UNIVERSIDADE FEDERAL DE VIÇOSA

PAULO VINÍCIUS DE MORAIS SANTOS

ENTERAL ELECTROLYTIC SOLUTIONS ADMINISTERED IN CONTINUOUS FLOW VIA NASO-RUMINAL ROUTE IN ADULT GOATS

VIÇOSA – MINAS GERAIS
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Dissertação apresentada à Universidade Federal de Viçosa, como parte das exigências do Programa de Pós-Graduação em Medicina Veterinária, para obtenção do título de *Magister Scientiae.*

Orientador: José Dantas Ribeiro Filho

Coorientador: Rinaldo Batista Viana

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Ficha catalográfica elaborada pela Biblioteca Central da Universidade Federal de Viçosa - Campus Viçosa

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S237e
2020

Santos, Paulo Vinicius de Morais, 1990-
Enteral electrolytic solutions administered in continuous flow via naso-ruminal route in adult goats / Paulo Vinícius de Morais Santos. – Viçosa, MG, 2020.
54 f. : il. ; 29 cm.

Inclui anexo.
Orientador: José Dantas Ribeiro Filho.
Dissertação (mestrado) - Universidade Federal de Viçosa.
Referências bibliográficas: f.44-50.

1. Equilíbrio ácido-base. 2. Hidratação. 3. Eletrólitos. 4. Soluções hipotônicas. I. Universidade Federal de Viçosa. Departamento de Veterinária. Programa de Pós-Graduação em Medicina Veterinária. II. Título.

CDD 22. ed. 636.39

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APROVADA: 24 de julho de 2020

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Autor

José Dantas Ribeiro Filho
Orientador

Dedico à clínica veterinária dos animais de produção.

AGRADECIMENTOS

Agradeço primeiramente a Deus por sempre me conduzir e me guiar durante toda a minha vida. Sem Ele, nada disso seria possível.

Agradeço eternamente aos meus amados pais, Gorete e Marivaldo, que são os responsáveis diretos por todos os acontecimentos da minha vida. Por acreditarem em mim e me agraciarem com todas as oportunidades para concluir meus estudos. Pelo amor incondicional que é extremamente fundamental em todos os momentos.

Aos meus irmãos, Gabriel e Theodoro, pelo companheirismo, pelas palavras, pelo exemplo de força e coragem num mundo cheio de maldade.

A minha noiva Sheila, que nunca me deixou desistir, que sempre acreditou que eu podia, e que é o meu apoio emocional. Obrigado por tornar minha vida mais leve e me fazer sorrir nos momentos mais difíceis.

Ao meu orientador, Professor Dantas, que me acolheu sem me conhecer, que me mostrou o caminho da pesquisa, pela confiança, pelas palavras, pelo conhecimento, por me ensinar o amor a clínica e pelo exemplo de profissionalismo.

Ao Professor Marcel pelo cuidado com o nosso trabalho, pelo acolhimento, pela amizade, pelas palavras, pela preocupação e por todos os conselhos.

Ao Professor Fabrício por estar sempre presente, acompanhando tudo de perto e sempre disposto a esclarecer todas as dúvidas.

Ao Professor Rinaldo da Universidade Federal Rural da Amazônia por toda ajuda no desenvolvimento do trabalho.

A Micheline e Samuel por toda a amizade e palavras de coragem e de incentivo, por me colocar na vida de vocês e por fazer sentir como se fossem da família.

A Caio, Lorena e Pedro, por desde o primeiro dia de laboratório me mostrarem o caminho da pesquisa e por toda ajuda durante esse processo.

As queridas Erica, Gabi e Lorraine e ao amigo Felipe, por estarem sempre presente e pela dedicação e comprometimento com o trabalho. Vocês vão longe!

A Rosi por todo o cuidado e carinho desde o primeiro dia como mestrando.

A Lidiany, por todo apoio, ajuda e pela Maple.

Aos amigos que, mesmo de longe estavam sempre me dando todo o apoio.

Ao setor de Clínica e Cirurgia de Grandes Animais de Departamento de Veterinária da Universidade Federal de Viçosa e aos funcionários por todo o apoio durante o experimento.

