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Original article

Effect of combinations of intravenous small-volume hypertonic sodium chloride, acetate Ringer, sodium bicarbonate, and lactate Ringer solutions along with oral fluid on the treatment of calf diarrhea

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Abstract

The aim of this study was to compare effect of combinations of intravenous isotonic sodium bicarbonate (NaHCO₃), acetate Ringer, lactate Ringer and small-volume hypertonic sodium chloride (NaCI) solutions along with oral electrolyte solutions (OES) on the treatment of neonatal calf diarrhea with moderate dehydration and metabolic acidosis. Thirty-two calves with diarrhea were used in the study. Calves were randomly assigned to receive acetate Ringer solution (n=8), lactate Ringer solution (n=8), isotonic NaHCO₃ (n=8) and 7.2% saline solutions (n=8), and two liters of OES were administrated to all calves orally at the end of intravenous administration. Blood samples for blood gas and biochemical analyses were collected at 0 hours and at 0.5, 1, 2, 4, 6 and 24 hours intervals. All the calves had mild to moderate metabolic acidosis on admission. Increased plasma volume and sodium concentration, but decreased serum total protein were observed within 0.5 hours following administration of hypertonic 7.2% NaCI + OES, compared to other 3 groups. In conclusion, administration of intravenous hypertonic 7.2% NaCI solution in small volume along with OES provided fast and effective improvement of dehydration and acid-base abnormalities within short time in treatment of calf diarrhea with moderate dehydration and metabolic acidosis.

Key words: calves, diarrhea, metabolic acidosis, fluid therapy

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Introduction

Calves with diarrhea lose large amounts of fluid and electrolytes (Phillips et al. 1971, Fisher and De La Fuente 1972), with attendant dehydration and acidosis that requires rehydration therapy (Groutides and Michell 1990). Fluids and electrolytes are usually administered orally or parenterally to ruminants. The method to be selected for fluid application in diarrhea depends on the presence or absence of a suckle reflex and the degree of dehydration. It is recommended to apply oral electrolyte solution to the calves with less than 8% dehydration and with suckle reflex. It is recommended that intravenous fluids should be given to the calves with no suckle reflex and more than 8% dehydrated (Roussel and Kasari 1990, Naylor 1996, Constable 2003, Smith 2009, Sen and Constable 2013). Sodium bicarbonate solutions are usually used in the treatment of severe metabolic acidosis where base excess is more negative than -10 mmol/L (Garcia 1999, Kasari 1999, Sen et al. 2009). For the treatment of mild to moderate acidosis, the lactate Ringer solutions or the acetate Ringer solutions could be used (Nakagawa et al. 2009). Small quantities of hypertonic sodium chloride solutions (7.2%) were shown to be an efficient treatment in animals with hypovolemic shock, severe dehydration (Senturk 2003) and endotoxemia (Constable et al. 1991a,b). Intravenous administration of hypertonic saline (HSS) can be combined with an oral alkalizing. Because the hypertonic saline alone does not improve acidosis (Constable 1999). HSS was found to be successful in the rehydration of hypovolemic calves (Constable et al. 1996, Walker et al. 1998) which were dehydrated experimentally by the administration of sucrose and diuretics. Until now, we did not find any study on effect to systemic alkalinization by intravenous four crystalloid solutions along with OES in the treatment of calf diarrhea.

The aim of this study was to compare effect of combinations of intravenous isotonic sodium bicarbonate, acetate Ringer, lactate Ringer and small-volume hypertonic sodium chloride solutions along with oral electrolyte solutions on the treatment of neonatal calf diarrhea with moderate dehydration and metabolic acidosis.

Materials and Methods

Calves

This study was done at Selcuk University, Faculty of Veterinary Medicine, Large Animal Clinic, and approved by Ethics Committee of the Faculty. Thirty-two calves with diarrhea were used in the study. Calves (n = 32) were enrolled to in the study if they had mild to moderate dehydration (as assessed by eye recession into the orbit of <3 mm (Constable et al. 1998) and metabolic acidosis (ie, jugular venous pH was approximately \geq 7.2). Exclusion criteria included the presence of concurrent severe health problem. Calves were less than 30 days old and with mean body weight range of 32.4±4.51 kg on admission. Venous catheter to V. auricularis was placed aseptically for administration of intravenous solutions.

Routine physical examination findings including extent of eyeball recession into the orbit, ability to stand, partly weak suckling reflex and decrease in cervical skin elasticity were recorded. Clinical assessment was done before the treatment and at periodically intervals within 24 hours post treatment. We did not attempt to identify the underlying cause of the diarrhea.

Treatment groups

After initial clinical and acid-base status assessment, calves were randomly allocated to 1 of 4 treatment groups.

Treatment group I (n=8); acetate Ringer solution (80 ml/kg) was given via intravenous route at rate of 30 ml/kg/h + Oral electrolyte solution (OES). Required acetate Ringer solution was given approximately within 180 minutes.

Treatment group II (n=8); lactate Ringer solution (80 ml/kg) was given via intravenous route at rate of 30 ml/kg/h + OES. Required lactate Ringer solution was given approximately within 180 minutes.

Treatment group III (n=8); Isotonic sodium bicarbonate (1.3% NaHCO₃) was given via intravenous route at rate of 20 ml/kg/h + OES. Required isotonic sodium bicarbonate was given approximately within 120 minutes.

Calculation of sodium bicarbonate needed for individual calves: sodium bicarbonate needed (mEq): negative base deficit (mmol/L) X 0.6 (factor for calves for extracellular fluid space) X BW (kg) and converted to mmol/L to gram of sodium bicarbonate, divided by 12 (Suzuki et al. 2002, Coskun et al. 2010, Trefz et al. 2012).

