http://dx.doi.org/10.1590/1678-4162-11348

Arq. Bras. Med. Vet. Zootec., v.72, n.1, p.18-24, 2020

Maintenance enteral electrolyte solutions for neonatal calves: sodium acetate and osmolarity effects

[*Soluções eletrolíticas enterais de manutenção para bezerros neonatos: efeitos do acetato de sódio e da osmolaridade*]

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ABSTRACT

The use of hypotonic electrolytic solutions in enteral fluid therapy is still understudied in calves. The objective of the present study was to evaluate the effects of maintenance enteral electrolytic solutions with different concentrations of sodium acetate and different osmolarities in calves. For this, 18 Holstein calves, six male and 12 female, 20 days old and weighing around 52kg, were used. The animals were randomly divided into three groups and each group received one of the treatments. The three electrolytic solutions contained the same components in different concentrations, resulting in a hyposmotic, an isosmotic and a hyperosmotic solution. Each animal was maintained in enteral fluid therapy for 12 hours with infusion rate of 15mL kg^{-1} h^{-1}. Abdominal circumference, body weight, feces consistency, glucose and plasma lactate, pH, pCO_2, HCO^-_3 and BE were measured at the following times: T0h, T6h, T12h and T24h. The hyposmotic solution did not generate the onset of diarrhea, while the isosmotic and the hyperosmotic did. Regardless of the dose used, acetate did not cause metabolic alkalosis in the evaluated animals. The results suggest that the use of hyposmotic solution in diarrheic calves, dehydrated and without metabolic acidosis, may be clinically important.

Keywords: diarrhea, fluid therapy, hypotonic solution, volemia.

RESUMO

O uso de soluções eletrolíticas hipotônicas na hidratação enteral ainda é pouco estudado em bezerros. O objetivo do presente estudo foi avaliar os efeitos de soluções eletrolíticas enterais de manutenção com diferentes concentrações de acetato de sódio e diferentes osmolaridades em bezerros. Para isso, foram utilizados 18 bezerros, seis machos e 12 fêmeas, holandeses, com 20 dias de nascidos e pesando por volta dos 52kg. Os animais foram divididos aleatoriamente em três grupos e cada grupo recebeu um dos tratamentos. As três soluções eletrolíticas continham os mesmos componentes, mas em diferentes concentrações, resultando em uma solução hiposmótica, uma isosmótica e uma hiperosmótica. Cada animal foi mantido em hidratação enteral durante 12 horas com taxa de infusão de 15mL $kg^{-1}h^{-1}$. Foram aferidos perímetro abdominal, peso corporal, consistência das fezes, glicose e lactato plasmático, pH, pCO_2, HCO^-_3 e excesso de base nos seguintes tempos: T0h, T6h, T12h e T24h. A solução hiposmótica não gerou aparecimento de diarreia, enquanto a isosmótica e a hiperosmótica geraram. Independentemente da dose utilizada, o acetato não causou alcalose metabólica nos animais avaliados. Os resultados sugerem que o uso da solução hiposmótica em bezerros diarreicos, desidratados e sem acidose metabólica, pode ser clinicamente importante.

Palavras-chave: diarreia, hidratação, solução hipotônica, volemia.

Recebido em 15 de fevereiro de 2019
Aceito em 14 de junho de 2019
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INTRODUCTION

The study with enteral fluid therapy using maintenance enteral electrolytic solutions is far from being finished, as there is still little information on their use, mainly in adult cattle. It is believed that research with maintenance enteral electrolytic solutions should emphasize the optimal osmolarity these solutions must have. This is due the fact that hyperosmotic enteral solutions in the intestinal tract may function as osmotic laxatives, resulting in diarrhea in the animals (McClure, 2001), while in isotonic solutions these adverse effects are not observed.

The use of hypotonic electrolyte solutions associated with enteral fluid therapy in calves remains understudied, despite studies in buffalo calves (Ermita *et al.,* 2016) and calves (Ribeiro Filho *et al.,* 2017). In horses this kind of solution has been more researched. When compared with isotonic solutions, they were effective in expanding volemia without causing plasma hyponatremia or a decrease in serum osmolarity, providing a new option for enteral fluid therapy (Ribeiro Filho *et al.,* 2014).

