NOTE

Internal Medicine

Rehydration and catabolic preventive effects depend on the composition of oral electrolyte solutions for diarrheic calves

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ABSTRACT. In this study, two commercially available oral electrolyte solutions (OES) with high sodium (CF) or with high glucose and glycine (SL), and two prototype OES were evaluated in terms of rehydration and preventing catabolism. Prototype OES based on CF were prepared by doubling the glucose amount (CFG) or by doubling both glucose and glycine (CFGG). Thirty-two diarrheic calves were randomly assigned four groups with eight calves in each group. Blood volume increased with CF and CFGG compared with that of other OES. The catabolic preventive effect was excellent in CFGG and SL. Our results suggest that both the amount of sodium, glucose, and glycine, and ratio of these factors aid dehydration and provide energy.

KEY WORDS: calf, catabolism, diarrhea, oral electrolyte solutions, sodium

Neonatal diarrhea remains the most common cause of death in beef and dairy calves, and continues to be a major cause of economic loss for the cattle industry [9]. Calves are more sensitive to fluid loss than adult cattle because they have higher total body water content and higher extracellular fluid volume than adults. Regardless of pathogen or mechanism involved, diarrhea increases the loss of electrolytes and water in feces and decreases milk intake [10]. In addition, diarrhea leads to overall loss of not only electrolytes and water, but also decreases absorption of carbohydrates, lipids, and amino acids in calves [3]. As a result, calves experience acute symptoms of dehydration and metabolic acidosis, which gradually leads to chronic exhaustion and negative energy balance. Negative energy balance continues during the diarrhea period [12]. Therefore, it is important to correct dehydration and metabolic acidosis, in order to prevent exhaustion long-term.

Diarrhea is the most common indication for fluid therapy in neonatal calves. Oral electrolyte solutions (OES) have classically been used to replace fluid losses, correct acid-base and electrolyte abnormalities, and provide nutritional support because OES are inexpensive and easy to administer on the farm [10]. OES can be categorized by high or low sodium and glucose concentration, by an agent (glucose, acetate, citrate, or glycine) that facilitates absorption of sodium and water from the intestine, or by an alkalinizing agent (acetate, citrate, or bicarbonate) to correct metabolic acidosis and osmolarity [10]. Because sodium is the principal determinant of the extracellular fluid (ECF) volume, it must be present in an OES to correct dehydration. Glucose is necessary to facilitate sodium absorption and provide an energy source for the diarrheic calves. The ideal ratio of glucose (along with glycine, if present) to sodium in OES is between 1:1 and 3:1 [2]. Commercially available OES with low (1:1) and high (3:1) glucose plus glycine ratios in the Japanese market are Calf-Lyte S (CF; Nippon Zenyaku Kogyo Co., Ltd., Fukushima, Japan) and Salaron (SL; Fujita Pharmaceutical Co., Ltd., Tokyo, Japan), respectively. However, the effect of different compositions of commercially available OES in Japan for diarrheic calves is poorly understood. Therefore, the present study was designed to test how differences in the composition of commercially available OES affect dehydration and prevent catabolism. In addition, we prepared two prototype OES to further evaluate differences in OES composition. Prototype OES based on CF were prepared by doubling the glucose amount (CFG) or by doubling both glucose and glycine (CFGG). The goals of oral fluid therapy are to replace fluid and acid-base deficits and to provide nutritional support [10]. In this study, dehydration correction, the alkalizing

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Table 1. Composition of the CF, CFG, CFGG, and SL used in this study

	Na^+ (mM)	Glucose (mM)	Glycine (mM)	Acetate (mM)	$Citrate^{3-}$ (mM)	Osmolality (mOsmol/l)	The ratio of glucose plus glycine to sodium
CF	100.1	57.2	57.3	40.2	-	359.0	1.1 : 1
CFG	100.1	116.8	57.3	40.2	-	396.0	1.7 : 1
CFGG	100.1	116.8	110.1	40.2	-	454.0	2.3 : 1
SL	73.9	116.8	110.1	-	19.3	441.0	3.1 : 1

CF: Calf-Lyte, CFG: Calf-Lyte + Glucose, CFGG: Calf-Lyte + Glucose + Glycine, SL: Salaron.

effect, and prevention of catabolism were measured.