Treatment group IV (n=8); 7.2% hypertonic saline (4 ml/kg) was given via intravenous route(Batmaz et al. 2003, Constable 2003a) + OES. Required 7.2% hypertonic saline was given approximately within 10 minutes.

The composition of fluids to be used for intravenous fluid treatment are presented in Table 1.

Oral electrolyte solution was immediately administrated to all calves orally at the end of administration intravenous. All calves (n=32) received 2 L of OES at room temperature ($20-22^{\circ}C$) by feeding bottle. Oral

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electrolyte solution included sodium acetate + glucose (25 gram/L) and had osmolarity of the 150 mmol/L (Sen et al. 2009). Ceftiofur hydrochloride (Cevtivil, Vilsan, Turkey) was administered (2.2 mg/kg IM, once in a day, 5 days) daily to all calves.

Blood samples collection

Jugular venous blood samples for blood gas and biochemical parameters were obtained at 0 hours (immediately prior to IV solutions administration) and after 0.5, 1, 2, 4 and 24 hours during the experiment. Venous blood samples for blood gas were taken into heparinized 1 ml syringes and were measured within 15 minutes. Blood samples for hematologic analyses were collected prior to IV solutions administration and at 24 hour of experiment. Blood samples for biochemical analysis were collected into plain tubes, allowed to clot at room temperature, centrifuged, and the serum was harvested and stored at -20°C until analyzed.

Calves were monitored closely for the first 24 h by a supervising veterinarian. After the 24 h study period additional supportive treatment was administered as needed until the calves were discharged from the veterinary hospital and treatments included alkalizing oral electrolyte solutions. Most of calves received additional OES after 24 h.

Laboratory analysis

Blood gas analysis was performed using a blood gas analyzer (GEM Premier 3000, Instrumentation Laboratory, Lexington, MA, USA), the values were corrected for rectal temperature, and the plasma bicarbonate concentration (HCO₃) and extracellular base excess (BE) values were calculated. Blood sodium (Na) and potassium (K) concentrations were measured using ion-selective electrodes and total protein (TP) concentration was measured in serum samples by a commercially available kit (ADS; Analytic Diagnostic Systems, Istanbul, Turkey) using a spectrophotometer (BT 3000 plus, Biotecnical Inc, SPA, Via lizenca, 18 00155, Rome, Italy). White blood cell (WBC) and hematocrit levels were determined by using hematological analyzer (MS4e Melet Schloesing Laboratories, France).

Determination of percentage change in plasma volume

Change in the plasma volume at time i was calculated from the serum protein concentration at time = 0 min (SP0) and the serum protein concentration at time i (SPi), whereby: Percent change in plasma volume at time i = $(SP0 - SPi) \times 100/SPi$ (van Beaumont et al. 1972).

Statistical analysis

Data were expressed as least squares mean and standard error of mean. P<0.05 was considered as significant. A statistical software program (SPSS 15.0 for Windows, SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. ANOVA and Tukey multiple range tests were used to evaluate differences of each treatment groups during the experiment and significance level of variation. Paired-Samples t-test was used to determine differences between pre-treatment (0th hour) and post-treatment (24th hour) hematological parameters.

Results

Clinical findings

All calves had diarrhea. According to history taken from the owners, the calves were affected by diarrhea for about 1 to 2 days. All the calves had also moderate acidemia ($pH \ge 7.2 < 7.35$) and < 8% dehydration with a degree of enophthalmos (< 3 mm). Most of calves had partly sucking reflex (not strongest), standing position, and a few calves had mild mental depression. Clinical findings in 32 calves are presented before treatment (baseline) and 24 hours after treatment administration in Table 2. There were no statistical difference in clinical findings (except CRT) at baseline between 4 groups.

In the meantime, there were no statistically different respiratory rate, pulse, body temperature and body weights between 4 treatments during the experiment, whereas there were statistically significant differences in CRT between treatments I and also treatment IV during the experiment compared to baseline (Table 2).

Fluid therapy

Each calf received intravenous + OES combination during the treatment. According to body weight of calves, calves in the treatment group I received approximately 1760 to 4120 ml of acetate Ringer solutions, calves in the treatment group II received approximately 1520 to 3760 ml of lactate Ringer solution, calves in the treatment group III received approximately 650 to 2177 ml of isotonic sodium bicarbonate solution, whereas calves in the treatment group IV received approximately 122 to 202 ml of hypertonic NaCI (7.2%) solutions. Each calf received 2 L of OES at the end of IV solution administration by feeding bottle. Calves had free access to water during to treatment. After administration of IV and oral solutions, all calves recovered with support treatment.



Acid-base analysis

All the calves had mild to moderate metabolic acidosis on admission, with jugular venous blood pH ranging from 7.24 to 7.27, pCO₂ ranging from 35.7 to 42 mm Hg, plasma bicarbonate concentration ranging from 16 to 19 mmol/L, base excess ranging from -7.84 to -11.1 mEq/L and lactate ranging from 1.48 to 2.76 mmol/L (Table 3). However, there were no statistically significant differences in blood gas values on admission among 4 groups (Table 3).

Intravenous administration of four different solutions along with OES to calves with mild to moderate acidosis caused increase in venous blood pH, HCO₃, BE (Table 3). However, there was no observed change in pCO₂ within 6 hours of treatment. The rate of systemic alkalinization showed similarity between the four treatment groups within 4 hours of the study period based on venous blood pH, HCO₃ and base excess. However, these blood gas parameters were corrected more early in hypertonic saline +OES group compared to other 3 groups.

While serum potassium concentrations decreased in 4 groups 30 minutes after treatment, serum sodium concentrations increased only in group 4 (Table 3).