Dehydrated suckling calves usually present metabolic acidosis and the addition of an alkalizing agent in the electrolytic solution is required (Bregadioli *et al.,* 2017). Acetate is only effective as an alkalizing agent after being metabolized and cannot be used in cases of severe metabolic acidosis. However, it does not present the disadvantages of bicarbonate when used in enteral solutions for neonatal calves, such as alkalinization of the abomasal pH, which does not allow milk to coagulate by interfering with its digestion, leading to the fermentation of undigested milk, lactic acidosis and worsening metabolic acidosis (Naylor *et al.,* 1990; Leal *et al.,* 2007; Constable *et al.,* 2009).

The aim of the present study was to evaluate the effects of maintenance enteral electrolytic solutions with different concentrations of sodium acetate and different osmolarities administered in a continuous flow through a small-caliber nasorruminal tube over 12 hours on newborn calves. It is hypothesized that the use of a hypotonic electrolyte solution causes no change in stool consistency and that the higher dose of sodium acetate may lead to the appearance of metabolic alkalosis.

MATERIALS AND METHODS

Six male and 12 female Holstein calves that were an average of 20 days old and had a median body weight of 52kg were used in this study. These calves were clinically healthy with no history of gastrointestinal disease, and underwent a clinical and laboratory evaluation prior to the experiment. Calves remained in individual pens (2×3m) and were provided with a wood shavings bed, which was changed daily. They were fed 1L of milk four times per day and were provided with water *ad libitum* during the experimental period.

Animals were randomly distributed into three equal-sized groups. Before starting treatments, a nasorruminal tube was introduced and attached to the halter of each animal. The probe was connected to a coil tube, through which the solution flowed from a 20L recipient positioned above the animal's head. Animals remained in individual stalls and received electrolyte solutions throughout the experimental period. All of the electrolyte solutions contained the same components but in different concentrations, resulting in a hypoosmotic solution – HypoSol – (200mOsmol L^{-1}): 4g sodium chloride, 0.5g potassium chloride, 1g sodium acetate, and 7.5g dextrose per liter; an isosmotic solution - IsoSol, (280mOsmol L^{-1}): 5g sodium chloride, 1g potassium chloride, 2g sodium acetate, and 10g dextrose per liter; and a hyperosmotic solution - HyperSol - (350mOsmol L^{-1}): 6g sodium chloride, 1g potassium chloride, 3g sodium acetate, and 15g dextrose per liter. Each animal received the appropriate solution for 12 hours at a rate of 15mL kg^{-1} hr^{-1} via nasorruminal tube (4mm diameter, 150cm long). During the fluid therapy phase, animals remained fasted, both food and water were withheld, and were kept without movement restrictions.

Abdominal circumference, body weight, stool consistency, plasma glucose and lactate, pH, pCO_2, HCO^-_3 and base excess (BE) were measured at the following times: T0h, immediately prior to the initiation of treatment; T6h, after 6 hours of treatment; T12h, after 12 hours of treatment (end of fluid therapy); and T24h, 12 hours after the end of fluid therapy. After one hour of the end of fluid therapy (T12h), the calves were fed 1L of milk, and water was again provided *ad libitum.* In the next

morning, after the last collection (T24h), they returned to the pre-experiment diet.

The abdominal circumference was measured by a tape measure at a midpoint of the paralumbar fossa for measurement in centimeters of the abdominal contour, while body weight was measured in bull scales. The feces were collected from the rectal ampoule. Subsequently, they were weighed, placed in aluminum trays, and placed in a kiln at 60°C for dehydration. The feces were then weighed daily until there were no changes in their weight. The moisture content of the feces was calculated by the formula: Moisture (%) = [(fresh weight - dry weight) / fresh weight] x 100.

Blood samples were collected in tubes with sodium fluoride to obtain the plasm to measure the glucose and lactate in plasma using an automatic analyzer. The samples for blood gas analysis were collected in 2mL disposable plastic syringes that had previously been heparinized with lithium heparin.

The statistical program SAEG 9.1 (Sistema…, 2007) was used for data analysis. Data were analyzed using repeated measures analysis of variance (ANOVA), which evaluated the effects of treatment and time, and the interaction between these. When the analysis was significant for one or more factor, Tukey's test was used to compare the mean values. Where the data did not meet the assumptions of ANOVA, Kruskal-Wallis test was applied. All analyses were interpreted considering a significance level of 5% ($P< 0.05$).

