Effect of a 24-hour infusion of an isotonic electrolyte replacement fluid on the renal clearance of electrolytes in healthy neonatal foals

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Objective—To determine the effects of a 24-hour infusion of an isotonic electrolyte replacement fluid (IERF) on weight, serum and urine electrolyte concentrations, and other clinicopathologic variables in healthy neonatal foals.

Animals—4 healthy 4-day-old foals.

Design—Prospective study.

Procedure—An IERF was administered to each foal at an estimated rate of 80 mL/kg/d (36.4 mL/lb/d) for 24 hours. Body weight was measured before and after the infusion period. Urine was collected via catheter during 4-hour periods; blood samples were collected at 4-hour intervals. Variables including urine production; urine and serum osmolalities; sodium, potassium, and chloride concentrations in urine and serum; urine and serum creatinine concentrations; urine osmolality-to-serum osmolality ratio (OsmR); transtubular potassium gradient (TTKG); and percentage creatinine clearance (Cr_{cl}) of electrolytes were recorded at 0, 4, 8, 12, 16, 20, and 24 hours during the infusion period. Immediately after the study period, net fluid and whole-body electrolyte changes from baseline values were calculated.

Results—Compared with baseline values, urine and serum sodium and chloride serum concentrations, urine and serum osmolalities, OsmR, and percentage Cr_{cl} of sodium and chloride were significantly increased at various time points during the infusion; urine production did not change significantly. After 24 hours, weight, TTKG, serum creatinine concentration, and whole-body potassium had significantly decreased from baseline values.

Conclusions and Clinical Relevance—Results suggest that administration of an IERF containing a physiologic concentration of sodium may not be appropriate for use in neonatal foals that require maintenance fluid therapy. (*J Am Vet Med Assoc* 2005;227:1123–1129)

Intravenous administration of fluids is performed in neonatal foals for a variety of clinical conditions. **Isotonic electrolyte replacement fluids (IERFs)** containing physiologic concentrations of sodium are commonly used in adult horses, and many practitioners administer these fluids to neonatal foals that require maintenance fluid therapy. However, maintenance fluid therapy requirements in foals are unknown, and recommendations are currently based on empirical information derived from other neonatal species and clinical experience.[1,2] It has recently been suggested that maintenance fluid therapy in sick neonatal foals should consist of fluids containing low concentrations of sodium and that the total parenteral sodium intake be limited to 2 to 3 mEq/kg/d (0.91 to 1.36 mEq/lb/d).[1,2]

Critically ill human neonates who are administered solutions containing physiologic concentrations of sodium are at risk of developing hypertension, edema, bronchopulmonary dysplasia, necrotizing enterocolitis, and patent ductus arteriosus.[3-9] Hypernatremia and volume overload (resulting from the limited ability of the kidneys to increase urinary sodium excretion) are thought to be the mechanism for these conditions.[3-7,10-14] These phenomena have been identified in neonatal humans, dogs, and sheep and are the basis for the recommendation to use fluids containing low sodium concentrations for maintenance fluid therapy in neonatal foals.[1,2,4,10-13,15,16]

Results of previous studies[17,18] in nursing neonatal foals have been used to establish reference values for urinary clearance of creatinine and electrolytes, percentage **creatinine clearance (Cr_{cl})** of electrolytes (fractional excretion), **urine osmolality (Osm_u)** and specific gravity, glomerular filtration rate, and effective renal plasma flow. In adult horses, IV administration of saline (0.9% NaCl) solution or 5% dextrose in water increases urinary excretion of sodium and chloride; however, information regarding the effects of administration of any type of fluid in neonatal foals is lacking.[19] The purpose of the study reported here was to determine the effects of 24-hour infusion of an IERF on body weight, serum and urine electrolyte (sodium, potassium, and chloride) concentrations, and other clinicopathologic variables in healthy neonatal foals.

Materials and Methods

Animals—Mares and foals from the University of Tennessee teaching and research herd were included in this study. Four healthy mixed-breed 4-day-old foals (2 males and 2 females) were used. Although precise gestational age was not known, foals were judged to have a gestational age of > 330 days on the basis of physical characteristics at the time of birth.[20] All foals stood and suckled within 2 hours after parturition, and no abnormalities were noted on gross examination of the placentas. All foals received adequate transfer of immunity (plasma IgG concentration, > 800 mg/dL) as determined 24 hours after parturition by use of an ELISA test kit.[a]

During the 24-hour study period, each mare and foal was housed in the same stall (3.7 × 3.7 m). Mares were each fed 2 kg of a concentrate and free-choice grass and alfalfa hay

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and had access to water ad libitum daily from parturition until after the study. Procedures were approved by the University of Tennessee Institutional Animal Care and Use Committee prior to beginning the study.