Hematologic Analyses

WBC of calves was high on admission (Table 3). However, WBC level decreased (except group 1) after treatment at 24 hours compared to baseline values.

Plasma Volume

Changes in plasma volume are presented before treatment and after treatment during 24 hours in Table 4. Plasma volume increased constantly in calves administered 7.2% NaCI 30 minutes after treatment. Plasma volume started to increase in calves administered acetate Ringer and NaHCO₃ in 60 minutes, but increased in lactate Ringer group 120 minutes after treatment (Table 4). The changes in plasma volume relative to baseline were significantly higher in calves of group IV at 0.5 h compared to other 3 groups.

Serum total protein concentration

There were no significant differences in serum total protein concentrations at baseline between 4 groups (Table 5). However, total protein concentrations were decreased significantly in 7.2% NaCl group 30 minutes after treatment.

Discussion

The present study has shown that administration of hypertonic NaCI + OES combination is useful reducing time and lowering the cost of treatment of diarrheic calves with mild to moderate metabolic acidosis. Dehydration and metabolic acidosis occur in almost all cases of calf diarrhea. IV and OES combination in rehydration therapy should be advised for both reducing time and lowering the cost of treatment of calf diarrhea. In the study, effects of 4 crystalloid solutions along with OES were evaluated on diarrheic calves with mild to moderate metabolic acidosis. It is generally accepted that any calf with a suckling reflex is suitable for OES. In the study, all of calves had suckling reflex, but it was not strong.

Oral electrolyte therapy is generally easier to perform on the farms in calves with diarrhea. Calves fed with hyperosmotic oral rehydrating solutions (600-717 mOsm/l) have a slower abomasal emptying rate compared to calves fed iso-osmotic oral rehydrating solutions (300-360 mOsm/l). Suckling an iso-osmotic oral rehydrating solution provides the fastest rate of solution delivery to the small intestine and a slightly faster rate of plasma volume expansion than does suckling or oesophageal intubation of a hypertonic oral rehydrating solution (Meganck et al. 2014). In the study, isotonic oral electrolyte solution that included acetate was used in calves. Sen et al. (2009) indicated that sodium acetate oral rehydrating solutions are more effective in expanding the plasma volume than sodium bicarbonate OES solutions. In diarrhea with no suckling reflexes, continuous IV infusion of isotonic fluids is recommended as treatment (Berchtold 1999). However, this treatment is troublesome and expensive. Alternatively, oral rehydration solutions are recommended for following rapid IV administration of hypertonic saline solution (Constable 2002). In veterinary medicine, HSS can be used in the treatment of hemorrhagic and endotoxemic shocks in various animals. HSS was also found to be successful for the treatment of hypovolemic calves (Constable et al. 1996, Walker et al. 1998) which were dehydrated experimentally by the administration of sucrose and diuretics (Koch and Kaske 2008). The hypertonic saline is administered intravenously at a dose of 4-5 ml / kg for 4-5 minutes (Suzuki et al. 1998, Constable 2003a). Oral rehydration solutions following rapid intravenous hypertonic saline administration are recommended (Koch and Kaske 2008). Until now, there is no information on the effect on systemic alkalinization of four crystalloid solutions along with OES in calves with diarrhea. In the study, the rate of systemic alkalinization showed similarity between the four treatment groups within 4 hours of experiment based on ef-

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	Na+ mEq/L	K+ mEq/L	Cl- mEq/L	Lactate mEq/L	Asetate mEq/L	Ca++ mEq/L	Mg++ mEq/L	Gluconate mEq/L	HCO ₃ - mEq/L	Fosfat
Acetate Ringer	141	5	98	-	27	-	3	23	-	1
Lactate Ringer	130	4	109.1	27.6	-	3	-	-	-	-
%1.3 NaHCO ₃	155	-	-	-	-	-	-	-	155	-
7.2 % NaCl	1232	-	1232	-	-	-	-	-	-	-

Table 1. Composition of the intravenous solutions used in this study.

Table 2. Changes in clinical parameters and body weight in calves given intravenous and oral electrolyte solution.