All procedures were in accordance with the National Research Council Guidelines for the Care and Use of Laboratory Animals (National Academy Press, 1996). Two commercially available OES, CF and SL, and two prototype OES were used. In one prototype OES (CFG), glucose was added to CF. In the other prototype OES (CFGG) glycine was added to CFG. Because of these adjustments, CFG contained glucose, but not glycine, equal to that of SL. CFGG contained glucose and glycine equal to that of SL. The ratio of glucose plus glycine to sodium in CF, CFG, CFGG and SL was 1.1:1, 1.7:1, 2.3:1 and 3.1:1, respectively. Table 1 shows the compositions of the four OES used.

Twenty-nine Holstein and three filial first-generation Japanese Black, 10.4 ± 3.7 days old were enrolled. In these calves, veterinary practitioners detected mild dehydration such that parenteral fluid therapy was not necessary, but moderate diarrhea was present based on physical examination. Blood gas analysis (i-STAT 1, Abbott Lab., Princeton, IL, U.S.A.) was performed on each calf. In 17 of the 32 calves (53.1%), *Cryptosporidium parvum* (*C. parvum*) was detected using a *C. parvum* rapid test kit (BOX-BIOK-155-10TEST, COSMO BIO Co., Ltd., Tokyo, Japan). Calves were randomly assigned to the CF, CFG, CFGG, and SL groups with 8 calves per group. Before OES administration, powder OES was dissolved in 2 l of warm water. The veterinary practitioner administered OES to calves using a feeding bottle with nipple, but did not administer other medication, such as antibiotics. All calves were offered two feedings of milk at the rate of 5% of body weight per feeding in the morning and afternoon, and had *ad libitum* access to concentrated feed (for growing calves at the nursing stage), hay, and water throughout treatment. Clinical findings and blood sampling were performed before (pre), and 1, 2, 4 and 24 hr after OES administration. Fecal status was assessed using a scoring system (0: firm, 1: pasty, 2: loose, and 3: watery) as described elsewhere [5]. Venous blood samples were anaerobically collected in a heparinized 1-ml syringe from the left jugular vein. Whole blood samples were analyzed for Ht, Hb, and base excess (BE) using an automatic gas analyzer (i-STAT 1, Abbott Lab.) and for beta-hydroxybutyrate (BHBA) concentrations by an automatic analyzer (Precision Xceed, Abbott Lab.). Changes in relative plasma volume (rPV) and relative BE (rBE) were calculated from Hb and Ht [4], and from actual BE concentration [11] using accepted formulas. Relative changes in BHBA (rBHBA) were derived from the following equation: $rBHBA = BHBA_{after} - BHBA_{before}$, where $BHBA_{before}$ and $BHBA_{after}$ are the BHBA concentrations immediately before and after administration, respectively.

The data are expressed as mean $\pm$ standard deviation. In diarrheic calves within group, mean values for each dependent variable were compared with the base value, using one-way ANOVA followed by Dunnet's test. Dependent variables were compared among groups for each sample collection period using one-way ANOVA followed by Tukey's HSD test. A statistical analysis was conducted using Excel Toukei 2010 (SSRI, Osaka, Japan). The significance level was $P<0.05$.