Ao setor de Caprinocultura do Departamento de Zootecnia da Universidade Federal de Viçosa por disponibilizar os animais para o estudo e aos funcionários que sempre nos receberam bem.

A Fapemig, ao Programa de Pós-Graduação em Medicina Veterinária da UFV e a Bioclin pelo fornecimento da estrutura e material necessário para o desenvolvimento desse estudo.

O presente trabalho foi realizado com apoio da Coordenação de Aperfeiçoamento de Pessoas de Nível Superior – Brasil (CAPES) – Código de Financiamento 001.

“O sofrimento é o intervalo entre duas felicidades.”

(Vinícius de Moraes)

ABSTRACT

SANTOS, Paulo Vinícius de Morais, M.Sc., Universidade Federal de Viçosa, July, 2020. **Maintenance enteral electrolytic solutions administered in continuous flow by the naso-ruminal route in adult goats**. Advisor: José Dantas Ribeiro Filho. Co-Advisor: Rinaldo Batista Viana.

This study aimed to investigate the effects of maintenance enteral electrolytic solutions administered naso-ruminally in continuous flow in adult goats subjected to water and food restriction. Six adult non-pregnant and non-lactating female goats, aged between two and five years old, were used in a crossover (6 × 2) study. Solution 1 (SEE1) comprised: 4.5 g sodium chloride (NaCl); 1 g potassium chloride (KCl); 0.5 g magnesium chloride (MgCl); 1 g calcium chloride in 1000 ml of water (measured osmolarity: 202 mOsmol L-1). Solution 2 (SEE2) comprised: 4.5 g of NaCl; 1 g of KCl; 0.5 g of MgCl; 2 g of calcium acetate in 1000 mL of water (measured osmolarity: 212 mOsmol L-1). The solutions were administered naso-ruminally at a dose rate of 15 mL kg h, for 12 hours. The animals were evaluated at times T−24, T0, T4, T8, T12, and T24. Both enteral electrolytic solutions were effective in expanding blood volume. SEE1 showed a low-intensity acidifying potential, while SEE2 showed behavior of a neutral enteral electrolytic solution.

Keywords: Acid-base balance. Electrolyte replacement. Enteral route. Fluid therapy. Hypotonic solutions.

RESUMO

SANTOS, Paulo Vinícius de Morais, M.Sc., Universidade Federal de Viçosa, julho de 2020. **Soluções eletrolíticas enterais de manutenção administradas em fluxo contínuo por via naso-ruminal em cabras adultas**. Orientador: José Dantas Ribeiro Filho. Coorientador: Rinaldo Batista Viana.

Este estudo teve como objetivo investigar os efeitos das soluções eletrolíticas enterais de manutenção administradas nasorruminalmente em fluxo contínuo em cabras adultas submetidas a restrição hídrica e alimentar. Seis cabras adultas não gestantes e não lactantes, com idades entre dois e cinco anos, foram usadas em um estudo *cross over* (6 × 2). A solução 1 (SEE1) composta por: 4,5 g de cloreto de sódio (NaCl); 1 g de cloreto de potássio (KCl); 0,5 g de cloreto de magnésio (MgCl); 1 g de cloreto de cálcio em 1000 ml de água (osmolaridade mensurada: 202 mOsmol L-1). A solução 2 (SEE2) composta por: 4,5 g de NaCl; 1 g de KCl; 0,5 g de MgCl; 2 g de acetato de cálcio em 1000 mL de água (osmolaridade mensurada: 212 mOsmol L-1). As soluções foram administradas por via naso-ruminal na dose de 15 mL kg h, durante 12 horas. Os animais foram avaliados nos tempos T-24, T0, T4, T8, T12 e T24. Ambas as soluções eletrolíticas enterais foram eficazes na expansão do volume sanguíneo. A SEE1 mostrou um potencial acidificante de baixa intensidade, enquanto a SEE2 apresentou comportamento de uma solução eletrolítica enteral neutra.

Palavras-chave: Equilíbrio ácido-base. Hidratação. Reposição de eletrólitos. Via enteral. Soluções hipotônicas.

