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Hypotonic enteral electrolyte solutions administered by nasoesophageal tube in continuous flow in dogs dehydrated by water restriction: Part 1

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[*Soluções eletrolíticas enterais hipotônicas administradas por sonda nasoesofágica em fluxo contínuo em cães desidratados por restrição hídrica: Parte 1*]

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ABSTRACT

The present study assessed and compared the effects of hypotonic enteral electrolyte solutions administered by nasoesophageal tube in continuous flow in dogs submitted to water restriction on packed cell volume; total serum protein and serum osmolarity concentrations; blood volume; plasma glucose and lactate levels; blood gas analysis, anion gap, and strong ion difference. Six adult dogs were used (four males and two females). All animals were submitted to both proposed treatments in a crossover design 6×2. The treatments were as follows: ESmalt consisting of 5g sodium chloride, 1g potassium chloride, 1g calcium acetate, 0.2g magnesium pidolate, and 9.6g maltodextrin that were diluted in 1.000mL water (measured osmotic concentration of 215mOsm L^{-1}) and ESdext consisting of 5g sodium chloride, 1g potassium chloride, 1g calcium acetate, 0.2g magnesium pidolate, and 9.6g dextrose that were diluted in 1.000mL water (measured osmotic concentration of 243mOsm L^{-1}). All solutions were administered at 15ml kg^{-1} h^{-1} for 4 hours. Both solutions increased the plasma volume in dehydrated dogs without causing adverse effects. However, ESmalt was more effective in promoting the increase in blood volume.

Keywords: canine, blood gas analysis, blood volume, enteral fluid therapy

RESUMO

O presente estudo avaliou e comparou os efeitos de soluções eletrolíticas enterais hipotônicas, administradas por sonda nasoesofágica em fluxo contínuo em cães submetidos a restrição hídrica, sobre o hematócrito, proteínas totais séricas, osmolaridade sérica, volemia, glicose e lactato plasmáticos, hemogasometria, ânion gap *e DIF. Foram utilizados seis cães adultos (quatro machos e duas fêmeas). Todos os animais foram submetidos aos dois tratamentos propostos, em um delineamento* crossover *6×2. Os tratamentos foram os seguintes: SEmalt – 5g de cloreto de sódio, 1g de cloreto de potássio, 1g de acetato de cálcio, 0,2g de pidolato de magnésio e 9,6g de maltodextrina, diluídos em 1.000mL de água (osmolaridade mensurada: 215mOsm L^{-1}); SEdext – 5g de cloreto de sódio, 1g de cloreto de potássio, 1g de acetato de cálcio, 0,2g de pidolato de magnésio e 9,6g de dextrose, diluídos em 1.000mL de água (osmolaridade mensurada: 243mOsm L^{-1}). Todas as soluções foram administradas no volume de 15mL kg^{-1} $hora^{-1}$, durante quatro horas, em fluxo contínuo. Ambas as soluções aumentaram o volume plasmático em cães desidratados, sem gerar o aparecimento de efeitos adversos. Porém, a SEmalt foi mais eficaz em promover a expansão da volemia.*

Palavras-chave: canino, hemogasometria, hipovolemia, hidratação enteral

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INTRODUCTION

Most diseases that affect dogs lead to changes in their homeostasis and result in varying degrees of dehydration. In addition to physical examination results, packed cell volume, total serum protein, urea, creatinine, serum or plasma electrolyte levels, urinary density and blood gas analysis are performed in clinical settings to estimate, monitor, and treat hydroelectrolytic and acid-base imbalances (Ribeiro Filho *et al*., 2008; Dibartola, 2012).

Dehydration is treated with fluid therapy, indicated for recovery, maintenance of cellular functions and correction of hydroelectrolytic and acid-base imbalances. Consequently, the fluid therapy improves homeostasis of the organism (Ribeiro Filho *et al*., 2008).

Crystalloids and colloids solutions are used to restore total blood volume. Depending on the kind of solution used, these hydroelectrolytic imbalances can be attenuated, corrected, or aggravated. Consequently, the fluid to be administered should be carefully chosen according to the patient clinical condition (Harold Davis *et al*., 2013). In dogs, the most commonly used fluid therapy routes of administration are intravenous, subcutaneous, oral, and intraosseous. The choice of the administration route depends on the nature and severity of the clinical disorder and the evolution of the dog's condition (Brown and Otto, 2008; Dibartola, 2012).