All calves had moderate diarrhea, accompanied with mild dehydration (Ht: $28.0 \pm 5.7\%$, Hb: 9.3 ± 1.9 g/dl), but no metabolic acidosis (pH: 7.37 ± 0.05, BE: 6.3 ± 4.5 mM). Clinical signs of eyeball recession into orbit and skin tent duration in the neck region were observed, but impaired central nervous system function including ataxia and coma were not observed. After administration of the OES, clinical signs, such as moist cough, jugular vein congestion, exophthalmos, salivation, and arrhythmia, were not observed throughout the experimental period for all groups. *C. parvum* was detected in 5/8 CF groups, 5/8 CFG groups, 4/8 CFGG groups, and 3/8 SL groups. The pre-OES administration fecal scores for CF, CFG, CFGG, and SL groups (2.1 ± 0.4, 2.3 ± 0.2, 2.3 ± 0.3 and 2.0 ± 0.4, respectively) were not significantly different to those after 4 hr OES administration (2.2 ± 0.3, 2.3 ± 0.3, 2.4 ± 0.4 and 2.2 ± 0.5, respectively).

Figure 1 shows the rPV in calves given each OES. The rPV of the CF group was significantly higher 2 hr after administration than the pre value, and this change remain high until the next day ($P<0.01$). In addition, the rPV of the CFGG group was significantly higher 4 hr after administration than the pre value ($P<0.05$). On the other hand, the rPV of the CFG and SL groups slightly and transiently increased, but these variances were not significant within the groups. CF and SL contained 100.1 and 73.9 mM of sodium, respectively. Research suggests that the ideal sodium concentration in OES to correct dehydration in calves is between 90 and 130 mmol/l [10]. In addition, Michell *et al.* [6] demonstrated that a commercial OES containing 73 mmol/l was not able to correct dehydration. Therefore, our results support research suggesting that higher sodium is needed to correct dehydration. However, when glucose was added to CF in the CFG prototype OES, the beneficial effects of sodium disappeared. The rPV of the CFG group was constant during the experimental period. When glycine was added to CFG in the CFGG prototype OES, the beneficial effect of increasing plasma volume was partly restored. Our results demonstrate that not only the sodium concentration in the OES, but also the glucose and glycine to sodium ratio are important for increasing plasma volume. The ratio of glucose to glycine to sodium present in CF, CFG, CFGG, and SL were 0.6:0.6:1.0, 1.2:0.6:1.0, 1.2:1.1:1.0 and 1.6:1.5:1.0, respectively. Even if the OES contained equal sodium amounts, differences in glucose or glycine concentration affected rehydration. The ratio
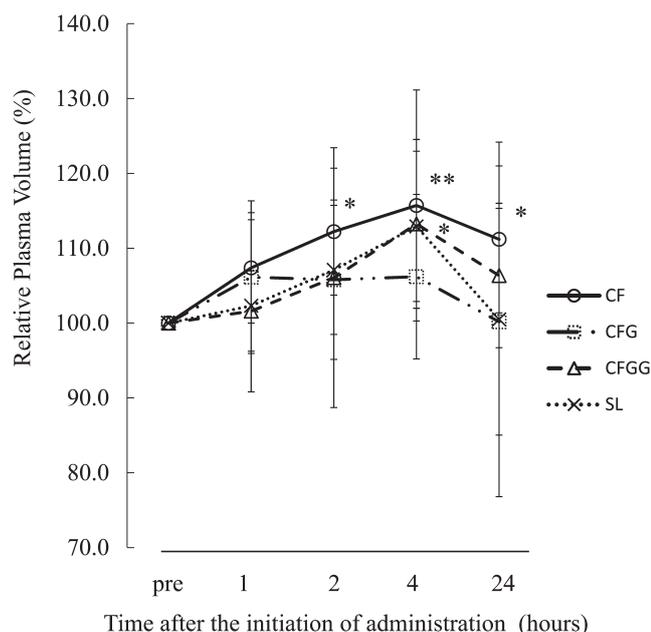
Fig. 1. Relative plasma volume (rPV) at pre, 1, 2, 4 and 24 hr after administration of CF, CFG, CFGG and SL. Pre: pre-infusion. Levels of significance indicated by *$P<0.05$, **$P<0.01$, versus pre-infusion values by Dunnet's test.
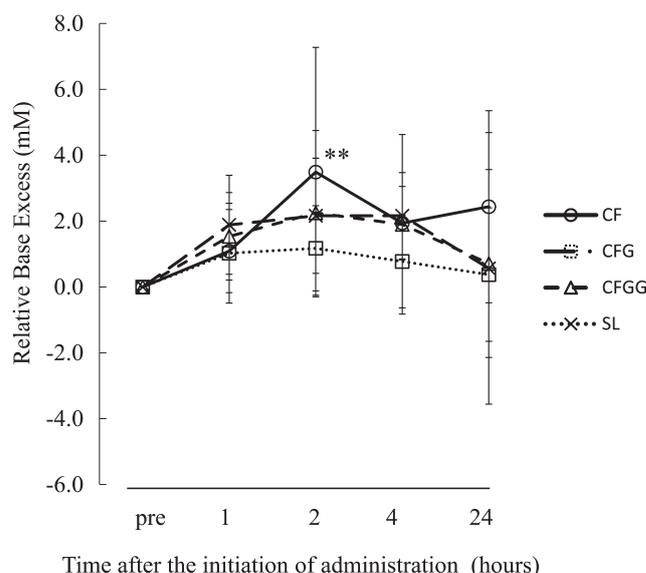
Fig. 2. Relative base excess (rBE) at pre, 1, 2, 4 and 24 hr after administration of CF, CFG, CFGG and SL. Pre: pre-infusion. Levels of significance indicated by *$P<0.05$, **$P<0.01$, versus pre-infusion values by Dunnet's test.