Procedures—Each foal was allowed to consume milk from birth through 3 days. On the fourth day, each foal was separated from its dam by placing it in a 1.2 × 1.8-m pen inside the mare's stall. The foal was able to stand, walk around, and lie down but did not consume milk or feed during the experimental period. Catheters were placed in the right and left jugular veins. One catheter was used for fluid administration, and the other was used for blood sample collection. Each foal was fitted with a sterile urinary catheter and a urinary collection apparatus consisting of latex tubing that attached the urinary catheter to a sterile 1-L urine collection bag. The apparatus was attached to the foal by a backpack and harness system.[b]

Body weight (kg) of each foal was measured immediately before and after the 24-hour study period by use of a walk-on digital scale. Prior to the start of the 24-hour urine collection, the bladder was emptied as completely as possible via the urinary catheter and baseline (0 hour) blood and urine samples were collected from the foals. After initial sample collections, administration of a continuous rate infusion of an IERF[c] (3.3 mL/kg/h [1.5 mL/lb/h], IV) via a standard coil administration set was begun. Fluid infusion rate was regulated by use of an infusion pump with a digital LCD readout.[d] To determine the actual amount of the IERF administered to each foal, the IERF bags were weighed before and after administration and the remaining volume in the bags was measured by use of a graduated cylinder.

Every 4 hours (ie, at 4, 8, 12, 16, 20, and 24 hours) during the infusion period, urine was collected and the volume was measured by use of a graduated cylinder. At the time of each urine collection, a 10-mL blood sample was collected from the jugular catheter; a 5-mL aliquot was placed in a serum separator tube without anticoagulant, and a 5-mL aliquot was placed in a tube containing the anticoagulant K_3-EDTA. Urinalysis was performed soon after urine collection, and a 10-mL aliquot was placed at 4°C for later analysis of electrolyte and creatinine concentrations and osmolality. The blood sample in the serum separator tube was allowed to clot and centrifuged for 15 minutes; serum was collected and stored at 4°C (39.2°F) for later analysis of electrolyte and creatinine concentrations and osmolality. The blood in the tube containing K_3-EDTA was analyzed immediately after collection for blood glucose concentration, PCV, and plasma total solid concentration. After each blood collection, the IV catheter was flushed with 5 mL of saline (0.9% NaCl) solution containing heparin (20 U of heparin sodium/mL). Urine and blood samples were stored at 4°C for a maximum of 16 hours before analysis.

Laboratory analyses—A commercial diagnostic strip was used to determine the effects of urinary catheterization. Urine samples were centrifuged for 5 minutes, and supernatants were analyzed for **urine sodium (Na_u)**, **potassium (K_u)**, **chloride (Cl_u)**, and **creatinine (Cr_u)** concentrations as well as for Osm_u, **specific gravity (USpG)**, and **volume (V_u)**. Urine electrolyte and Cr_u concentrations were measured via automated analysis with a standard chemistry analyzer.[e] Osmolality was measured via the vapor pressure method by use of an osmometer,[f] and USpG was measured via refractometry. **Urine production rate (UPR)** was determined by use of the following calculation:

$$UPR\ (mL/h/kg) = V_u/4\ h/body\ weight\ (kg).$$

A linear change in body weight was assumed for the calculation because the foals were weighed only before and after the study.

Serum sodium (Na_s), **potassium (K_s)**, **chloride (Cl_s)**, and **creatinine (Cr_s)** concentrations were measured by use of a standard chemistry analyzer.[e] **Serum osmolality (Osm_s)** was measured via the vapor pressure method by use of an osmometer.[f] Plasma total solids concentration was measured by use of a hand-held refractometer, and PCV was determined by use of a capillary tube method after centrifugation for 60 seconds. Blood glucose concentration was determined by use of a calibrated handheld glucometer.[g]