Oral or enteral fluid therapy has been used to correct cases of mild-to-moderate dehydration, but it is not often used to correct severe cases of hypovolemia. In addition to being a "physiological route", other advantages include its lower cost and safety than the other fluid therapy routes (Brown and Otto, 2008). Current studies had reported results from experimental assays related to several clinical disorders associated with hydroelectrolytic and acid-base imbalances treated by enteral or oral fluid therapy in dogs (Spandorfer *et al*., 2005; Reineke *et al*., 2013; Forbes *et al*., 2015). Experimental trials using enteral fluid therapy administered by a continuous flow by nasoesophageal tube have not been found in the literature.

Consequently, this study aimed to evaluate the effects of hypotonic electrolyte solutions containing energy sources administered by a nasoesophageal tube in continuous flow during the fluid therapy phase on the blood parameters of healthy dogs submitted to water restriction. We hypothesized that the use of hypotonic enteral electrolyte solution during the fluid therapy phase would increase blood volume without causing adverse effects.

MATERIAL AND METHODS

The experiment was approved by the Ethics Committee on Animal Research under protocol no 96/15. The research was performed in the city of Viçosa, Minas Gerais, Brazil, which is located at an altitude of approximately 640m at latitude of −20° 73′ 56.03″ and longitude of −42° 85′ 76.62″. The temperature recorded during the study period ranged from 21.7°C to 33.1°C, and the relative humidity ranged from 43.6% to 89.6%. Six healthy Golden Retrievers, two females and four males aged 2-6 years with an average body weight of 33.5kg and body score of 3 (Feitosa, 2008) were used. Before the start of the experiment, the animals were clinically evaluated, followed by laboratory tests. Twelve hours before the fluid therapy treatment, dogs were placed in individual cages with water and food restriction. All animals were submitted to both proposed treatments in a crossover design 6×2. A 7-days interval was used between treatment cycles. The animals in the ESmalt group received an electrolytic solution containing 5g sodium chloride, 1g potassium chloride, 1g calcium acetate, 0.2g magnesium pidolate, and 9.6g maltodextrin that were diluted in 1.000mL of water (measured osmotic concentration of 215mOsm L^{-1}). Those in the ESdext group received an electrolytic solution containing 5g sodium chloride, 1g potassium chloride, 1g calcium acetate, 0.2g magnesium pidolate, and 9.6g dextrose that were diluted in 1.000mL of water (measured osmotic concentration of 243mOsm L^{-1}). Nasoesophageal tubes 3mm diameter and 100cm length (Long nº 8 nasoesophageal tube-Embramed. Distributed by Embramed Ind. Com. Ltda. São Paulo, SP, Brazil) were used to administer the solutions; they were introduced into the right nostril of the dogs and fixed with a superglue (Superbonder®, Henkel Ltda. São Paulo, SP, Brazil) at the dorsal nasal region. All solutions were administered at

$15mL^{-1}$ kg^{-1} h^{-1} through a 4h period in a continuous flow.

To perform laboratory evaluations, blood samples were collected after skin disinfection by jugular venipuncture. Vacuum-sealed vials containing EDTA (Vacuntainer BD, Juiz de Fora, MG, Brazil) were used to collect total blood samples to measure the packed cell volume (PCV%) by the microhematocrit technique. Plasma samples were obtained from blood collected in vacuum-sealed vials with sodium fluoride (Vacuntainer BD, Juiz de Fora, MG, Brazil) for measurement of glucose and lactate levels. Serum samples were obtained from blood and stored in vacuum-sealed vials with no anticoagulants to measure total serum protein (Biochemical device-HumaStar 300 - Human. Distributed by in vitro Diagnóstica Ltda. Itabira, MG, Brazil) and serum osmolarity using an osmometer (Advanced Micro-Osmometer Model 3320; Advanced Instruments Inc., Norwood, MA, United States). Venous blood samples (2mL) were collected using sterile syringes containing lithium heparin (Polypropylene syringe containing a 0.5-2mL heparinized disk. PICO50 - Radiometer Copenhagen; Radiometer Medical 248 ApS, Brønshøj-Copenhagen, Denmark) for blood gas analysis (ABL 80 Flex - Radiometer Copenhagen; Radiometer Medical 248 ApS, Brønshøj-Copenhagen, Denmark) and measurement of electrolytes. The following parameters were measured in these samples: blood pH (pH); partial carbon dioxide pressure (pCO_2); bicarbonate concentration ($cHCO_3^-$); total carbon dioxide concentration (tCO_2); base concentration (cBase); anion gap, sodium, potassium, and chloride. Blood volume was calculated using the following formula: %VP= (TP1/TP2) −1×100, where VP is the plasma volume, TP1 is the initial total protein concentration, and TP2 is the final total protein concentration. described by Boyd (1981). The strong ion difference (SID) was determined using the following formula: $SID = (Na^+ + K^+) - (Cl^-)$ (Stewart, 1983).