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LIST OF ABBREVIATIONS

AG – Anion gap

Alb – albumin

BE – Concentration of titratable bases

Ca^{2+} – Ionic calcium

$cHCO_3^-$ – Bicarbonate concentration

Cl^- – Chloride

Creat – Creatinine

dL – Deciliter

EDTA – Ethylenediamine tetraacetic acid

EFC – Extracellular fluid compartment

FL – Filtered load

G – Gauge

g – Gram

Gluc – Glucose

GT – Grouped in time

H^+ – Hydrogen

H_2CO_3 – Carbonic acid

HCl – Hydrochloric acid

HPO_4^{2-} – Phosphate ions

IFC – Intracellular fluid compartment

K^+ – Potassium

kg – Kilograms

L – Liter

Lac – Lactate

m – Meter

m^2 – Square meter

mEq – Milliequivalents

mg – Milligrams

Mg^{2+} – Magnesium

mL – Milliliter

mm – Millimeter

mmHg – Millimetre of mercury

mmol – Millimole

mOsmol – Milliosmole

Na^+ – Sodium

Osm – Osmolarity

P – Phosphorus

pCO_2 – partial pressure of carbon dioxide

PCV – Packed cell volume

pH – Potential of hydrogen

PTH – Parathyroid hormone

Σ – Summation notation

SEE1 – Solution 1

SEE2 – Solution 2

SID – Strong ion difference

TPP – Total plasma proteins

uCa^{2+} – Urinary total calcium

uCl^- – Urinary chloride

uE – Urinary Electrolyte

uK^+ – Urinary potassium

uMg^{2+} – Urinary magnesium

uNa^+ – Urinary sodium

upH – Urinary pH

Ur – urea

USG – Urine specific gravity

V – Volume

SUMMARY

1. Introduction

Among the metabolic disorders that affect adult ruminants, metabolic alkalosis stands out as one of the mains acid base disorders (Roussel, 2014), which can be caused by prolonged periods of fasting and dehydration. Correction of this disorder can be achieved by several means, where the choice of the most effective treatment depends on the intensity of the condition the patient experiences.

Among the possibilities for correcting acid base imbalances, enteral fluid therapy is an effective option. However, similar to cattle, the administration of enteral electrolytic solutions in goats is performed via the oro-ruminal route. In order to avoid stress and lesions in the pharyngeal and esophageal mucosa of the animals, caused by the use of this technique, enteral fluid therapy via the naso-ruminal route in a continuous flow can also be used in this kind of animal. This technique has already been tested in experimental trials with several animal species (Alves et al., 2019; Ermita et al., 2016; Ribeiro Filho et al., 2017, 2011) and it has been successfully used in the clinical routine practiced by the authors of this manuscript for a number of years.

The main challenge in correcting hydroelectrolytic and acid base imbalances in adult ruminants by an enteral modality remains the administration of electrolytic solutions that are effective and economically viable. Except for the study carried out by Atoji-Henrique et al. (2012), there are no experimental tests with enteral electrolytic solutions in adult goats, which makes the present clinical trial relevant, since the composition of maintenance enteral electrolytic solutions for the species remains unknown. In addition, clinical trials with hypotonic enteral electrolytic solutions have not been performed in adult goats to date. However, considering the positive results of this type of solution in other animal species, it is assumed that they would also be satisfactory in adult goats.

Thus, the aim of this study was to investigate the effects of two maintenance hypotonic enteral electrolytic solutions administered via the naso-ruminal route in a continuous flow through a small-gage nasogastric tube for 12 hours in adult goats subjected to water and food restriction. It was hypothesized that the use of the solution with a higher concentration of chloride and a strong ion difference (SID) equal to zero (SEE1), in addition to increasing blood volume, would have a low acidifying effect in animals.

2. Literature Review

2.1. Body water

The animal organism is composed mainly of water, which corresponds to approximately 60% of the body weight. This percentage can vary according to some factors, such as age and breed. The water is divided into two main compartments, the intracellular fluid compartment (IFC) and the extracellular fluid compartment (EFC). The IFC is responsible for storing about two-thirds of the body's water, and the rest is located in the EFC, which is composed of the interstitial, intravascular and transcellular fluid compartments. In addition, there are differences between the electrolytic compositions of each compartment (Walz and Taylor, 2012).