The **transtubular potassium gradient (TTKG)** was calculated by use of the following equation:

$$TTKG = K_u/(Osm_u/Osm_s)/K_s.$$

Urine osmolality-to-serum osmolality ratio (OsmR) was calculated by use of the following equation:

$$OsmR = Osm_u/Osm_s.$$

Net fluid volume ($fluid_{net}$) and **net whole-body sodium (Na_{net})**, **potassium (K_{net})**, and chloride **concentrations** gained or lost were determined on the basis of differences between the amounts of each variable infused and the amounts excreted in the urine during the 24-hour period; the net values were calculated by use of the following formula:

$$X_{net}\ (mEq/L/kg) = (X_{in} - X_{out})/weight\ (kg),$$

where X_{in} is the total fluid volume (L) or amount of electrolyte (mEq/L × volume [L]) in the volume infused and X_{out} is the total urine volume (L) or amount of electrolyte (mEq/L × V_u) excreted in urine. Mean values of weight at baseline or at the 24-hour time point were used for this calculation.

Percentage Cr_{cl} rates or **fractional excretion rates for sodium (Na_{FE})**, **potassium (K_{FE})**, and **chloride (Cl_{FE})** were calculated for each blood and urine sample collected at 4-hour intervals by use of the following formula:

$$X_{FE} = ([X_u/X_s] \cdot [Cr_s/Cr_u]) \cdot 100\%,$$

where X_u is the electrolyte concentration in urine and X_s is the electrolyte concentration in serum.

Creatinine clearance was calculated for each blood and urine sample collected at 4-hour intervals by use of the following formula:

$$Cr_{cl} = (Cr_u \times V_u)/(Cr_s \times 240\ min \times wt\ [kg]).$$

A linear change in weight was assumed for the calculation of Cr_{cl} because foals were weighed only before and after the study.

Data and statistical analyses—Descriptive data are presented as median and range unless otherwise specified. Differences in total fluid volume, sodium, potassium, and chloride concentrations between IV fluid input and urine output and differences in weight of foals during the 24-hour observation period were evaluated by use of a paired *t* test, Wilcoxon signed rank test, or sign test, depending on the distribution of the data. A mixed-model repeated-measures ANOVA was used to compare the change in value of the following dependent variables at 4-hour intervals during the 24-hour period, beginning with baseline (0 hour): blood glucose concentration; PCV; plasma total solid concentration; Na_s, Cl_s, K_s, and Cr_s concentrations; Osm_s and Osm_u; Na_u, Cl_u, K_u, and Cr_u concentrations; USpG; Na_{FE}, K_{FE}, and Cl_{FE}; OsmR; and TTKG. Changes in dependent variables V_u and Cr_{cl} were evaluated in the same manner; however, baseline values were not available, and the first measurement was taken at 4 hours after the start of the 24-hour experimental period. The independent variable in the model was time, and foal was included in the

model as a random factor. A multiple range test according to the Tukey method was used to distinguish among the various levels of time.[21] Values for each of the dependent variables evaluated in the mixed model are presented as least square means and ranges. Significance was defined as a value of $P \leq 0.05$.

Results

None of the baseline urine samples contained blood or protein. However, in 3 of 4 foals, blood (range, trace to 3+) and protein (range, 1+ to 2+) were detected in urine samples obtained at each of the subsequent collection periods. The USpG increased from 1.009 at baseline to 1.015 during the study period, but this difference was not significant (**Table 1**). At baseline, Osm_u was 209.75 mOsm/L, and this value increased to 476.25 mOsm/L at the 24-hour time point; this difference was significant.

Over the 24-hour infusion period, there was a significant decrease in weight of the foals from a median

Table 1—Variables in urine samples* collected from four 4-day-old foals before and during a 24-hour infusion with an isotonic electrolyte replacement fluid.