The laboratory tests were performed at the following time points: T-12h (immediately before water and food restriction); T0h (immediately before the start of fluid therapy); T4h (end of fluid therapy) and T8h (4h after the end of fluid therapy).

Descriptive statistics were performed to obtain the means ± standard deviations of all variables. Data were evaluated using Lilliefors test and Cochran's & Bartlett's test to assess the normality of data and homogeneity of variances, respectively. Analysis of variance (ANOVA) was performed when the data attempted the prerequisites of normality and homogeneity. Variables that did not meet the criteria for ANOVA evaluation were subjected to non-parametric analysis by Kruskal–Wallis and Wilcoxon tests. The Minitab 17.0 software (Minitab Inc., Pennsylvania, USA) was used.

RESULTS AND DISCUSSION

The objective of the water restriction in which the animals were submitted was to evaluate the therapeutic potential of enteral enteric solutions. The dose of $15mL^{-1}kg^{-1}$ h^{-1} used in this test animal was based on pilot studies, because there is no dose for enteral fluid therapy reported in the literature in dogs. It is important to emphasize that Balbinot *et al.* (2011) administered intravenously the volume of $25mL^{-1}$ kg^{-1} $12h^{-1}$ (body weight × degree of dehydration + maintenance rate) in experimentally dehydrated dogs, while Davis *et al.*, (2013) described the volume to be administered in the replacement phase based on the formula body weight (kg) × % dehydration. Both values are approximate to that used in the present study.

The small-caliber nasoesophageal tube used during the fluid therapy phase did not cause stress in the animals, and none of the dogs attempted to try to remove the tube. This fluid therapy technique is often used in animals of other species (Ribeiro Filho *et al*., 2011; Atoji *et al*., 2012; Ribeiro Filho *et al*., 2015). Furthermore, the enteral administration of the electrolyte solutions in continuous flow at $15mL^{-1}$ kg^{-1} h^{-1} was well tolerated by the dogs with no cases of abdominal distention or pain. The absence of these adverse effects has been described in adult bovines (Ribeiro Filho *et al*., 2011), goats (Atoji *et al*., 2012), horses (Ribeiro Filho *et al*., 2015), buffalo calves (Ermita *et al*., 2016) and calves (Ribeiro Filho *et al*., 2017). All the mentioned authors used a volume similar to that used in the present study and did not report the incidence of these abnormalities during the fluid therapy period. It is important to emphasize that the present study was the first controlled trial

using this therapeutic modality of fluid therapy for dogs.

The PCV did not change between the groups (P> 0.05). However, a difference was detected in the time point evaluation in both groups (P< 0.05). In both groups, a decrease in the PVC values were observed at the end of the fluid therapy period (T4h), what persisted until T8h (Table 1). These results demonstrated that electrolyte solution with maltodextrin (ESmalt) and electrolyte solution containing dextrose (ESdext) promoted an increase of the blood volume in dogs. This result shows us the efficiency of this fluid therapy modality. The total serum protein concentrations confirmed the result of the blood volume increased trough time, particularly in the animals that received ESmalt (Table 1).

The evaluation of the serum osmolarity, showed no difference between the groups or time points of this study (P> 0.05; Table 1). Just as showed before, there was no significant difference in the blood volume between the groups (P> 0.05), but, when we look the entire study period, there was a significant increase in the blood volume in the ESmalt group at T4h (Table 1). Experimental studies in humans (Rautanen *et al*., 1993) and animals (Ribeiro Filho *et al*., 2014) demonstrated that hypotonic solutions allow better water absorption than isotonic solutions. Since the ESmalt used in the present study had a lower osmolarity (215mOsm L^{-1}), the results obtained in the ESmalt group showed that the electrolytic enteral hypotonic solution led to significant water absorption, even in a short period (4h), making this solution a good option of fluid therapy to increase the plasma volume in dehydrated dogs.

There were no statistic differences in plasma glucose and lactate levels between or within the groups during the study period (P> 0.05). Moreover, the values for both variables remained within the normal range for the animals of this species. In horses, Ribeiro Filho *et al*. (2014 and 2015) obtained similar results to those in the present study, when comparing enteral electrolyte solutions containing maltodextrin and dextrose.