RESULTS AND DISCUSSION

As expressed in Table 1, the animals that received HypoSol treatment had no change in the consistency of the feces at the end of the fluid therapy phase (T12h), whereas in one (16.66%) of the animals that received the IsoSol treatment, diarrhea was detected. In the same period, two animals (33.33%) of the HyperSol treatment showed diarrhea. These results demonstrate that the hypotonic solution (HypoSol) was absorbed in greater quantity by the intestinal tract, evidencing that this solution is an alternative for the enteral fluid therapy of calves with diarrhea, which is the main cause of dehydration and death of neonatal calves. The isotonic solution, when used in these patients, may increases the intensity of diarrhea. In children, oral hypotonic electrolyte solution reduces fecal production by 20%, vomiting episodes by 30% and intravenous hydration use by 33%, it began to be used on a global scale in 2005 (Oral…, 2006).

Table 1. Frequency of fecal consistency in healthy neonatal calves treated with hypotonic (HypoSol), isotonic (IsoSol) and hypertonic (HyperSol) enteral electrolyte solutions administered by continuous nasogastric tube for 12 hours

	Fecal Consistency				
Time (h)	Dry	Well-formed pasty	Pasty	Diarrheal	Total
		HypoSol			
0h	0^{+} $(0)^{++}$	83.33 (5)	16.67 (1)	0 (0)	25 (6)
6h	0 (0)	83.33 (5)	16.67 (1)	0 (0)	25 (6)
12h	0 (0)	33.33 (2)	66.67(4)	0 (0)	25 (6)
24h	0 (0)	83.33 (5)	16.67 (1)	0 (0)	25 (6)
Total	0 (0)	70.83 (17)	29.17 (7)	0 (0)	100 (24)
		IsoSol			
0h	0 (0)	83.33 (5)	16.67 (1)	0 (0)	25 (6)
6h	0 (0)	83.33 (5)	16.67 (1)	0 (0)	25 (6)
12h	0 (0)	66.67(4)	16.67 (1)	16.67 (1)	25 (6)
24h	0 (0)	83.33 (5)	0 (0)	16.67 (1)	25 (6)
Total	0 (0)	79.17 (19)	12.5 (3)	8.3 (2)	100 (24)
		HyperSol			
0h	0 (0)	83.33 (5)	16.67 (1)	0 (0)	25 (6)
6h	0 (0)	50 (3)	33.33 (2)	16.67 (1)	25 (6)
12h	0 (0)	16.67 (1)	50 (3)	33.33 (2)	25 (6)
24h	0 (0)	66.67(4)	33.33(2)	0 (0)	25 (6)
Total	0 (0)	54.17 (13)	33.33 (8)	12.5 (3)	100 (24)

$^{+}$Frequency of fecal consistency (%); $^{++}$ Number of animals.

In turn, diarrhea that appears during the use of hypertonic enteral electrolyte solutions (HyperSol) was caused by the fact that the electrolyte solution was not completely absorbed, and consequently, the volume remaining in the intestinal lumen caused softening of the stool.

The animals of all treatments presented a slight increase in the abdominal circumference and body weight, but without difference (P> 0.05), which can be attributed to the administration of enteral electrolyte solutions. The animals received on average 8.2 liters of solution, about 15% of their body weight in 12 hours, which may have generated this increase (Table 2). Similar results were reported in cattle by Ermita *et al* (2018) and in goats by Atoji *et al.* (2012).

Table 2. Mean values and standard deviations of abdominal circumference (cm), weight (kg), plasma glucose (mg/dL) and plasma lactate (mMol/L) in healthy neonatal calves treated with hypotonic enteric electrolyte solutions (HypoSol), isotonic (IsoSol) and hypertonic (HyperSol) administered by continuous nasogastric tube for 12 hours

Treatment	T0h	T6h	T12h	T24h
		Abdominal circumference (cm)		
HypoSol	93.17±4.91	97.83±4.87	101.50±6.62	96.83±5.77
IsoSol	92.17±9.11	93.50±7.19	100.50±7.71	96.50±7.92
HyperSol	95.33±12.5	101.50±10.86	103.33±12.26	95.50±6.73
		Weight (kg)		
HypoSol	56.67±11.15	58.34±11.34	60.00±10.71	57.83±10.14
IsoSol	51.50±14.81	53.34±14.68	54.34±14.53	51.84±14.49
HyperSol	55.67±13.59	58.50±13.92	60.50±15.64	57.00±13.53
		Plasma glucose (mg/dL)		
HypoSol	84.67±11.48	72.83±9.15	73.33±7.06	101.17±19.49
IsoSol	92.17±14.59	83.83±16.58	80.00±13.55	92.83±17.27
HyperSol	91.83±17.86	105.83±33.20	96.17±17.97	103.83±32.79
		Plasma lactate (mMol/L)		
HypoSol	0.96±0.38	1.07±0.73	1.15±0.36	1.15±0.30
IsoSol	1.14±0.43	1.05±0.41	1.06±0.40	1.19±0.49
HyperSol	1.0±0.43	1.08±0.36	1.09±0.52	1.06±0.41

(P< 0.05) by the Tukey test.