		Time after start of infusion (h)						
Variable	**Reference range[17]**	**0 (Baseline)**	**4**	**8**	**12**	**16**	**20**	**24**
Sodium (mEq/L)	NE	10[a] (7–13)	40[a] (19–71)	118[b] (78 –165)	167[c] (129–195)	176[c] (153–204)	164[b,c] (130–191)	162[b,c] (132–211)
Potassium (mEq/L)	NE	79.6[a] (24.0–212.0)	80.3[a] (32.0–126.0)	47.4[a] (26.2–86.0)	54.1[a] (27.0–89.4)	37.6[a] (14.6–54.0)	31.4[a] (15.6–46.0)	28.5[a] (4.6–39.0)
Chloride (mEq/L)	NE	37[a] (16–72)	43[a] (24–62)	84[a,b] (67– 118)	113[b] (83– 127)	116[b] (104–134)	115[b] (79–136)	119[b] (95–162)
Urine production (mL/kg/h)	6.16[17]	ND	2.2[a] (0.6–5.5)	3.3[a] (1.3–5.7)	2.7[a] (1.3–3.3)	3.8[a] (2.5–5.5)	3.2[a] (2.4–4.1)	2.5[a] (1.6–3.5)
Creatinine (mg/dL)	26.5 ± 13.7[17]	65.6[a] (15.0–182.7)	91.0[a] (24.0–158.4)	56.4[a] (33.2–99.0)	56.6[a] (36.0–92.2)	41.9[a] (35.0–51.0)	38.6[a] (25.3–53.1)	47.1[a] (28.0–76.9)
Urine osmolality (mOsm/L)	101.7 ± 24[17]	210[a] (63–513)	326[a,b] (130–524)	351[a,b] (224–526)	475[b] (323–606)	431[a,b] (298–494)	433[a,b] (343–518)	476[b] (360–641)
Urine specific gravity	1.001–1.027[17]	1.009[a] (1.002–1.021)	1.014[a] (1.004–1.025)	1.013[a] (1.008–1.018)	1.015[a] (1.010–1.022)	1.013[a] (1.012–1.015)	1.014[a] (1.012–1.015)	1.015[a] (1.010–1.018)

Data are presented as least square means (range).
*Aliquots of urine collected during a 4-hour period.
NE = Not estimated. ND = No data.
[a-c]Values for a given variable with different superscript letters are significantly ($P \leq 0.05$) different. To convert kilograms to pounds, multiply by 2.2.

Table 2—Clinicopathologic variables in four 4-day-old foals before and at 4-hour intervals during a 24-hour infusion with an isotonic electrolyte replacement fluid.

		Time after start of infusion (h)						
Variable	**Reference range[17,22]**	**0 (Baseline)**	**4**	**8**	**12**	**16**	**20**	**24**
Serum sodium (mEq/L)	142 ± 19[22]	137[a] (136–138)	140[a,b] (136–145)	141[b] (139–144)	141[b] (138–143)	140[a,b] (137–142)	139[a,b] (138–141)	139[a,b] (136–141)
Serum potassium (mEq/L)	4.8 ±1.4[22]	4.1[a] (3.9–4.2)	4.3[a] (4.2–4.6)	4.1[a] (3.9–4.2)	4.3[a] (4.1–4.7)	4.1[a] (4.0–4.4)	4.1[a] (3.9–4.1)	4.1[a] (3.9–4.2)
Serum chloride (mEq/L)	101 ± 11[22]	96[a] (92, 100)	99[a,b] (94–107)	99[b] (94–106)	99[a,b] (93–106)	99[b] (94–106)	99[a,b] (95–105)	99[a,b] (94–105)
Serum creatinine (mg/dL)	1.0 ± 0.1[17]	1.0[a] (0.8, 1.3)	0.9[b] (0.7–1.1)	0.8[b] (0.7–1.1)	0.8[b] (0.7–1.1)	0.8[b] (0.6–1.0)	0.7[b] (0.6–0.9)	0.8[b] (0.7–0.9)
Serum osmolality (mOsm/L)	244.5 ±18.7[17]	267[a] (261, 272)	269[a] (265, 278)	273[a,b] (267–279)	275[a,b] (270–279)	272[a,b] (266–277)	274[a,b] (271–276)	281[b] (273–292)
PCV (%)	30–46[22]	37.0[a] (36–38)	34.8[a] (33–36)	34.8[a] (33–36)	33.0[a] (31–36)	33.3[a] (32–35)	35.5[a] (31–39)	33.3[a] (29–36)
Plasma total solids (g/dL)	5.3–7.9[22]	5.7[a] (4.6–6.2)	5.7[a] (4.5–6.4)	5.7[a] (4.4–6.4)	5.7[a] (4.3–6.4)	5.8[a] (4.4–6.8)	5.8[a] (4.4–6.9)	6.0[a] (5.0, 6.8)
Blood glucose (mg/dL)	101–226[22]	137[a] (116–158)	129[a,b] (108–150)	110[a,b] (89–130)	108[a,b] (87–129)	100[a,b] (79–121)	100[b] (79–121)	104[a,b] (83– 125)

Data are presented as least square means (range).
[a,b]Values for a given variable with different superscript letters are significantly ($P \leq 0.05$) different.