Parameters	Base	eline	Time after administration (h)					
	0 th h	0.5^{th} h	$1^{\mathrm{th}}\mathrm{h}$	$2^{\rm th} h$	$4^{th} h$	6 th h	$24^{th} h$	
Temperature (°C)							
Group 1	38.7±0.35	38.5±0.19	38.5±0.17	38.4±0.22	38.7±0.18	38.7±0.18	38.9±0.14	
Group 2	38.2±0.33	38.2±0.29	38.4±0.29	38.4±0.27	38.6±0.19	38.9±0.19	38.8±0.21	
Group 3	38.8±0.18	38.6±0.18	38.6±0.16	38.8±0.24	38.8±0.20	38.9±0.20	39.0±0.14	
Group 4	38.9±0.28	38.9±0.2	38.8±0.26	39.0±0.20	39.2±0.21	39.3±0.17	38.9±0.11	
Pulsation/min								
Group 1	108±11.5	112±12.7	109±13.3	110±12.6	122±11.8	124±9.73	106±11.5	
Group 2	126±12.7	131±13.1	131±13.3	127±11.0	138±8.43	130±9.75	124±8.66	
Group 3	116±9.80	114±11.6	120±9.94	122±9.17	122±8.25	117±9.67	120±7.77	
Group 4	110±9.73	114±9.63	114±8.48	111±8.04	113±7.39	117±6.94	103±6.37	
Respiratory rate/	min							
Group 1	27.5±4.17	26.0 ± 2.27	26.9±1.94	23.8±3.03	25.3±2.90	23.8 ± 2.40	25.6±3.87	
Group 2	36.3±4.96	36.0±6.13	33.4±6.51	32.3±4.85	35.5±4.84	32.3±5.32	35.1±7.06	
Group 3	30.5±3.70	27.5 ± 2.53	25.0±2.07	23.5±2.77	22.3±1.98	24.9±1.60	28.0±3.32	
Group 4	31.1±3.93	30.5±3.02	30.3±3.73	28.0 ± 2.48	29.9±3.70	25.4±3.43	35.6±4.44	
CRT (sec)								
Group 1	4.63±0.46 ^{bB}	3.50±0.27 ^{AB}	3.25±0.41 ^{AB}	2.75±0.37 ^A	2.38±0.26 ^A	2.13±0.13 ^A	2.50±0.19 ^A	
Group 2	3.25 ± 0.45^{ab}	3.00 ± 0.38	3.00±0.33	2.63 ± 0.32	2.38±0.18	2.25 ± 0.16	2.25 ± 0.16	
Group 3	3.13±0.23ª	2.75 ± 0.25	2.75 ± 0.25	2.63 ± 0.18	2.63 ± 0.18	2.50 ± 0.19	2.25 ± 0.16	
Group 4	3.88 ± 0.30^{abB}	3.75±0.31 ^B	3.25±0.31 ^{AB}	3.00±0.33 ^{AB}	2.75 ± 0.25^{AB}	2.63±0.38 ^{AB}	2.38 ± 0.18^{A}	
BW (kg)								
Group 1	32.4±4.51	-	-	-	-	-	33.0.±4.66	
Group 2	33.2±1.10	-	-	-	-	-	33.7±1.22	
Group 3	37.4±1.89	-	-	-	-	-	37.6±2.02	
Group 4	39.2±3.36	-	-	-	-	-	40.1±3.05	

CRT: Capillary refill time, BW: body weight.

Different letters in the same rows (A, B) and columns (a, b) point statistically significant differences (p<0.05).

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Table 3. Changes in blood gases and hematologic parameters in calves given intravenous and oral solution.