of glucose to glycine to sodium present in CF have maximized sodium absorption, and additional glucose and glycine may affect sodium absorption or lead to osmotic diarrhea.

The pre-administration venous pH values of the CF, CFG, CFGG, and SL groups (7.36 ± 0.05, 7.37 ± 0.03, 7.37 ± 0.06 and 7.38 ± 0.05, respectively) were not significantly different to those after 2 hr OES administration (7.40 ± 0.05, 7.38 ± 0.03, 7.39 ± 0.03 and 7.40 ± 0.05, respectively). The pre-administration HCO_3^- concentrations of the CF, CFG, CFGG, and SL groups (32.9 ± 5.9, 31.6 ± 3.8, 32.8 ± 3.6 and 32.4 ± 5.2, respectively) were not significantly different to those after 2 hr OES administration (34.6 ± 6.3, 32.9 ± 3.2, 34.9 ± 4.1 and 34.5 ± 4.8, respectively). The pre-administration PCO_2 concentrations of the CF, CFG, CFGG, and SL groups (57.2 ± 5.2, 54.8 ± 4.5, 56.6 ± 9.9 and 54.5 ± 4.2, respectively) were not significantly different to those after 2 hr OES administration (55.5 ± 5.1, 56.0 ± 3.6, 57.0 ± 5.6 and 57.3 ± 4.0, respectively). However, only CF administration decreased concentrations of PCO_2 2 hr after OES administration. Figure 2 shows the rBE in calves given each OES. The rBE of the CFG, CFGG, and SL groups slightly increased at 2 hr after OES administration (1.2 ± 1.3, 2.3 ± 2.5 and 2.2 ± 1.7 mmol/*l*, respectively), but these variances were not significant within the groups. Only CF administration significantly increased rBE 2 hr after OES administration (3.5 ± 3.8 mmol/*l*). The sequential changes in rBE for CF, CFG, CFGG, and SL were not significantly different among those groups. Acetate is alkalinizing agent and has alkalinizing effects similar to bicarbonate [8]. Citrate is alkalinizing agent too, but Naylor *et al*. [7] demonstrated that citrate was unsuitable for use in intravenous fluid. There were no differences in rBE between the CFGG and SL groups. Although both acetate and citrate are effective alkalinizing agents in OES, only CF administration markedly corrected acid-base status. The cause of this was unclear, but CF may improve plasma volume and decrease concentrations of PCO_2 by the potential alkalinizing effect attributed to aerobic metabolism. Aerobic metabolism accelerates clearance of lactate [1]. In addition, CF have twice the amount of acetate compared to the amount of citrate in SL could be explained.