Table 3—Creatinine clearance, percentage creatinine clearance (fractional excretion) of electrolytes, urine osmolality-to-serum osmolality ratio, and transtubular potassium gradient values in four 4-day-old foals before and during a 24-hour infusion with an isotonic electrolyte replacement fluid.

Variable	Reference range[17]	Time after start of infusion (h)						
		0 (Baseline)	4	8	12	16	20	24
Creatinine clearance (mL/min/kg)	2.8 ± 0.55 [17]	ND	2.4[a] (2.0–2.9)	3.1[a] (2.0–4.5)	3.0[a] (2.8–3.4)	3.6[a] (2.1–5.3)	2.7[a] (2.2–3.2)	2.4[a] (1.5–3.3)
Fractional excretion of sodium (%)	0.31 ± 0.18 [17]	0.25 [a] (0.05–0.62)	0.32[a] (0.19–0.60)	1.30[b] (1.05–1.66)	1.78[b,c] (0.98–2.57)	2.25[c] (1.90–2.81)	2.28[c] (1.81–2.71)	2.07[c] (1.58–2.67)
Fractional excretion of potassium (%)	13.26 ± 4.49[17]	32.93[a] (18.62–52.84)	20.85[a] (10.09–34.9)	17.70[a] (9.08–34.9)	18.07[a] (9.08–24.50)	16.31[a] (5.58–22.57)	14.89[a] (8.68–21.44)	14.93[a] (1.14–25.00)
Fractional excretion of chloride (%)	0.42 ± 0.32[17]	0.90[a] (0.41–1.73)	0.53[a] (0.33–1.02)	1.29[a,b] (0.98–1.72)	1.70[b,c] (0.95–2.11)	2.08[b,c] (1.93–2.47)	2.22[c] (1.83–2.71)	2.12[c] (1.56–2.75)
Urine osmolality-to- serum osmolality ratio	0.41 ± 0.09[17]	0.8[a] (0.2–1.9)	1.2[a,b] (0.5–1.9)	1.3[a,b] (0.8–1.9)	1.7[b] (1.2–2.2)	1.6[a,b] (1.1–1.8)	1.6[a,b] (1.3–1.8)	1.7[a,b] (1.3–2.3)
Transtubular potassium gradient	NE	23.7[a] (19.3–28.3)	16.1[b] (10.2–20.0)	9.0[b,c] (5.1–11.6)	7.3[c] (4.0–11.1)	6.3[c] (2.0–12.1)	5.0[c] (3.0–8.0)	4.8[c] (0.5–7.6)

Values were calculated by use of data obtained from serum samples (collected at 4-hour intervals) and urine samples (4-hour collection period) and are presented as least square means (range).
See Table 1 for remainder of key.

value of 51.4 kg (113.1 lb; range, 49.5 to 53.1 kg [108.9 to 116.8 lb]) at baseline to 48.4 kg (106.5 lb; range, 46.8 to 51.4 kg [103.0 to 113.1 lb]) at the 24-hour time point, which represented a median loss of 2.7 kg (5.9 lb; range, 1.8 to 3.2 kg [4.0 to 7.0 lb]) or 5.5% (range, 3.4% to 5.9%) of body weight.

By the 8-hour time point, there was a significant increase in Na_u concentration, compared with the baseline value (Table 1). By the 12-hour time point, there was a significant increase in Cl_u concentration. The K_u concentration decreased from 79.6 mEq/L at baseline to 28.5 mEq/L at the end of the 24-hour infusion, but this difference was not significant. The UPR increased from 2.2 mL/kg/h (1.0 mL/lb/h) to a maximum of 3.8 mL/kg/h (1.73 mL/lb/h) at the 16-hour time point, but this difference was not significant.

Compared with baseline values, there were significant increases in Na_s and Cl_s concentrations at the 8-hour time point and a significant decrease in Cr_s concentration at the 4-hour time point (**Table 2**). The Osm_s increased over time, but the only significant difference from the baseline value was at the 24-hour time point. The K_s concentration, Osm_s, PCV, and plasma total solids concentration values did not change significantly during the study period. Blood glucose concentration decreased significantly during the infusion and reached its lowest value of 99.8 mg/dL at the 20-hour time point. Only 1 foal had a blood glucose concentration < 80 mg/dL (ie, 79 mg/dL) at any of the time points.

