic *Escherichia coli* and *Cryptosporidia,* the likely inciting causes of the calf's diarrhea.

Necropsy revealed no gross lesions. Histopathology revealed vesiculation of neuronal nuclei of the cerebral cortex, leading to a diagnosis of cerebral cortical degeneration.

Calf B

An 8-day-old male Hereford × Holstein (calf B) weighing 32 kg was presented to the Veterinary Teaching Hospital at the University of Guelph with a history of diarrhea of 4 days' duration. Prior therapy had consisted of twice-daily oral electrolyte solution of an undetermined quantity. Despite this therapy, the calf became dehydrated, was depressed to the point of being unable to rise, and had lost its suckle reflex.

At the time of admission, the calf was tachypneic (48 breaths/min) and tachycardic (126 beats/min) and had a subnormal body temperature of 36.5°C. Other clinical abnormalities noted were dehydration of approximately 6% of body weight, marked depression, absent suckle reflex, and the passage of loose, pale feces.

The dehydration was presumed to be due to ongoing fluid losses from diarrhea that had not been entirely corrected by oral electrolyte solutions. Depression and the concomitant absence of suckle reflex were presumed to be due to coexisting metabolic acidosis, which results from excess bicarbonate losses in fluid feces.

The diagnostic evaluation included venous blood gas analysis and serum electrolytes (sodium, potassium, and chloride). Feces were collected and submitted for bacterial, parasitologic, and virologic studies.

Treatment of calf B consisted of intravenous lactated Ringer's solution initially at 500 ml/h over 4 hours to replace fluid deficits, followed at 60 ml/kg for 24 hours for maintenance and ongoing losses. In addition, 240 mEq of sodium bicarbonate was administered intravenously during the initial 4-hour period to treat the metabolic acidosis that had been confirmed on blood gas analysis (data not shown).

Within 3 hours of the start of fluid therapy, the calf was able to stand, had an improved demeanor, and had regained its suckle reflex. Passage of feces appeared to be infrequent, and stool was taking on a formed consistency.

At 9½ hours postadmission, blood gas analysis demonstrated a continued, though reduced, degree of metabolic acidosis (data not shown). An additional 240 mEq of sodium bicarbonate was administered intravenously, and since the diarrhea was abating, fluid therapy was altered from intravenous to oral administration. At 14 hours postadmission, the calf was fed 1 l of a commercial oral electrolyte solution (Table 2) mixed with 1 l of whole milk. The calf suckled vigorously and consumed the solution in its entirety. Electrolytes just before the feeding had not changed markedly over admission values (Table 1).

The following morning the calf was found recumbent, markedly depressed, and exhibiting fine muscle tremors. With the possibility of bacterial meningoencephalitis causing these signs, the calf was started on a potentiated sulfonamide‡ at 30 mg/kg every 12 hours IV and placed on intravenous lactated ringers solution (60 ml/kg for 24 hours). Cytology of cerebrospinal fluid obtained from the lumbosacral junction was within normal limits. Blood gas and serum electrolyte samples revealed mild metabolic acidosis (data not shown) with marked hypernatremia (208 mEq/l) and hyperchloremia (177.6 mEq/l) (Table 1). At this time, it was determined that the calf had received an entire liter of the concentrated electrolyte solution at the 14-hour feeding rather than a properly diluted solution of oral electrolyte solution. With label direc-

† Lasix, Hoechst, Montreal, Quebec.

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tions indicating the addition of 60 ml of the concentrate to 940 ml of water, a 15-fold excess of the electrolytes had been administered (Table 2).

Therapy was therefore altered to 5% dextrose IV at 40 ml/kg for 24 hours, furosemide at 2.2 mg/kg IV every 12 hours, and dexamethasone 1 mg/kg IV every 24 hours.

With the change in therapy to treat hypernatremia, the calf gradually became brighter in demeanor. However, on day 3 postadmission, the calf was again noted to be depressed and subsequently developed periods of convulsions, became comatose, and died. Serum electrolytes were monitored throughout the clinical course and showed steady decline toward normal concentrations (Table 1). *Cryptosporidium* was the only enteric pathogen found on fecal analysis.

Necropsy revealed pulmonary edema and congestion as the only gross lesions. Histopathologic examination of the brain demonstrated lesions of acute laminar cerebral necrosis.

Experimental Induction

Animals

For experimental induction of hypernatremia, three clinically normal male Holstein calves weighing 44 to 56 kg and less than 2 weeks of age were used. Calves were accustomed to being fed (by bucket) 2 liters of whole milk twice daily and had water free choice. Two calves served as the principals and were given, via calf nipple bottles, one liter of a concentrated oral electrolyte solution§ (Table 2), mixed with 1 l of whole milk in the place of a normal morning feeding. This duplicated the toxic feeding calf B was given. The third calf served as a control and was given, also via a calf nipple bottle, 1 l of the above oral electrolyte solution that had been diluted according to label directions (Table 2) and mixed with 1 l of whole milk. Water was not available to the calves during the experimental period. Each calf consumed its allotted feeding readily and completely.