The main electrolytes in the EFC are sodium, chloride and bicarbonate, while in IFC it is possible to find, mainly, potassium, phosphate and proteins. Despite the different resources and electrolytic compositions, IFC and EFC are in osmotic balance, where water and electrolytes can diffuse between them through hydrostatic and oncotic forces. (Walz and Taylor, 2012).

This balance is one of the body's mechanisms which, when in harmony, is called homeostasis.

2.2. Acid base balance

It is necessary to be aware of acid base imbalances, which are present in several diseases that affect ruminants. These conditions are often caused by the producer himself to ignore the environmental and nutritional needs of his herd. Ruminants may exhibit mild and non-specific symptoms, such as reduced food consumption and apathy. Therefore, constant observation is necessary for early intervention in any imbalance in these animals. (Peek and Diver, 2018).

Free hydrogen (H^+) plays an important role in cell metabolism. The amount of this element in the IFC and EFC is regulated by a delicate balance between acids and bases present in the body. Some reactions can release or remove the H^+ proton from the organism, examples of those reactions that release H^+ are hydrochloric acid (HCl) and carbonic acid (H_2CO_3) when dissociated in water they can form H^+ and Cl^- molecules or H^+ and bicarbonate (HCO_3^-) molecules, respectively. The bases can do the reverse, removing these H^+ ions from the organism, for example, the bicarbonate itself, the phosphate ions (HPO_4^{2-}) and proteins. (Hall, 2011; Carson and Bruss, 2008).

There are several mechanisms responsible for the concentration of H^+ in the body, among them, we can highlight the buffer systems, which can occur through the bicarbonate buffer with the aid of the carbonic anhydrase enzyme (Hall, 2011), the phosphate buffer where the kidney has a fundamental role , since it has a great capacity to excrete or concentrate phosphate ions depending on the need of the organism (Fry and Karet, 2007) and the protein buffer for the vast amount, such as hemoglobin and

albumin, present in IFC and EFC, however, the latter occurs slowly (Martin-Terezo e Martens, 2014).

Another important mechanism in regulating the amount of hydrogen ions present in the body is the respiratory system. The body constantly produces high levels of CO_2 through cellular metabolism, these can be diffused into the interstitial fluid and then into the blood. CO_2 is eliminated together with H^+ ions, and this is how, by increasing the respiratory rate, it can eliminate more sources of H^+ or do the opposite in cases where an increase in the quantity of these ions is necessary through a decrease in the respiratory frequency (Hall, 2011).

The most efficient and important mechanism of the body to control the acid base balance is renal system. HCO_3^- is continuously filtered in the tubules and, if they are excreted in the urine, this removes the base of the blood. Too much H^+ is also secreted in the tubular lumen, thus removing acid from the blood. If more H^+ is secreted than HCO_3^- is filtered, there will be a net loss of acid from the extracellular fluid. On the other hand, if more HCO_3^- is filtered than H^+ is secreted, there will be a net loss of base (Hall, 2011). The kidneys can control the volume of other electrolytes, which are excreted through the urine, and can eliminate non-volatile products that the lungs cannot eliminate. (Madias and Adrogué, 2013).

2.3. Electrolytic balance

2.3.1. Sodium

The main and most abundant EFC cation is sodium (Na^+), being the main responsible for regulating the osmolarity of this same space. It is estimated that sodium, together with some anions with which it can associate, such as chloride and

bicarbonate, represent about 94% of extracellular solutes. Therefore, changes in its concentration can directly affect the volume and osmolarity of the EFC (Hall, 2011).

Although its concentrations are controlled by multiple gastrointestinal, renal and endocrine mechanisms, sodium and, consequently, the osmolarity of the EFC, are regulated by two primary systems. One of them is the feedback system of the ADH osmoreceptor, where an increase in the EFC osmolarity leads to the secretion of ADH which, through the bloodstream, reaches the kidneys and increases the water permeability in the distal tubules, cortical collecting tubules and ducts medullary collectors. This increase in permeability causes greater reabsorption of H_2O, and consequently of Na^+, causing concentrated urine with less volume to be excreted. (DiBartola et al, 2012a)

The other system of importance for sodium regulation is the thirst mechanism. Several areas in the brain form the center of the thirst, the place that controls all this mechanism. There are several ways for this mechanism to be activated, and more than one of them can happen at the same time. One of the most important is the increased osmolarity of the EFC, which causes an intracellular dehydration in the center of the thirst promoting the sensation of thirst. Other forms of activation are the decrease in EFC volume along with blood pressure and the secretion of Angiotensin II (Hall, 2011).