Table 1. Means and standard deviations of packed cell volume (PCV), total serum protein, osmolarity, blood volume, glucose and lactate levels of dogs dehydrated by water restriction subjected to two protocols of continuous enteral fluid therapy trough time

		Times			
Parameters	Groups	T-12h	T0h	T4h	T8h
PCV (%)	ESmalt	46.2±2.6^{Aa}	46.0±3.4^{Aa}	37.8±5.5^{Ab}	37.4±3.5^{Ab}
	ESdext	45.0±2.3^{Ab}	46.8±3.6^{Aa}	35.6±2.5^{Ab}	37.4±5.7^{Ab}
Total protein g dL^{-1}	ESmalt	7.3±0.5^{Aab}	7.7±0.6^{Aa}	6.5±0.3^{Ab}	6.7±0.5^{Ab}
	ESdext	7.1±0.6^{Aa}	7.1±0.4^{Aa}	6.7±0.5^{Aa}	7.1±0.6^{Aa}
Osmolarity mOsm L^{-1}	ESmalt	303.4±5.0^{Aa}	307.2±7.3^{Aa}	301.4±5.9^{Aa}	302.2±0.83^{Aa}
	ESdext	304.0±5.6^{Aa}	308.6±7.0^{Aa}	303.2±4.1^{Aa}	306.4±6.7^{Aa}
Blood volume	ESmalt	0.0±0.0^{Ab}	-3.7±10.5^{Ab}	19.0±13.3^{Aa}	-3.0±6.2^{Ab}
	ESdext	0.0±0.0^{Aa}	0.94±11.9^{Aa}	5.6±10.3^{Aa}	-4.5±2.9^{Aa}
Glucose mg dL^{-1}	ESmalt	100.4±6.4^{Aa}	97.8±5.0^{Aa}	115.8±26.3^{Aa}	99.0±7.5^{Aa}
	ESdext	97.8±4.9^{Aa}	96.0±4.5^{Aa}	103.6±6.0^{Aa}	97.2±8.2^{Aa}
Lactate mg dL^{-1}	ESmalt	13.4±2.0^{Aa}	13.4±4.0^{Aa}	9.8±2.4^{Aa}	10.8±3.6^{Aa}
	ESdext	12.2±4.5^{Aa}	9.2±4.0^{Aa}	12.4±8.8^{Aa}	14.0±5.4^{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).

A difference was observed in blood pH (P< 0.05) in both groups only over time (Table 2). At T0h, pH values were lower than those at T8h. Despite the increase observed in the mentioned period, these values remained within the physiological limits mentioned by Balbinot (2007) and Dibartola (2012), indicating the results were clinically insignificant. No difference in pCO_2

was observed between or within the groups over the time (P> 0.05), which indicated that the tested solutions had no effect on the respiratory component of blood gas analysis.

Table 2. Means and standard deviations of pH, pCO_2, $cHCO_3^-$, tCO_2, cBase, anion gap, and strong ion difference (SID) of dogs dehydrated by water restriction and subjected to two protocols of continuous enteral fluid therapy trough time

		Times			
Parameters	Groups	T-12h	T0h	T4h	T8h
pH	ESmalt	7.37 ± 0.02^{Aab}	7.35 ± 0.02^{Ab}	7.36 ± 0.01^{Aab}	7.42 ± 0.02^{Aa}
	ESdext	7.39 ± 0.03^{Aab}	7.36 ± 0.02^{Ab}	7.41 ± 0.08^{Aab}	7.41 ± 0.01^{Aa}
pCO_2 mmHg	ESmalt	39.3 ± 5.5^{Aa}	40.5 ± 5.0^{Aa}	35.9 ± 2.5^{Aa}	35.4 ± 1.7^{Aa}
	ESdext	38.7 ± 1.8^{Aa}	41.3 ± 1.8^{Aa}	35.9 ± 8.8^{Aa}	37.2 ± 2.8^{Aa}
$cHCO_3^-$ mmol L^{-1}	ESmalt	21.9 ± 1.7^{Aab}	21.2 ± 2.0^{Aab}	19.4 ± 1.2^{Ab}	22.7 ± 1.8^{Aa}
	ESdext	22.5 ± 1.8^{Aab}	22.4 ± 1.9^{Aab}	19.1 ± 2.8^{Ab}	23.2 ± 1.9^{Aa}
tCO_2 mmol L^{-1}	ESmalt	23.0 ± 1.8^{Aa}	22.3 ± 2.1^{Aa}	20.5 ± 1.2^{Aa}	23.5 ± 1.7^{Aa}
	ESdext	23.6 ± 1.8^{Aab}	23.6 ± 1.9^{Aab}	20.0 ± 3.0^{Ab}	24.2 ± 2.0^{Aa}
cBase mmol L^{-1}	ESmalt	1.8 ± 1.1^{Aa}	-3.0 ± 1.3^{Aab}	-4.5 ± 1.2^{Ab}	-0.4 ± 1.9^{Aa}
	ESdext	-1.0 ± 1.9^{Aab}	-1.9 ± 2.1^{Aab}	-3.8 ± 1.4^{Ab}	-0.2 ± 2.0^{Aa}
Anion gap mmol L^{-1}	ESmalt	14.3 ± 3.6^{Aab}	7.5 ± 5.4^{Ab}	11.6 ± 3.9^{Aab}	14.8 ± 1.0^{Aa}
	ESdext	14.7 ± 1.5^{Aa}	4.1 ± 3.6^{Ab}	13.2 ± 2.4^{Aa}	14.7 ± 0.5^{Aa}
SID	ESmalt	40.2 ± 10.5^{Aab}	30.2 ± 13.8^{Ab}	35.3 ± 3.1^{Aab}	40.9 ± 1.2^{Aa}
	ESdext	40.7 ± 10.2^{Aa}	30.8 ± 8.9^{Ab}	36.0 ± 1.7^{Aab}	41.2 ± 1.3^{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).