Parameters -	Base 0 th h	0.5 th h	1 th h	Time 2 th h	24 th h		
all	0 h	0.5 ^m h	1 n	2 n	4 th h	6 th h	24 n
pH Crown 1	7 27 + 0 024	7 21 - 0.024	7 20 - 0.014	7 20 + 0 0234	7 24 ± 0 02 AB	7.40 ± 0.02 B	7 40 + 0.01B
Group 1	$\frac{7.27 \pm 0.02^{A}}{7.24 \pm 0.01^{A}}$	7.31±0.03 ^A 7.27±0.01 ^A	$\frac{7.30 \pm 0.01^{A}}{7.28 \pm 0.02^{AB}}$	$\frac{7.29 \pm 0.02^{aA}}{7.30 \pm 0.02^{aAB}}$	$\frac{7.34 \pm 0.02^{\text{aAB}}}{7.36 \pm 0.02^{\text{abBC}}}$	$\frac{7.40 \pm 0.02^{\text{B}}}{7.42 \pm 0.02^{\text{C}}}$	$7.40 \pm 0.01^{\text{B}}$ $7.39 \pm 0.02^{\text{C}}$
Group 2	$7.24 \pm 0.01^{\text{A}}$ $7.26 \pm 0.02^{\text{A}}$	$7.32 \pm 0.01^{\text{A}}$	7.28 ± 0.02^{AB} 7.32 ± 0.03^{AB}	7.36 ± 0.02^{abBC}	$7.36 \pm 0.02^{\text{abBC}}$ 7.41 ± 0.03 ^{abBC}	$7.42 \pm 0.02^{\circ}$ $7.46 \pm 0.03^{\circ}$	$7.39 \pm 0.02^{\circ}$ $7.45 \pm 0.02^{\circ}$
Group 3				$7.38 \pm 0.02^{\text{bBC}}$			
Group 4	$7.27 \pm 0.03^{\text{A}}$	7.28 ± 0.02^{A}	7.33 ± 0.02^{AB}	7.38±0.02	7.44 ± 0.02^{bC}	$7.44 \pm 0.01^{\circ}$	7.40 ± 0.02^{BC}
Crown 1	37.0 ± 2.20^{A}	34.8±3.29 ^A	37.5±2.37 ^A	39.5±2.15 ^{AB}	39.8±1.74 ^{AB}	43.6±2.63 ^{AB}	48.5±2.77 ^B
Group 1 Group 2	37.0 ± 2.20^{4} 42.0±2.65 ^A	$39.4 \pm 1.87^{\text{A}}$	39.8±2.32 ^A	$40.4 \pm 2.19^{\text{A}}$	$\frac{39.8 \pm 1.74^{\text{A}}}{42.0 \pm 1.98^{\text{A}}}$	45.6±2.38 ^{AB}	46.5 ± 2.77^{2} 52.5 ± 2.24^{B}
Group 2 Group 3	35.9±2.85 ^A	37.6±2.15 ^A	39.3±2.41 ^A	40.4 ± 2.19 40.8 ± 1.91^{AB}	$\frac{42.0 \pm 1.98}{39.0 \pm 2.45^{\text{A}}}$	43.0 ± 2.58 41.8 ± 1.67^{AB}	48.9±1.22 ^B
Group 3	42.0±4.02	38.8±1.97	37.5±2.10	40.9±1.94	42.9±1.62	43.1±2.16	47.0 ± 2.46
O ₂ (mm Hg)	42.0±4.02	30.0±1.97	57.5±2.10	40.9 ± 1.94	42.9±1.02	43.1±2.10	47.0±2.40
Group 1	29.3±2.35 ^{AB}	32.5±3.36 ^B	29.3±2.70 ^{AB}	26.6±1.99AB	27.6±1.45 ^{AB}	26.4±1.60 ^{AB}	22.0±2.67 ^A
Group 2	29.5 ± 2.55 22.5 ± 1.75^{AB}	28.0±1.49 ^{BC}	25.8±2.14 ^{ABC}	30.1±1.48 ^c	27.3±1.93 ^{ABC}	24.1±1.13 ^{AC}	22.0±2.07 20.6±1.19 ^A
Group 2	27.0±1.90	26.8±2.19	27.8±1.54	25.9±0.72	27.5 ± 1.93 26.5 ± 1.93	24.1±1.13 22.8±1.25	20.0±1.19 24.8±1.45
Group 3	21.4±2.83	29.3±2.34	27.6±1.07	26.4±1.34	24.6±1.76	24.9±1.80	24.0 ± 1.45 23.0 ± 1.45
Na ⁺ (mmol/L)	21.4±2.05	29.3 ± 2.34	27.0±1.07	20.4 ± 1.34	24.0±1.70	24.9±1.00	23.0±1.43
Group 1	133±3.05	136±2.63	133±3.35	134±2.57	137±2.24	139±2.48	141±2.09
			133 ± 3.35 135 ± 1.98	134 ± 2.57 135 ± 1.22			141 ± 2.09 138±1.57
Group 2 Group 3	135±2.18 134±6.69	135 ± 2.16 138 ± 6.39	135 ± 1.98 138 ± 6.17	135 ± 1.22 140 ± 5.89	137±1.19 142±5.97	138±1.07 144±4.56	138 ± 1.57 140 ± 3.52
	134 ± 0.09 130 ± 3.51	138 ± 0.39 141±3.10	138 ± 0.17 138±3.40	140 ± 3.89 138±3.18	142 ± 3.97 137±3.04	144 ± 4.50 139 ± 2.22	140 ± 3.52 136 ± 2.27
Group 4 K+ (mmol/L)	150±5.51	141±3.10	130±3.40	130±3.18	13/±3.04	139±2.22	130±2.27
Group 1	4.70±0.41 ^в	3.95±0.32 ^{AB}	4.14±0.45 ^{AB}	3.91±0.36 ^{AB}	3.31±0.26 ^{AB}	3.04±0.22 ^A	3.65±0.25 ^{AB}
Group 1 Group 2	4.70 ± 0.41^{5} 4.81 ± 0.44	$\frac{3.95 \pm 0.32^{\text{AB}}}{4.51 \pm 0.42}$	4.14 ± 0.45^{AB} 4.53 ± 0.46	$3.91 \pm 0.36^{\text{AB}}$ 4.20 ± 0.43	3.31 ± 0.26^{AB} 3.98 ± 0.36	3.04 ± 0.22^{A} 3.34 ± 0.28	3.65 ± 0.25^{AB} 3.80 ± 0.29
	4.81 ± 0.44 $4.38 \pm 0.26^{\circ}$	4.51 ± 0.42 3.80 ± 0.16^{BC}	$\frac{4.53 \pm 0.46}{3.66 \pm 0.12^{B}}$	$\frac{4.20\pm0.43}{3.55\pm0.16^{B}}$	3.98 ± 0.30 3.13 ± 0.14^{AB}	2.79±0.17 ^A	3.28±0.07 ^{AB}