Calves were monitored clinically for the development of signs of hypernatremia, at which time they were euthanatized with an intravenous barbiturate.

Samples

Venous blood samples for determination of serum electrolytes (sodium, potassium, and chloride), pH, packed cell volume (PCV), base excess, and total protein were obtained from each calf immediately prior to administering the oral electrolyte/milk solution, 1 h postfeeding, then every second hour until the appearance of overt clinical signs of hypernatremia.

Cerebrospinal fluid for sodium, potassium, and chloride concentrations was collected from each calf at the lumbosacral space at the time of appearance of clinical signs in the principal calves and at a similar time for the control.

§ Electrolyte Concentrate, Austin, Joliette, Quebec.

TABLE 2. Constituents and Directions for Dilution of Concentrated Oral Electrolyte Solution* Used in Calves B, C, D in the Concentrate Form and Calf E Diluted as per Label Instructions

Each 60 ml contains:	Sodium chloride	5.9 g
	Calcium chloride	0.23 g
	Magnesium chloride	0.30 g
	Sodium acetate	3.8 g
	Potassium acetate	1.0 g
	Dextrose	27 g

Directions: Mix 60 ml concentrate to 940 ml water.
Oral dose: 1 l or more as recommended by veterinarian.

* Electrolyte Concentrate, Austin Laboratories, Joliette, Quebec.

Analyses for sodium, potassium, and chloride were performed by ion-selective electrode (Nova 5, Nova Biomedical, Newton MA); total protein, by a refractometer (American Optical, Buffalo, NY); and pH and base excess, on an automated blood gas analyzer (Radiometer, Copenhagen, Denmark).

Results

Clinical Findings

Each calf suckled readily and consumed the entire amount of fluids in the bottle. One of the principal calves (calf C) showed temporary mild abdominal discomfort for approximately 15 minutes following fluid consumption; the other principal and the control calf showed no untoward reactions to consuming the solution.

The principal calves became depressed and recumbent and could not be induced to rise by vigorous stimulation within 5 hours of fluid administration; whereas the control remained clinically unaffected. Additionally, calf C of the principals developed a tense, distended abdomen and fluid yellow/mucoid feces at 5½ hours post-fluid administration. Calf C was euthanatized at 6 hours post-fluid administration, and calf D was euthanatized at 5 hours post fluid administration.

Blood and CSF Samples

Shown in Table 3, the serum sodium and chloride rose markedly in the principals but remained stable in the control calf. The base excess rose in the principal calves when compared with the control calf, presumably due to metabolization to bicarbonate of the large amount of acetate present in the electrolyte concentrate. Serum potassium did not change remarkably with time in either the principals or the control. The total protein showed mild elevations in both principal calves but not in the control. In all calves, the PCV fell marginally over the experiment. Electrolyte values of CSF taken at the end of the experiment paralleled simultaneous serum electrolyte values (Table 3).

TABLE 3. Levels of Serum Sodium, Potassium, Chloride, pH, Base Excess, Packed Cell Volume, and Total Protein in Blood of Control and Principal Calves During Experimental Induction of Hypernatremia and CSF Electrolytes at the Termination of the Experiment

Calf	Sample Time (Hours Post-administration)	Sodium (mEq/l)	Potassium (mEq/l)	Chloride (mEq/l)	pH	BE (mmol/l)	PCV (%)	TP (g/dl)
C (principal)	0	136.3	5.9	100.1	7.32	5.2	24	5.4
	1	149.6	4.6	110.4	7.36	5.7	23	5.4
	3	173.0	5.5	125.6	7.29	10.2	27	6.0
	5*	176.0	5.1	127.0	7.36	13.8	21	5.9
	6	178.6	4.2	128.7	7.34	14.0	21	6.1
CSF	6	175.6	4.3	143.1		NA		
D (principal)	0	139.4	4.1	107.3	7.37	0.3	30	5.6
	1	151.2	4.8	114.9	7.35	3.8	29	5.7
	3	168.9	4.4	129.5	7.33	7.3	29	5.9
	5*	179.8	4.2	137.1	7.32	10.3	28	6.1
CSF	5	172.9	4.3	142.1		NA		
E (control)	0	141.8	5.1	106.3	7.33	1.6	27	5.9
	1	141.5	4.8	107.0	7.36	2.9	25	5.6
	3	142.3	5.1	108.3	7.39	4.4	24	5.9
	5	141.1	4.8	107.1	7.41	4.9	24	5.9
	6	140.7	4.8	107.1	7.36	3.6	24	5.6
CSF	6	140.8	3.2	120.9		NA		

CSF: cerebrospinal fluid; BE: base excess; PCV: packed cell volume; TP: total protein; NA: not available.
* Onset of clinical signs of hypernatremia.