During the 24-hour study period, TTKG values significantly decreased, compared with the baseline value (**Table 3**). The OsmR increased from the baseline value with time, but this difference was significant only at the 12-hour time point. There were significant increases in Na_{FE} and Cl_{FE} values at the 8-hour and 12-hour time points, respectively, compared with baseline values. During the infusion, K_{FE} decreased (albeit not significantly) from the baseline value, and the values at any time point were not significantly different. Creatinine clearance did not change significantly during the study period, although no true baseline (0 hour) value was obtained prior to commencement of the infusion.

Table 4—Net change (gain or loss) in whole body electrolytes and total fluid in four 4-day-old foals after a 24-hour infusion with an isotonic electrolyte replacement fluid.

Variable	Sodium (mEq/kg)	Potassium (mEq/kg)	Chloride (mEq/kg)	Fluid (mEq/kg)
Intake via infusion	9.67[a] (9.28–11.40)	0.28[a] (0.27–0.33)	6.77[a] (6.49–7.98)	76.28[a] (66.27–81.41)
Loss	8.36[a] (7.91–12.51)	2.78[b] (1.57–4.34)	5.81[a] (5.22–8.53)	70.4[a] (46.26–92.73)
Net change	0.59 (–1.75–2.14)	–2.50 (–3.91– [–1.31])	0.59 (–1.00–1.54)	2.74 (–15.68–14.97)

Data are presented as median value (range).
See Table 2 for remainder of key.

After the 24-hour infusion, the gain and loss of electrolytes and fluid were assessed and the net gain or loss was calculated (**Table 4**). During the 24-hour study period, there was no significant change in whole-body values of fluid, sodium, or chloride, but there was a significant loss of potassium. The correlation between weight loss and K_{net} loss was not significant ($r = 0.93$; $P = 0.06$).

Discussion

All foals tolerated the experimental procedures well and remained bright, alert, and active, despite the

lack of oral intake of fluid. No complications were observed in any foal during the 24-hour period after removal of the IV and urinary catheters.

After 24 hours without oral alimentation, blood glucose concentrations in the 4 foals were within the reference range for adult horses used by our hospital and only slightly below values reported for 4-day-old nursing foals.[22,23] Blood glucose concentrations would be expected to decrease in a neonate from which feed is withheld. Blood glucose concentration values are interpreted as an indication of anabolic versus catabolic status, and it is important to note that the blood glucose concentrations remained relatively stable during the 24-hour study period. Healthy 4-day-old neonatal foals may have adequate fat reserves to maintain blood glucose concentration when food is withheld for a short period.[24]

During the study period, urine samples obtained via the urinary catheters were assessed by use of urinary reagent strips and the results for blood and protein ranged from negative to 3+ and negative to 2+, respectively. These findings are consistent with values for urine samples collected via free catch or catheter from neonatal foals that have been previously reported.[17] In the foals of our study, the UPR was lower than the value in nursing foals, as previously reported.[17] Although UPR was not measured before commencement of the infusion in foals of our study, higher UPRs in nursing foals may reflect a higher consumption of milk, compared with the volume (77 mL/kg/d [35 mL/lb/d]) administered IV to the foals of our study. This is supported by results of another study,[25] which indicated that urine production in foals maintained with parenteral nutrition and saline (0.9% NaCl) solution was decreased, compared with urine production in foals that were nursing their mares. The lower UPR determined for foals of the present study may be attributable to an increase in the circulating concentration of arginine vasopressin and active reabsorption of water by the kidneys; this is supported by the significant increases in Osm_u, Osm_s, and OsmR during the experimental period. An increase in serum arginine vasopressin concentration would increase water reabsorption from the distal convoluted tubule and collecting ducts, resulting in a decreased V_u and UPR. Serum arginine vasopressin concentration was not measured in the present study because it was our intent to evaluate whether retention of sodium in neonatal foals was similar to that of other species.

Urine specific gravity was low in baseline samples and variable in samples obtained throughout the experimental period. The urine was hypo-osmolar initially but became hyperosmolar during the study period. These data suggest that Osm_u may be a better indicator of renal concentrating ability in foals than USpG, as previously reported[26] in adult horses.

The OsmR value significantly increased from 0.8 at baseline to 1.7 at the end of the 24-hour study period. The OsmR has been used to differentiate prerenal from renal azotemia in adult horses and is an indicator of the ability of kidneys to conserve water.[27] In the foals of the present study, increases in Osm_u and OsmR during the infusion period may have indicated the release of arginine vasopressin, which resulted in reabsorption of water from the distal convoluted tubules and collecting ducts in an effort to conserve free water. The significant increases in Na_s concentration and Osm_s determined in our study would support this mechanism because increased Na_s concentration and Osm_s are potent stimulators of arginine vasopressin release. Furthermore, changes in the OsmR may be useful in assessing renal concentrating ability and determining excessive fluid loss in foals that are administered IERFs.