Figure 3 shows the rBHBA in calves for each OES. The rBHBA in the CF and CFG groups remained constant until 4 hr after OES administration. The rBHBA of the CFGG and SL groups significantly decreased, reaching -0.09 ± 0.06 and -0.06 ± 0.05 at 4 hr after OES administration, respectively ($P<0.05$). Subsequent changes in rBHBA for the CF, CFG, CFGG and SL groups were not significantly different. The pre-administration plasma glucose concentrations for the CF, CFG, CFGG and SL groups (90.1 ± 14.2, 97.6 ± 28.9, 84.4 ± 10.7 and 103.1 ± 16.1 mg/d*l*, respectively) did not significantly change until 4 hr after OES administration (92.1 ± 13.5, 107.4 ± 19.3, 86.5 ± 19.1 and 113.8 ± 19.2 mg/d*l*, respectively). The glucose concentration of CF was 57.2 mmol/*l*, and those of CFG, CFGG and SL were 116.8 mmol/*l*. CFG, which has a large amount of glucose and small amount of glycine, was not effective in preventing catabolism. This suggests that the concentration of glucose in the OES is not the only factor for preventing catabolism. The ratio of glucose to glycine in CF, CFG, CFGG, and SL was 1.0:1.0, 2.0:1.0, 1.1:1.0 and 1.1:1.0, respectively, which suggests that a ratio around 1.0:1.0 is optimal for preventing catabolism. Therefore, it may be not only the amount of glucose, but also the ratio of glucose to glycine that is important for providing energy.

Our results demonstrated that not only the amount of sodium, glucose, and glycine, but also ratio of these factors is important
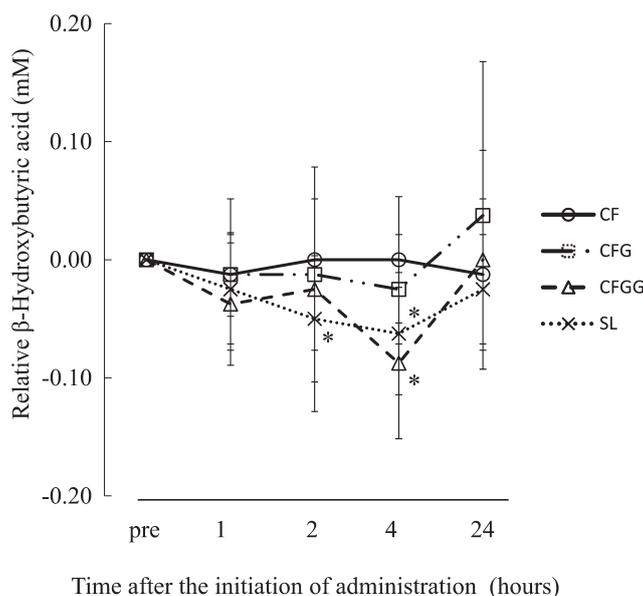
Fig. 3. Relative beta-hydroxybutyrate (rBHBA) values at pre, 1, 2, 4 and 24 hr after administration of CF, CFG, CFGG and SL. Pre: pre-infusion. Levels of significance indicated by *$P<0.05$, versus pre-infusion values by Dunnet's test.

for correcting dehydration and preventing catabolism. From commercially available OES in Japan, administration of CF increased plasma volume and corrected BE, but did not prevent catabolism. Administration of SL did not improve plasma volume or correct BE. However the catabolic preventive effect was excellent, since SL have more rapid prevention of catabolism and maintain low value in rBHBA compared with CF. This suggests that it is necessary to use CF and SL properly. CF should be used in the early stages of diarrhea for calves with dehydration and metabolic acidosis, but not in the later stages of exhaustion. On the other hand, SL may beneficial for wasting diarrheic calves with dehydration.

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