The animal organism can prevent Na^+ losses that are also happening through the renin-angiotensin-aldosterone system. When there is a decrease in blood pressure, there is a stimulus for the release of renin, which in turn promotes the release of angiotensin I and II, angiotensin II acts on the kidneys by decreasing the renal flow and providing the secretion of aldosterone which increases the reabsorption of Na^+, preventing its elimination by the kidneys (Jerry Kaneko et al., 2008).

Serum Na^+ levels in dairy goats reared under confinement, according to Atoji-Henrique et al. (2012) is 140 mEq/L. Changes in these values are of great importance for the animal's health. In cases where the sodium values are below this value, we may have a condition called hyponatremia. Generally, hyponatremia is associated with large losses of fluid by the body and, under these conditions, homeostasis will be impaired, since large amounts of water are allowed to migrate from the plasma to the interstitium, which may cause cell edema and irreversible lesions. (Hall, 2011).

Hypernatremia, increased serum or plasma Na^+ levels, is often related to the early stages of diarrhea, vomiting or kidney disease where there is a greater loss of water than electrolytes. Hypernatremia can occur when salt intoxication in ruminants is associated with water restriction. As long as water is available, this intoxication will not occur (Jerry Kaneko et al., 2008).

2.3.2. Potassium

Potassium (K^+) is the ion in greater quantity in the IFC, being responsible for the transmission of stimuli and for the communication between cells, playing the role in several essential functions. Changes in their concentrations can occur in a wide variety of clinical circumstances, which can trigger intense neuromuscular effects due to changes in the potential of the cell membrane (Jerry Kaneko et al., 2008).

One of the protection mechanisms against changes in the concentrations of H^+ ions in the EFC is the exchange with the K^+ ions present in the IFC. This occurs when the blood pH value decreases. This same mechanism can also occur, but in reverse, in cases of metabolic alkalosis. Insulin also acts on the regulation of potassium, it stimulates its absorption in cells (Hall, 2011).

The kidney plays a key role in regulating potassium. It is filtered through the glomerulus, where approximately 70% is reabsorbed by the proximal tubules together

with water and sodium, 10 to 20% are reabsorbed in the ascending branch of the loop of Henle and the remaining 10 to 20% are directed to the distal nephrons where they are adjusted what will be reabsorbed and what will be secreted (DiBartola e De Morais, 2012).

According to Ward (1966), the frequent use of diuretics and a decrease in food intake are the main causes of hypokalemia. It is also possible that these animals show losses of K^+ in cases of diarrhea or vomiting. Hypokalaemia does not usually show clinical signs in patients, the animal may rarely have muscle weakness, polyuria or polydipsia (DiBartola and De Morais et al, 2012).

In cases where the animal has a plasma potassium concentration above the reference levels, or hyperkalaemia, the damage caused can be more serious and the signs become noticeable when these patients have a greater or equal increase in the serum concentration of only 3 to 4 mEq/L can cause cardiac arrhythmias, and higher concentrations can lead to cardiac arrest or fibrillation. Hyperkalaemia is uncommon in cases where the kidneys are healthy (Hall, 2011).

The replacement of this ion can be performed parenterally or enterally, and can be found in some commercial solutions such as Ringer lactate, which has 4 mEq/L of K^+ in its composition, which is sufficient for the maintenance of this electrolyte in patients, but insufficient in cases where there is a deficit, supplementation is necessary to correct the values according to the needs of each patient.

An enteral electrolyte solution containing potassium is the safest way to administer this electrolyte when the dose and speed of the solution are done correctly. Added to this is the ability of the intestinal mucosa to control the speed of absorption of electrolytes, thus preventing larger doses from reaching the bloodstream and causing unwanted effects (Weiner and Wingo, 1997).