During the experimental period, foals did not consume milk or receive other sources of energy; compared with baseline values, the foals' weight significantly decreased, which may have been related to a negative energy balance. During the first week of life, foals should gain approximately 0.5 to 1.4 kg/d (1.1 to 3.1 lb/d).[28] However, the foals in our study lost 2.7 kg (5.9 lb) during the study period. To our knowledge, there are no reports regarding weight changes in neonatal foals undergoing feed deprivation for 24 hours. Newborn foals have poor glycogen stores but possess sufficient metabolizable fat to meet the metabolic rate for more than 24 hours.[24] Colostrum and milk provide enough energy to support metabolism and spare the use of fat reserves. In 1 study,[25] it was determined that 4-day-old foals nursing their mares consume 123.6 kcal/kg. Compared with nursing foals, foals maintained with parenteral nutrition (75 kcal/kg/d [34.1 kcal/lb/d]) and saline solution for 3 days had lower energy expenditure and a negative energy balance available for growth. Foals receiving parenteral nutrition gained less weight than nursing foals.[25] Electrolyte intake and loss in urine and feces were not measured in that study.

Another explanation for the weight loss in foals receiving parenteral nutrition may be associated with fluid and potassium losses secondary to the IERF administration. In suckling 10- and 11-day-old foals (mean weight, 59 kg [129.8 lb]), fluid intake was 15.1 kg (33.2 lb) and fluid loss was 14.2 kg (31.2 lb), resulting in a net gain of 0.95 kg/d (2.1 lb/d).[29] These data can be used to estimate $fluid_{net}$ retention of 15.8 mL/kg/d (7.2 mL/lb/d). Comparatively, foals in the present study had a minimal amount of $fluid_{net}$ retention (2.74 mL/kg/d), which was not significantly associated with weight loss. However, a correlation between weight loss and K_{net} loss was suggested, although this correlation was not significant. Administration of fluids containing sodium may have induced a natruresis in these foals, leading to an increased urinary potassium secretion that resulted in a total body potassium deficit. This phenomenon has been reported in other species.[30,31] Furthermore, a strong correlation between potassium loss and weight loss as a result of feed deprivation has been reported in adult horses.[32] The mechanism for potassium-induced weight loss is as follows: potassium loss in the urine leads to a decreased plasma potassium concentration and movement of potassium from the intracellular compartment to the vascular space. Loss of intracellular potassium results in a loss of intracellular water, which results in cell shrinkage.[32-35] A shift in water from the intracellular space to extracellular space will lead to weight loss as the extracellular

expansion is corrected by increasing urine production and osmole excretion. Because there was no $fluid_{net}$ loss, this mechanism is less likely caused by a negative energy balance than by weight loss. Insensible fluid losses were not measured but may have exceeded the fluid retention, which would validate the theory of weight loss and fluid loss secondary to sodium natruresis.

Loss of K_{net} was 0.11 mEq/kg/h (0.05 mEq/lb/h) for the duration of the study. At the fluid administration rate of 80 mL/kg/24 h (36.4 mL/lb/24 h), the loss of K_{net} could be met by supplementing the fluid with an additional 31 mEq of potassium/L. The use of KCl for fluid supplementation would also add 31 mEq of chloride/L to the infusion, further imbalancing the physiologic concentrations of the fluid. The effects of an infusion of fluid containing a high concentration of chloride have not been studied in neonatal foals, but it is theorized that the recipient foals would become acidemic according to the strong ion theory.[36] Although other means of providing potassium supplementation are available, a better choice may be the use of certain commercially available crystalloid maintenance fluids[h,i] that contain a higher concentration of potassium (13 mEq/L) and lower concentrations of sodium (40 mEq/L) and chloride (40 mEq/L). Administration of these products at a rate of 80 mL/kg/d to foals such as those used in the present study would provide 3.2 mEq/kg/d of sodium and chloride. Although this exceeds the amount of sodium (0.59 mEq/kg) retained by foals in our study, the lower concentration of sodium in these products, compared with that of IERFs, would decrease the level of natruresis and result in less loss of potassium. However, use of crystalloid fluids does not address energy needs of neonates.[28]

Although there was some loss of potassium in the urine and a decrease in K_{net}, the K_u, K_s, and K_{FE} values did not change significantly during the experimental period. This is contrary to findings of other studies[37,38] in adult horses, in which there was good agreement between potassium balance and changes in K_{FE}. However, at the end of the infusion period of the present study, K_{FE} of the foals was 14.93%, compared with 32.93% at baseline, which suggests an attempt to compensate for urinary potassium loss.