As expressed in Table 2, $cHCO_3^-$, tCO_2, and cBase demonstrated similar tendencies trough time points. There was a slight, but significant, decrease (P< 0.05) in the values of these variables at T4h, with the exception of tCO_2, what remained unaltered in the animals of the SEmalt group during the entire study period (P> 0.05). This decrease was caused by the effect of enteral electrolyte solutions demonstrating their effect on some blood acidification properties trough time in dogs. However, we cannot say that the solutions caused metabolic acidosis. According to Russel *et al.* (1996) and Dibartola (2012), metabolic acidosis occurs when the value of the component (cBase) is negative and find himself below the reference range of normality for these animals. Even with the decrease in $cHCO_3^-$, tCO_2, and cBase, the dogs did not become in metabolic acidosis because the values of cBase remained in the normal range for the specie as described by Balbinot (2007).

Fluid therapy time is another important aspect that should be considered when evaluating the effects of electrolyte solutions on $cHCO_3^-$, tCO_2, and cBase. In the present study, the animals were rehydrated for just 4h of replenishment period. Therefore, it can be concluded that the administration of these enteral solutions for a longer period may have had a blood acidifying effect, what was not observed in the present study.

The anion gap showed alterations in both groups only trough time evaluation (P< 0.05). The lowest value was noted at T0h (Table 2). The anion gap method of diagnosis is mainly used to identify metabolic acidosis, and this acidosis is only significant when the values of anion gap show higher values than the upper reference limit to the species. According to Wellman *et al.* (2006), the reference range is between 12 and 24mmol L^{-1}. For this diagnostic method (anion gap), the enteral fluid therapy did not cause metabolic acidosis.

The calculation of SID, a difference over time (P< 0.05) was observed in both groups (Table 2). The smaller values at T0h (P< 0.05), slightly increased at T4h, and returned to baseline at T8h

(P< 0.05). SID results showed that dogs that were submitted to a short period of water and food restriction (12h) developed metabolic acidosis. According to Morais and Constable (2006), values <36mmol L^{-1} indicate metabolic acidosis, while values >42mmol L^{-1} indicate metabolic alkalosis. The administration of the enteral electrolyte solutions used in the present study increased the SID value at T4h, even though not significantly (P> 0.05), can demonstrate the capability of the enteral solutions to restore homeostasis, even in a short period of time (4h). The metabolic acidosis observed in the animals in both groups at T0h (end of the dehydration period) was due to hyperchloremia. By that time, the chloride levels were 121.3±2.2mmol L^{-1} in the animals in the ESmalt group and 119.5±4.3mmol L^{-1} in those in the ESdext group.

This finding confirms the results by Dibartola (2012), who indicated that dehydration could cause hyperchloremic metabolic acidosis, as observed in the animals of the present study.

CONCLUSION

Hypotonic enteral electrolyte solutions containing 9.6g/L of maltodextrin (ESmalt) and 9.6g/L of dextrose (ESdext) administered at 15mL kg^{-1} h^{-1} for 4 hours by a nasoesophageal tube in continuous flow were effective to increase blood volume without causing adverse effects in dogs. These results demonstrate the effectiveness of hypotonic enteral electrolyte solutions containing energy sources in dogs, making them important therapeutic options in fluid therapy for animals of this species.

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