2.3.3. Chloride

Chloride constitutes approximately two-thirds of the anions in the plasma and the rest of the EFC. It is also the main anion filtered by the glomeruli and reabsorbed in the renal tubules. Chloride plays an important role in maintaining osmolarity and actively participates in the regulation of the acid base balance (De Morais and Biondo, 2012). The average value of chloride in the plasma of goats is 109 mEq/L (Atoji-Henrique et al., 2012).

Changes in the plasma chloride concentration are directly related to disturbances in the acid base balance, this is due to its indirect action in the plasma bicarbonate concentration. Acidosis can be caused by hyperchloremia due to a decrease in the concentration of bicarbonate in the blood. This is a way of compensating for negative charges in the EFC, in an attempt to maintain electroneutrality (Constable, 2003; Alves et al, 2019).

The kidneys act as an electro-neutralizer by expelling or retaining charges to maintain homeostasis. Thus, in situations where chloride is reduced, the kidney retains ions with negative charges, such as chloride and bicarbonate, which can generate metabolic alkalosis (De Morais and Biondo, 2012).

2.3.4. Magnesium

Magnesium (Mg^{2+}), one of the cations with two valences present in the body, is the second most abundant positive charge electrolyte in IFC after potassium. Even so, most of it is not found inside cells but in bones (Stewart, 2015). More than half the concentration of Mg^{2+} is bound to proteins, mitochondria or substrates (Hall, 2011).

Magnesium is involved in several biochemical processes in the body, which include the activation of many enzymes, and precisely for this reason, its concentration must be strictly regulated. Because it is present in the normal diet of the animals and

is also dependent on it to maintain its adequate levels, it is estimated that its daily intake is on average 250 to 300 mg, where only half of this value is absorbed by the gastrointestinal system. (Hall, 2011).

In situations of lack of appetite and fluid therapy with solutions without a source of magnesium, the serum values of this electrolyte decrease, leading to hypomagnesaemia (Avanza et al., 2009). Long-term magnesium deficiency can cause several unwanted effects on the cardiac and neuromuscular systems, in addition to electrolyte disturbances (Hall, 2011).

2.3.5. Calcium

With an important role in muscle activity, intracellular signaling and being a cofactor of the blood coagulation system, calcium (Ca^{2+}) stands out as one of the main plasma electrolytes (Aguilera-Tejero, 2015). Approximately 99% of the calcium in the body is deposited in the bones. Of the small value (1%) found in plasma, half of it is in ionized form, that is, it has biological activity in cell membranes. The rest are linked to proteins or linked to other anions such as phosphate, bicarbonate, sulfate, citrate and lactate (Schenck et al, 2012).

In this way, only about 50% of the calcium in the plasma can be filtered in the glomerulus. Typically, about 99% of the filtered calcium is reabsorbed by the tubules, with only about 1% of the filtered calcium being excreted. About 65% of the filtered calcium is reabsorbed in the proximal tubule, 25 to 30% is reabsorbed in the loop of Henle and 4 to 9% is reabsorbed in the distal tubules (Hall, 2011).

Calcium is mainly acquired through food, and can also be removed from the bones when necessary through parathyroid hormone (PTH). When the calcium concentration in the EFC falls below normal, the parathyroid glands are stimulated leading to an increase in PTH secretion. This hormone acts directly on the bones to

increase the resorption of salts from the bone and to release large amounts of calcium into the extracellular fluid, thus returning calcium levels back to normal. The same occurs the other way around, and excess calcium is deposited in the bones (Hall, 2011).

Measurement of calcium can be done using serum or plasma samples. Total calcium and ionized calcium can be measured. Whenever possible, the best method of evaluation is ionized calcium, as it is the safest variable to demonstrate the amount of this electrolyte available in the bloodstream (Schenck et al, 2012).