Plasma glucose values (Table 2) did not show differences between treatments and treatments over time (P> 0.05). Similar results were reported by Gomes *et al.* (2014), who analyzed solutions containing glucose precursors and did not observe variation in glycemia of treated animals. Ribeiro Filho *et al.* (2014), using 15g/L of dextrose in the elaboration of enteral electrolytic solutions for horses, reported an increase in glycemia during the fluid therapy period. In cattle, Ribeiro Filho *et al.* (2011) reported that when using an enteral electrolyte solution containing 5g/L dextrose, the animals did not show any difference in glycemia during the treatment period. However, these authors reported that the other solution used, containing a precursor of glucose propylene glycol in the volume of 15mL/L, promoted an increase of plasma glucose during treatment and that this persisted until 24 hours after the end of the fluid therapy.

In the HyperSol, a slight increase in glycemia was observed during the experimental phase, which persists until time T24h (Table 2). The animals received electrolytic solution containing 15g/L of dextrose and 3g/L of sodium acetate, which when oxidized, metabolizes into glucose and carbon dioxide (Leal *et al.,* 2007), which caused this slight increase in glycemic levels. Plasma glucose concentrations did not show changes between treatments and over time in treatments (P> 0.05). In addition, their values remained within the reference range for the studied age (Table 2).

The amount of glucose used in the electrolyte solutions observed in the present assay was not enough to promote a significant increase in the glycemic rate in the animals. This result indicates that if there is a need to correct cases of hypoglycemia, the amount of energy source should be higher.

As expressed in Table 2, no difference was detected in mean plasma lactate values between treatments and over time in treatments (P> 0.05). The sources of energy commonly used in enteral electrolyte solutions, when too much, can lead to the risk of allowing unabsorbed glucose to carry over into the large intestine, where glucose may be fermented to short-chain volatile fatty acids and exacerbate fecal water loss as quoted by Nouri and Constable (2006). The values verified in the present study demonstrate that even the amount used in the hypertonic solution (HyperSol), 15g/L dextrose, was not enough to increase the lactate concentration in the blood and to determine the appearance of adverse effects. According to Nouri and Constable (2006) the upper limit of glucose in an oral electrolyte solution (OES) for a calf of 45kg-body weight may be 1.0-3.6g/kg-body weight.

It was suggested to increase the amount of dextrose to provide a more expressive effect on the glycemic rate of animals. However, there is a possibility that the increase of carbohydrate in the electrolytic solution causes an increase in blood lactate concentration. As there was no increase in its values (Table 2), this procedure can be performed, though the possibility that the increase of the energy source in the electrolytic solution predisposes to the appearance of acidosis should not be excluded.

No changes were observed in mean blood pH values between treatments (P> 0.05). In the HyperSol treatment, at time T24h, there was a variation (P< 0.05) of the mean values in relation to the time T12h (Table 3). This increase in pH occurred, possibly, due to the end of fluid therapy and the return of feed. The same behavior was observed in the solutions HypoSol and IsoSol, although not significant, the return of the mean values to basal concentrations (T0h) occurred. Despite the difference, values remained within the reference range for neonatal calves, from 7.32 to 7.40 (Lisbôa *et al.*, 2002).

Table 3. Mean values and standard deviations of blood pH, pCO_2 (mmHg), $cHCO^-_{3v}$ (mMol/L) and $cBase_v$ (mMol/L) in healthy neonatal calves treated with hypotonic (HypoSol), isotonic (IsoSol) and hypertonic (HyperSol) enteral electrolyte solutions administered by continuous nasogastric tube for 12 hours