Discussion

This paper demonstrates the potential dangers of mixing errors involving the use of oral electrolyte solutions for rehydration in diarrheic calves and expands the reported clinical settings in which hypernatremia can occur in cattle.

The two principal animals utilized in the experimental induction of hypernatremia, as well as the known clinical induction (calf B), show clear and similar clinicopathologic changes. Although the low number does not allow statistical comparison, the experimental calves help corroborate the findings in the clinical cases. It is possible the hypernatremia found in calf A was due to excess pure water loss and not the result of faulty oral electrolyte preparation; however, calves with similar clinical histories seldom have elevated serum sodium concentrations.[13,14]

It was considered important that the two healthy, hungry calves readily consumed the highly concentrated solution, and that the solution as mixed with milk was palatable.

The effect of hypernatremia on brain cells is inhibition of glycolysis,[9] hence the depression noted in experimental calves. Depression in the clinical cases was likely a combination of hypernatremia, dehydration, and acidosis. During states of hyperosmolarity, in this case due to hypernatremia, the brain cells produce substances termed "idiogenic osmoles," which serve to protect the brain against adverse effects of hyperosmolarity.[15] These substances can, in turn, exert continued elevation of brain intracellular osmolarity during resolution of the hypernatremic state. As a result of the reduction of extracellular osmolarity, water enters the brain cells causing brain swelling within the cranial vault, which can manifest clinically as convulsions.

Only in the clinical cases was this brain swelling a clinical consideration, as the calves that had induced hypernatremia were euthanatized before efforts were undertaken to reduce serum sodium concentrations. Therefore, convulsions were not to be expected in the experimental calves.

Necropsy findings, although considered diagnostic in swine,[16] are seldom conclusive in cattle and include nonspecific changes of cerebral edema[2] or encephalomalacia.[1]

Each of the two clinical cases was dehydrated and acidotic, presumably from the diarrhea. The hypokalemia was presumed to represent a total body deficit of potassium due to fecal loss and inadequate intake. Both acidosis and hypernatremia can contribute to signs of depression. The combination of dehydration and hypernatremia presents a therapeutic dilemma. Fluid therapy is necessary for combating dehydration and should be sodium-poor to dilute the high concentrations of serum sodium. However, rapid reduction of serum sodium concentrations can lead to brain swelling resulting in convulsions.[17]

Successful intravenous therapy for hypernatremic dehydration that has not been associated with post-therapy convulsions in children has been described.[18] This involved the use of an initial rehydrating solution of 75 to 80 mEq/l of sodium in 5% glucose with the anion portion being comprised of ⅔ chloride and ⅓ bicarbonate, acetate or lactate. Twenty-five to 50 ml/kg of this fluid was administered during the initial 4–5 hours until urine

formation was noted. Correction of the remaining volume deficit was gradual over 2 days with a 2.5 to 5% glucose solution containing 25–40 mEq/l sodium, 40 mEq/l potassium, and the anion 25% base as lactate or acetate. The diarrheic calves treated in this study were rehydrated with 5% dextrose, but this may have been given too rapidly. Oral, rather than intravenous, fluid therapy with 2.5% dextrose has been shown to decrease the incidence of seizures in hypernatremic rabbits.[17] The oral route would therefore be preferred if animals would tolerate oral fluids. However, clinical cases with ileus, abdominal distension, or malabsorptive abnormalities, as may be found in many diarrheic calves, may prevent the use of the oral route.

Diuretic therapy in the clinical cases was used to enhance renal sodium ion excretion, as the calves' renal natriuretic capacity would likely have been blunted by extracellular volume contraction. However, this therapy will also increase water loss, which, without supportive fluid therapy, can have severe consequences in an already dehydrated animal.

The toxicity demonstrated due to known mixing error of an oral electrolyte solution supplied in excess of 15 times the quantity of sodium ions that would normally be given at one treatment. It is likely that some lower degree of sodium excess through mixing errors of oral electrolytes can be tolerated by calves. The therapeutic efficacy of commercially available oral electrolyte solutions for rehydration in neonatal calf diarrhea remains unquestioned. However, as serum sodium concentrations of the patient are seldom known at the time of treatment, and the clinical sign of depression can result from either acidosis or hypernatremia, the clinician should be alert to the possibility of mixing errors inducing hypernatremia in those calves undergoing oral electrolyte therapy that become depressed or remain so after appropriate fluid therapy.

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