Goats with high milk production can present hypocalcemia, reaching values of 4 to 5 mg/dL soon after parturition. This happen because the body requires a high demand for calcium, but the body needs one or more days to synthesize all the enzymes necessary to remove calcium from the bones. This disease is common when a diet rich in calcium is provided, causing a decrease in PTH synthesis. The low amount of this hormone results in decreased calcium mobilization of bones and intestines (Rankins and Pugh, 2012)

2.4. Metabolic Disorders in Goats

Ruminants are commonly affected by diseases that can cause some type of metabolic disorder. Among the main metabolic disorders found in ruminants, we can highlight ruminal acidosis, tympanism, urea intoxication, ketosis and several pathologies that can secondarily cause acidosis or metabolic alkalosis (Neto et al, 2014).

Metabolic alkalosis is the change in the acid base balance most commonly found in adult cattle that have conditions that alter their normal conditions due to dehydration, lack of appetite or changes in abomasal emptying (Roussel, 2014).

It is believed that due to the increased need of the body for sodium, in order to control the plasma volume reduction process, this electrolyte can be exchanged more efficiently for protons to the tubular lumen, and thus generate a metabolic alkalosis of contraction in the individual (Garella et al., 1975). Other authors claim that contraction alkalosis may be caused by hypochloremia due to a reduction in plasma volume or administration of hypochloremic solutions (Luke and Galla, 2012).

The proteins in the cortical collecting ducts of the nephron exchange chloride ions from the tubular fluid to the intracellular medium for bicarbonate, which generates protons. When the plasma volume decreases or hypochloremic solutions are administered, this protein stops eliminating bicarbonate, since chloride is not available in the tubular light causing the bicarbonate to accumulate, which causes a metabolic alkalosis (Luke and Galla, 2012). Thus, the presence of metabolic alkalosis may be associated with subclinical or initial levels of dehydration.

The correction of this disorder can be carried out by several methods, where the choice of the most effective treatment depends on the intensity of the patient's condition. In cases where there is no severe dehydration or hypovolemic shock, enteral hydration has been shown to be as efficient as intravenous hydration. (Dias et al, 2019).

2.5. Enteral fluid therapy in continuous flow

As they are frequent conditions in the clinical routine, the evaluation of hydroelectrolytic and acid base imbalances are essential components in the examination of sick animals, the correction of these imbalances being a priority for the success of the specific therapy to be employed and the reestablishment of homeostasis (Carlson and Bruss, 2008; Jones and Navarre, 2014).

Regardless of the origin, for the correction of dehydration and electrolyte disturbances and acid base fluid therapy is the therapeutic practice adopted (Constable, 2003; Roussel, 2014). In addition, it assists in maintaining cardiac output and improves tissue perfusion (Jones and Navarre, 2014). In this way, fluid therapy needs to be rationally planned so that the specific deficiencies of the patient can be met and anticipated, which can change throughout the treatment (Speirs and Wrigley, 1997).

In ruminants, the most widely used fluid administration routes are intravenous and oro-ruminal (Constable, 2003; Ribeiro Filho et al., 2013). The parenteral (intravenous) route is indispensable in cases of severe dehydration, with the risk of hypovolemic shock and in cases of sepsis, for example, as it allows rapid infusion of replacement fluid (Constable, 2003; Ribeiro Filho et al., 2011). This route, however, requires thorough care with the permanent observation of the patient, the handling of solutions and placement of the venous catheter, which increases the risk of contamination of the patient, in addition, it requires sterile solutions, which increases the cost of treatment (Lopes et al., 2002; Ribeiro Filho et al., 2011).

Enteral fluid therapy is an effective alternative to the parenteral route. It consists of the administration of electrolytic solutions by means of an oro-ruminal or naso-ruminal probe (Ribeiro Filho et al., 2009). It is a route widely used in the ruminant clinic, due to the ease of the technique and the possibility of administering large amounts of electrolyte solution in the rumen, solutions that do not require sterilization (Constable, 2003; Ribeiro Filho et al., 2009; Roussel, 2014). The cost of enteral fluid therapy is a factor that contributes a lot to the dissemination and adoption of the technique among veterinarians who attend outside the dependencies of a veterinary hospital (Ribeiro Filho et al., 2011), the value of the liter of solution, for

oral use, can be up to 97% lower, when compared to solutions for parenteral use (Ribeiro Filho, 2011).