Group 3	$4.38 \pm 0.20^{\circ}$ 4.81 ± 0.40^{B}	3.80 ± 0.10^{AB}	3.91 ± 0.22^{AB}		$3.48 \pm 0.24^{\text{A}}$	3.40±0.21 ^A	4.11±0.25 ^{AB}
Group 4		3.80±0.15 [™]	3.91±0.22 ⁻¹⁰	3.61 ± 0.27^{A}	3.48±0.24 [™]	3.40±0.21 [™]	4.11±0.25 ^m
Lactate (mmol		1.2(+0.22	1.21 + 0.27	1 20 + 0 26	1 14 + 0 22	1 (4 + 0.20	1 22 + 0 20
Group 1	1.48 ± 0.31	1.26±0.22	1.21±0.27	1.20±0.26	1.14±0.22	1.64±0.38	1.33 ± 0.29
Group 2	2.76 ± 1.09	2.89 ± 1.16	2.63 ± 1.01	2.56 ± 0.90	1.95 ± 0.73	1.76 ± 0.54	1.71 ± 0.35
Group 3	1.56 ± 0.67	1.25 ± 0.47	1.20 ± 0.32	1.11±0.35	1.35±0.38	1.50 ± 0.47	1.03 ± 0.19
Group 4	2.36±1.04	1.85 ± 0.75	1.70 ± 0.64	1.83 ± 0.66	1.49 ± 0.41	1.35 ± 0.34	1.39 ± 0.38
HCO ₃ ⁻ (mmol/I		17.0 + 1.244	10.2 + 1.104	10.1 + 1.1734	21 Q + 1 5 2aAB	27.0 + 1.65BC	20.4 + 1.070
Group 1	$17.0 \pm 1.25^{\text{A}}$	17.0±1.24 ^A	18.3 ± 1.10^{A}	19.1 ± 1.17^{aA}	21.8 ± 1.52^{aAB}	27.0 ± 1.65^{BC}	30.4±1.96 ^c
Group 2	17.8 ± 0.97^{A} 16.0 ± 1.30^{A}	18.1±0.91 ^A 19.6±1.07 ^{AB}	$\frac{18.7 \pm 1.16^{\text{A}}}{20.5 \pm 1.30^{\text{AB}}}$	$\frac{20.1 \pm 1.55^{aA}}{23.1 \pm 0.82^{abB}}$	$\frac{23.8 \pm 1.72^{abAB}}{24.4 \pm 1.17^{abBC}}$	$\frac{30.0 \pm 2.51^{\text{BC}}}{29.8 \pm 1.64^{\text{CD}}}$	32.5±2.31 ^c 34.3±1.35 ^b
Group 3							
Group 4	19.0 ± 0.79^{A}	18.2 ± 1.13^{A}	$20.7 \pm 0.94^{\text{A}}$	$25.2 \pm 1.29^{\text{bAB}}$	$29.0 \pm 1.33^{\text{bB}}$	29.0 ± 1.45^{B}	25.6±3.59 ^{AB}
TCO ₂ (mm Hg		10.0 + 1.224	10.4 + 1.164	20.2 + 1.2234	22.0 + 1.57aAB	20.2 + 1.71BC	21.0 + 2.040
Group 1	18.1±1.30 ^A	18.0±1.33 ^A	19.4 ± 1.16^{A}	20.3 ± 1.23^{aA}	23.0 ± 1.57^{aAB}	28.3 ± 1.71^{BC}	31.9±2.04 ^c
Group 2	19.1±1.04 ^A	$19.3 \pm 0.97^{\text{A}}$	19.9±1.22 ^A	21.3 ± 1.60^{aA}	25.0 ± 1.78^{abAB}	31.4 ± 2.58^{BC}	34.1±2.35 ^c
Group 3	17.1±1.39 ^A	20.7±1.12 ^{AB}	21.7±1.34 ^{AB}	24.3 ± 0.84^{abB}	25.6±1.19abBC	31.1±1.65 ^{CD}	35.8±1.34 ^D
Group 4	20.3±0.87 ^A	19.3 ± 1.17^{A}	21.9 ± 0.97^{AB}	$26.4 \pm 1.34^{\text{bBC}}$	30.3±1.36 ^{bC}	$30.3 \pm 1.51^{\circ}$	30.8±1.81 ^c
BE (mmol/L)	10.0 + 1.414	0 40 + 1 174	6 22 + 2 284	7 46 + 1 2224	2 04 + 1 772AB	2 15 + 1 77BC	5 (4 + 0.070
Group 1	-10.0 ± 1.41^{A}	-9.40 ± 1.17^{A}	-6.33±2.28 ^A	-7.46 ± 1.33^{aA}	-3.94 ± 1.77^{aAB}	2.15 ± 1.77^{BC}	$5.64 \pm 2.07^{\circ}$
Group 2	-9.61±0.98 ^A	-8.81±1.01 ^A	-8.11±1.32 ^A	-6.33 ± 1.77^{aA}	-1.76±1.99ªAB	5.45±2.86 ^{BC}	7.58±2.64 ^c
Group 3	-11.1±1.45 ^A	-6.48 ± 1.20^{AB}	-5.56 ± 1.58^{AB}	-2.33 ± 1.05^{abB}	-0.26 ± 1.42^{abBC}	5.98±1.96 ^{CD}	$10.3 \pm 1.65^{\text{D}}$
Group 4	$-7.84 \pm 0.85^{\text{A}}$	-8.65 ± 1.38^{A}	-5.25±1.13AB	$0.30 \pm 1.46^{\text{bBC}}$	4.84±1.55 ^{bC}	$4.71 \pm 1.56^{\circ}$	$4.55 \pm 1.91^{\circ}$
$O_2 \text{ SAT}(\%)$	44.1 - 5.20	51 4 - 5 05	20 (. (72	10.0 . 1 . 1	46.0 + 0 10	40.4 - 2.05	260.655
Group 1	44.1±5.39	51.6±5.87	38.6±6.73	40.9±4.61	46.9±3.42	48.1±3.96	36.9±6.55
Group 2	28.1±4.01 ^A	42.3±3.26 ^{AB}	37.9±5.08 ^{AB}	49.3±2.68 ^B	47.0±4.69 ^B	44.0±2.75 ^{AB}	33.9±3.63AB
Group 3	38.9±4.10	43.5±5.57	46.1±4.78	44.5±2.15	48.8±5.61	43.6±4.46	48.3±4.72
Group 4	29.6±7.36	45.3±5.16	46.2±3.03	48.3±3.73	39.1±6.50	46.8±4.66	40.0±4.57
WBC $(10^3/\text{mm}^3)$							160 207
Group 1	14.3±1.31	-	-	-	-	-	16.9±2.35 ^b
Group 2	15.2±2.02	-	-	-	-	-	12.2 ± 1.60^{ab}
Group 3	18.6±2.10	-	-	-	-	-	$10.2 \pm 1.64^{ab^*}$
Group 4	14.3±3.10	-	-	-	-	-	$8.15 \pm 1.14^{a^*}$
Hematocrit (%							
Group 1	30.5±1.39	-	-	-	-	-	26.5±1.37*
Group 2	25.3±1.10	-	-	-	-	-	23.6±0.77
Group 3	27.4±2.65	-	-	-	-	-	24.8±2.46*
Group 4	30.5 ± 0.97	-	-	-	-	-	26.9 ± 2.06