Treatment	T0h	T6h	T12h	T24h
		Ph		
HypoSol	$7.38±0.019^{Aa}$	$7.37±0.015^{Aa}$	$7.35±0.031^{Aa}$	$7.39±0.021^{Aa}$
IsoSol	$7.35±0.046^{Aa}$	$7.36±0.037^{Aa}$	$7.32±0.046^{Aa}$	$7.37±0.042^{Aa}$
HyperSol	$7.37±0.016^{Aab}$	$7.37±0.015^{Aab}$	$7.36±0.018^{Ab}$	$7.40±0.036^{Aa}$
		pCO_2 (mmHg)		
HypoSol	48.33±2.63	48.83±2.40	50.50±2.17	49.20±1.92
IsoSol	52.33±4.46	48.50±4.37	50.33±1.97	50.67±3.78
HyperSol	51.0±4.15	50.33±2.34	52.67±2.34	50.0±2.61
		$cHCO^-_{3v}$ (mMol/L)		
HypoSol	27.72±1.18	26.73±1.25	26.60±2.88	28.70±2.25
IsoSol	30.68±3.29	28.30±3.13	28.85±3.45	30.48±2.94
HyperSol	27.90±3.53	25.60±3.08	24.93±2.91	27.48±2.51
		$cBase_v$ (mMol/L)		
HypoSol	$3.22±1.06^{Aa}$	$2.25±1.07^{Aa}$	$1.62±2.87^{Aa}$	$4.20±2.3^{Aa}$
IsoSol	$4.3±1.47^{Aa}$	$2.1±1.38^{Aab}$	$1.04±1.34^{Ab}$	$4.16±1.4^{Aa}$
HyperSol	$3.71±1.81^{Aab}$	$3.03±1.46^{Ab}$	$3.81±0.5^{Aab}$	$5.63±2.2^{Aa}$

Mean values followed by different capital letters in the same column or by different lowercase letters in the same row differ from each other (P< 0.05) by the Tukey test.

In the mean values of the partial pressure of carbon dioxide, there were no differences (P> 0.05) between treatments and in the treatments over time. Although not significant, a decrease of the means during the fluid therapy period in the IsoSol and HyperSol solutions can be observed (Table 3). As with bicarbonate (Table 3) and base excess (BE), the slight reduction in pCO_2 values was possibly due to the higher amount of sugar and chloride in these solutions, which would lead to an acidification that was compensated by the respiratory buffer system, causing a decrease of pCO_2 values. However, this variation had no clinical significance, as the

means were within the normal range (48 to 60mmHg) reported by Lisbôa *et al.* (2002) in healthy bovine calves and buffalo calves by Silva *et al.* (2010).

Mean values of BE had no difference between treatments (P> 0.05). In the evaluation over time, a difference (P< 0.05) was detected in the groups of electrolytic solutions IsoSol and HyperSol (Table 3). In the IsoSol solution a reduction in BE at the final moment of the fluid therapy (T12h) was observed when compared to T0h (before the period of fluid therapy) and T24h (12 hours after the end of the fluid therapy). In turn, the animals hydrated with the HyperSol solution presented a significant decrease in T6h in relation to T24h.

The reduction of BE during the fluid therapy phase in IsoSol (T12h) and HyperSol (T6h) treatments can be attributed to the composition of referred electrolytic solutions (Table 3). Two substances possibly influenced this result: chloride and dextrose. Chloride participation was discussed previously (bicarbonate concentration). The other possibility is related to the amount of dextrose in the electrolytic solutions used, because according to Zhang *et al.* (2003), the carbohydrates are metabolized by bacteria in the gastrointestinal tract, producing organic acids, having an elevation of these in the plasma. Lactate isomers (L-lactate and D-lactate) are some of the organic acids produced by bacterial metabolism (Fall and Szerlip, 2005). D-lactate is metabolized slowly in most mammals, causing a serum accumulation of this organic acid, reducing blood pH, bicarbonate and BE (Ewaschuk *et al.*, 2005).

The increase in the values of BE occurred in the three treatments at T24h, returning to values similar to T0h, possibly due to the end of fluid therapy and the return of feed, as occurred with the pH (Table 3). It should be noted that the amount of sodium acetate contained in the treatment solutions, mainly HypoSol and IsoSol, were not enough to cause an increase in the BE, signaling that in calves with metabolic acidosis it should be higher than that used in the present test.

CONCLUSIONS

The HypoSol did not generate the onset of diarrhea, while the IsoSol and HyperSol did. Regardless of dose used, acetate did not cause metabolic alkalosis in the animals in the present study. The results suggest that the use of the HypoSol in diarrheal calves, dehydrated and without metabolic acidosis may be clinically important.

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