Further evidence of the severe potassium losses in the foals of our study was indicated by the significant decrease in TTKG from the baseline value during the infusion period. The calculated TTKG is an indirect measure of the effect of aldosterone on urinary potassium excretion, after correcting for reabsorption of solute-free water by the kidney. This value may be helpful in evaluating K_{net} status in neonatal foals that are receiving IV fluid therapy.[30,39] Although reference values have not been established for neonatal foals, the decrease in TTKG detected in the foals of our study suggests a decreasing effect of aldosterone on the collecting duct with time. Decreased production of aldosterone by the cortex of the adrenal glands would be expected as a result of sodium administration via infusion with no potassium supplementation. Unfortunately, serum aldosterone concentration was not measured in our study.

During the 24-hour study period, there was no significant change in Cr_{cl} in the foals. Although baseline urine samples were not collected, the range of Cr_{cl} values (2.4 mL/min/kg after 4 hours to 3.6 mL/min/kg at 16 hours) is consistent with reference values reported for nursing 4-day-old foals.[17] This information is important because Cr_{cl} can be used to approximate glomerular filtration rate and changes in glomerular filtration rate can affect the kinetics of drugs excreted by the kidneys.[17] In the foals of our study, the IERF infusion caused significant increases in Na_{FE} and Cl_{FE} within 8 and 12 hours of commencement of the infusion, respectively. This finding is in agreement with results of another study,[19] which indicated that Na_{FE} and Cl_{FE} changed significantly from baseline values in adult horses that received either 5% dextrose in water or saline solution IV for 6 hours. In the present study, the increase in Na_{FE} and Cl_{FE} from baseline values was rapid and resulted in excretion of most of the sodium administered IV during the 24-hour study period. Previous reported values for renal sodium clearance of nursing foals are 0.5 mEq/kg/d (0.23 mEq/lb/d). If a foal consumes 2.0 mEq of sodium/kg/d (0.9 mEq of sodium/lb/d) orally (consistent with consumption of an amount of mare's milk [with a sodium concentration of 10 mEq/L] equivalent to 20% of its body weight), the Na_{net} retention would be 1.5 mEq/kg/d (0.68 mEq/lb/d), assuming no loss of sodium in the feces. This is in close agreement with the predicted sodium requirements of neonatal foals of 2 to 3 mEq/kg/d (0.9 to 1.4 mEq/lb/d).[1] In the present study, there was a Na_{net} retention of approximately 0.59 mEq/kg/d (0.27 mEq/lb/d; range, –1.75 to 2.14 mEq/kg/d [–0.79 to 0.97 mEq/lb/d]). These data suggest that healthy 4-day-old foals are able to effectively increase sodium and chloride excretion in response to infusion of an IERF containing physiologic concentrations of sodium. This is in contrast to other neonatal species in which there is a minimal increase in renal excretion of sodium when fluids containing physiologic concentration of sodium are administered.[1,2,4,10-13,15,16]

In neonatal foals, a 24-hour infusion of an IERF containing physiologic concentrations of sodium and potassium resulted in increased renal clearance of sodium, K_{net} loss, and weight loss. The latter 2 findings suggest that an IERF may not be an appropriate choice for maintenance fluid therapy in foals. Additional studies are required to determine the optimal sodium and potassium content of replacement and maintenance fluids that are administered to neonatal foals.

a. SNAP Foal, Abbott Laboratories, Greensboro, NC.
b. Mila International Inc, Florence, Ky.
c. Normosol R, Abbott Laboratories, Chicago, Ill.
d. Heska Corp, Fort Collins, Colo.
e. Hitachi 911 automatic analyzer, Boehringer Mannheim, Indianapolis, Ind.
f. Wescor osmometer, Wescor Inc, Logan, Utah.
g. Medi Sense Precision QID, Abbott Laboratories, Bedford, Mass.
h. Normosol M, Abbott Laboratories, Chicago, Ill.
i. Plasmalyte 56, Baxter Healthcare, Deerfield, Ill.

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