pH: concentration of hydrogen ions, PCO₂: partial pressure of carbon dioxide, PO₂ partial pressure of oxygen, Na⁺; sodium, K⁺; potassium HCO₃: bicarbonate, TCO₂; total amount of carbon dioxide, BEecf: base excess of extracellular fluid, O₂SAT. %: oxygen saturation, WBC; white blood cell. Different letters in the same rows (A, B, C, D) and columns (a, b, c) point statistically significant differences (p<0.05). * Indicates statistically significant between 0 and 24 hours (p<0.05).

Effect of combinations of intravenous small-volume ...

Parameters	В	aseline	Time after administration (h)					
	0 th h	0.5 th h	1 th h	2 th h	4 th h	6 th h	24 th h	
Group 1	0 ^A	7.53 ± 4.32^{AB}	15.6±3.63 ^{AB}	26.3±3.58 ^B	19.4 ± 7.94^{AB}	16.4 ± 7.62^{AB}	10.1 ± 6.82^{AB}	
Group 2	0	8.07±6.46	14.36±8.01	19.7±7.28	17.1±8.34	27.5±9.20	10.9 ± 7.61	
Group 3	0	5.04 ± 4.57	21.1±11.5	22.6±7.61	23.9±11.7	21.0±9.96	6.78±7.04	
Group 4	0 ^A	20.0 ± 1.46^{BC}	19.5±3.71 ^{BC}	25.2±3.37 ^{BC}	29.3±6.98 ^c	27.3±3.57 ^{BC}	11.1±3.32 ^{AB}	

Table 4. Changes in plasma volume in calves given intravenous and oral solution.

Different letters in the same rows (A, B, C) point statistically significant differences (p<0.05).

Table 5. Changes in total protein level in calves given intravenous and oral solution.

Parameters –	Baseline		Time after administration (h)						
	0 th h	0.5 th h	1 th h	2 th h	4 th h	6 th h	24 th h		
Group 1	6.33 ± 0.34	5.91±0.29b	5.50±0.32 ^b	5.03 ± 0.28	5.38 ± 0.32	5.55±0.41 ^b	5.90±0.44 ^b		
Group 2	5.80 ± 0.66	5.45 ± 0.38^{ab}	5.46 ± 0.46^{b}	4.90 ± 0.49	5.00 ± 0.43	4.61 ± 0.42^{ab}	5.24 ± 0.38^{ab}		
Group 3	4.90 ± 0.35	4.70 ± 0.19^{a}	4.13 ± 0.18^{a}	4.00 ± 0.14	4.10±0.30	4.11 ± 0.20^{a}	4.60 ± 0.16^{a}		
Group 4	$5.60 \pm 0.19^{\text{B}}$	4.68 ± 0.18^{aA}	4.70 ± 0.16^{abAB}	4.50±0.21 ^A	4.12±0.27 ^A	4.44 ± 0.24^{abA}	5.06 ± 0.21^{abAB}		

Different letters in the same rows (A, B) and columns (a, b,) point statistically significant differences (p<0.05).

fects on jugular venous blood pH, HCO_3 and base excess. However, administration duration of the HSS was short compared with other groups. In addition, volume of HSS that was administrated to calf was also very small compared to other solutions and the combination was cheaper than the others. Plasma volume increased constantly in calves administered 7.2% hypertonic NaCl 30 minutes after treatment, whereas total protein concentrations were decreased significantly in hypertonic NaCl group at 30 minutes after treatment. The hypertonic saline solution is used to increase plasma volume rapidly in severely dehydrated ruminants (Constable 2003a,b).

Lactate and acetate are metabolizable bases and they are found in popular polyionic solutions (lactated Ringer and acetate Ringer). These two substances are predominantly metabolized to bicarbonate, therefore they have an alkalising effect. Acetated Ringer's solution is theoretically superior to lactated Ringer's solution because acetate is metabolized faster and alkalinization is more rapid. Acetate would not exacerbate D- and L-lactic acidosis (Kasari and Naylor 1985). A disadvantage of commercially available acetated Ringer's solutions is that it contains gluconate, which is slowly metabolized by neonatal calves. Despite some disadvantages, the lactated Ringer solution is popular and still widely used by practitioners (Naylor and Forsyth 1986, Berchtold 2009). Our results show that bicarbonate induced a significantly greater increase in the BE concentration than acetate and lactate. Lactate and acetate do not act as fast as alkaline sodium bicarbonate (Berchtold 2009).

The results of the present study showed that the administration of four treatment groups solutions were similarly effective in improving acid base abnormalities in calves with mild to moderate metabolic acidosis. However, hypertonic sodium-chloride solutions + OES group improved venous acid-base balance and dehydration abnormalities at 30 minutes after treatment.

In conclusion, it could be said that administration of 7.2% hypertonic sodium chloride solution in small volumes + OES combinations provided a quick, economic, practical and effective improvement of acid-base and dehydration abnormalities (depending on decreased TP concentrations and increased in plasma volume) within very short time in diarrheic calves with mild to moderate metabolic acidosis.

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References

- Batmaz H, Yılmaz Z, Topal A, Görgül OS, Şentürk S (2003) Effects of hypertonic sodium chloride, hypertonic sodium chloride + sodium bicarbonate and hypertonic sodium chloride + ringer's lactate solution in the treatment of dogs with experimentally induced endotoxaemia. Turk J Vet Anim Sci 27: 339-347.
- Berchtold J (1999) Intravenous fluid therapy of calves. Vet Clin North Am Food Anim Pract 15: 505-531.
- Berchtold J (2009) Treatment of calf diarrhea: intravenous fluid therapy. Vet Clin North Am Food Anim Pract 25: 73-99.
- Constable PD, Gohar HM, Morin DE, Thurmon JC (**1996**) Use of hypertonic saline-dextran solution to resuscitate hypovolemic calves with diarrhea. Am J Vet Res 57: 97-104.
- Constable PD, Schmall LM, Muir WW 3rd, Hoffsis GF, Shertel ER (**1991a**) Hemodynamic response of endotoxemic calves to treatment with small volume hypertonic saline solution. Am J Vet Res 52: 981-989.
- Constable PD, Schmall LM, Muir WW 3rd, Hoffsis GF (1991b) Respiratory, renal, hematologic and serum biochemical effects of hypertonic saline solution in endotoxemic calves. Am J Vet Res 52: 990-998.
- Constable PD, Walker PG, Morin DE, Foreman JH (**1998**) Clinical and laboratory assessment of hydration status of neonatal calves with diarrhea. J Am Vet Med Assoc 212: 991-996.
- Constable PD (2003a) Fluid and electrolyte therapy in ruminants. Vet Clin North Am Food Anim Pract 19: 557-597.
- Constable PD (2003b) Hyperchloremic acidosis: the classic example of strong ion acidosis. Anesth Analg 96: 919-922.
- Constable PD (**1999**) Hypertonic saline. Vet Clin North Am Food Anim Pract 15: 559-585.
- Constable PD (2002) The treatment of the diarrheic calf: an update. In: Kaske M (ed) Recent developments and perspectives in bovine medicine. Keynote Lectures of the XXII World Buiatrics Congress, Klinik fur Rinderkrankheiten, Hannover, pp 132-143.
- Coskun A, Sen I, Guzelbektes H, Ok M, Turgut K, Canikli S (2010) Comparison of the effects of intravenous administration of isotonic and hypertonic sodium bicarbonate solutions on venous acid-base status in dehydrated calves with strong ion acidosis. J Am Vet Med Assoc 236: 1098-1103.
- Fisher EW, De la Fuente GH (**1972**) Water and electrolyte studies in newborn calves with particular reference to effects of diarrhoea. Res Vet Sci 13: 315-322.
- Groutides CP, Michell AR (**1990**) Intravenous solutions for fluid therapy in calf diarrhoea. Res Vet Sci 49(3): 292-297.
- Kasari TR, Naylor JM (1985) Clinical evaluation of sodium bicarbonate, sodium L-lactate, and sodium acetate for the treatment of acidosis in diarrheic calves. J Am Vet Med Assoc 187: 392-397.
- Kasari TR (**1999**) Metabolic acidosis in calves. Vet Clin North Am Food Anim Pract 15: 473-486.
- Koch A, Kaske M (2008) Clinical efficacy of intravenous hypertonic saline solution or hypertonic bicarbonate solu-

tion in the treatment of inappetent calves with neonatal diarrhea. J Vet Intern Med 22: 202-211.

- Meganck V, Hoflack G, Opsomer G (2014) Advances in prevention and therapy of neonatal dairy calf diarrhoea: a systematical review with emphasis on colostrum management and fluid therapy. Acta Vet Scand 56: 75.
- Nakagawa M, Suzuki K, Takahashi F, Kamikatano K, Koiwa M, Taguchi K (2009) Comparison of the alkalizing effects of bicarbonate precursors in calves with experimentally induced metabolic asidosis. J Vet Med Sci 71: 807-809.
- Naylor J (1996) Neonatal ruminant diarrhea. In: Smith BP (ed) Large animal internal medicine, 2nd ed., St Louis, Mosby, pp 396-417.
- Naylor JM, Forsyth GW (**1986**) The alkalinizing effects of metabolizable bases in the healthy calf. Can J Vet Res 50: 509-516.
- Perez Garcia J (1999) A practitioner's views on fluid therapy in calves. Vet Clin North Am Food Anim Pract 15: 533-543.
- Phillips RW, Lewis LD, Knox KL (**1971**) Alterations in body water turnover and distribution in neonatal calves with acute diarrhea. Ann N Y Acad Sci 176: 231-243.
- Roussel AJ, Kasari TR (**1990**) Using fluid and electrolyte replacement therapy to help diarrheic calves. Vet Med (Praha) 85: 303-311.
- Sen I, Constable PD (2013) General overview to treatment of strong ion (metabolic) acidosis in neonatal calves with diarrhea. Eurasian J Vet Sci 29: 114-120.
- Sen I, Altunok V, Ok M, Coskun A, Constable PD (2009) Efficacy of oral rehydration therapy solutions containing sodium bicarbonate or sodium acetate for treatment of calves with naturally acquired diarrhea, moderate dehydration, and strong ion acidosis. J Am Vet Med Assoc 234: 926-934.
- Senturk S (2003) Effects of a hypertonic saline solution and dextran 70 combination in the treatment of diarrhoeic dehydrated calves. J Vet Med A 50: 57-61.
- Smith GW (2009) Treatment of calf diarrhea: oral fluid therapy. Vet Clin North Am Food Anim Pract 25: 55-72.
- Suzuki K, Kato T, Tsunoda G, Iwabuchi S, Asano K, Asano R (2002) Effect of intravenous infusion of isotonic sodium bicarbonate solution on acidemic calves with diarrhea. J Vet Med Sci 64: 1173-1175.
- Suzuki K, Ajito T, Iwabuchi S (1998) Effect of a 7.2% hypertonic saline solution infusion on arterial blood pressure, serum sodium concentration and osmotic pressure in normovolemic heifers. J Vet Med Sci 60: 799-803.
- Trefz FM, Lorch A, Feist M, Sauter-Louis C, Lorenz I (2012) Metabolic acidosis in neonatal calf diarrhea-clinical findings and theoretical assessment of a simple treatment protocol. J Vet Intern Med 26: 162-170.
- van Beaumont W, Greenleaf JE, Juhos L (1972) Disproportional changes in hematocrit, plasma volume, and proteins during exercise and bed rest. J Appl Physiol 33: 55-61.
- Walker PG, Constable PD, Morin DE, Foreman JH, Drackley JK, Thurmon JC (1998) Comparison of hypertonic saline-dextran solution and lactated Ringer's solution for resuscitating severely dehydrated calves with diarrhea. J Am Vet Med Assoc 213: 113-121.