The direct deposition of electrolyte solutions in the rumen, allows the formation of a reserve of water and electrolytes, which supports a continuous absorption of these elements for a certain time (Constable, 2003). Also, for this reason, a disadvantage of the oro-ruminal route is abdominal distension, followed by discomfort, caused by the large amount of fluid deposited in one time in the rumen (Ribeiro Filho et al., 2011) and the risk of injury to the pharynx and esophagus, in addition to stress, caused by the successive surveys necessary in this therapeutic modality (Ribeiro Filho et al., 2013).

An alternative to the classic oral route is enteral fluid therapy via naso-ruminal, using a small-caliber probe. This route is already widely used, and with success, in horses (Avanza et al., 2009; Gomes et al., 2012; Ribeiro Filho et al., 2014), cattle (Ribeiro Filho et al., 2011; Ribeiro Filho et al., 2013), buffalo calves (Ermita et al., 2016) and has also been tested in goats (Atoji-Henrique et al., 2012). In adult ruminants this pathway is called naso-ruminal.

In addition to the notable advantages of enteral fluid therapy, this technique allows the infusion of the electrolyte solution slowly and continuously (Lopes et al., 2004; Ribeiro Filho, 2011). As the equine urethral probe used is 5 x 7 mm in diameter and 1.5 m long, this way, probing is facilitated, therefore, the discomfort caused to the animal by the passage and presence of the probe is minimal, not preventing the access and food intake by the patient (Atoji-Henrique et al., 2012; Ribeiro Filho et al., 2013).

2.6. Osmolarities of electrolyte solutions

According to Wellman et al. (2012), osmolarity is defined as the number of osmoles, particles that exert a certain osmotic pressure, in a liter of solution and should be measured in the serum, preferably, because the presence of the anticoagulant can cause changes in the measurement.

In both human and veterinary medicine, the osmolarity of electrolyte solutions (ES), whether for parenteral or enteral use, is still the subject of much discussion among researchers. For the World Health Organization (WHO) one of the most important advances in human medicine in the 20th century was the development of an oral rehydration solution (Smith, 2009; Smith and Berchtold, 2014). At first, a hyperosmolar solution (311 mOsm/L) had been developed, which significantly contributed to reducing child mortality in countries where cholera was endemic. In the search for improvements in clinical results, researchers developed a solution that reduced the need for parenteral hydration by 33% and the incidence of vomiting by 30%, for this, it was only necessary to reduce the osmolarity of the electrolyte solution to 245 mOsm/L (Mahalanabis et al., 1995; WHO, 2018).

A point that should be called attention is that the changes promoted in the osmolarities of the rehydration solutions are mainly due to changes in the amount of sodium and/or sugar, present in the formulation. That is, in hypotonic solutions, the amount of sodium and glucose available is usually lower. As a concrete example, we have the standard oral rehydration solution from the WHO, whose first solution (hypertonic: 311mOsm/L) held 90 mEq/L of sodium and 111 mEq/L of glucose, while the new solution (hypotonic: 245 mOsm/L) presented an equimolar mixture of 75 mEq/L of sodium and glucose (WHO, 2018).

Despite the benefits that this change in the osmolarity of the solutions can promote, with regard to the greater absorption of the solution, some authors call

attention to the appearance of hyponatremia, promoted by the solutions of less osmolarity, especially if used in maintenance therapy (Alves et al., 2011; McNab et al., 2015). Likewise, care must be taken with solutions of high osmolarity, to avoid the so-called 'salt intoxication' or hypernatremia (Kirchner et al., 2013). Even so, there is still a lack of studies to better assess the conditions under which low osmolarity solutions can cause hyponatremia (Beck, 2007).

In ruminants, the intrinsic needs of each age group vary greatly, in order to render the same treatment inappropriate when it is applied to animals of different ages (Roussel, 2014). In adult animals, the use of low osmolarity electrolytic solutions (hypotonic) has been predominant and has shown satisfactory results (Constable, 2003; Atoji-Henrique et al., 2012; Ribeiro Filho et al., 2013; Jones and Navarre, 2014; Roussel, 2014; Alves et al., 2019). We have, therefore, that the osmolarity of ES for enteral use, will play a decisive role in the absorption of water and electrolytes.

3. Material and Methods

The experimental procedures were approved by the ethics committee in animal use of Universidade Federal de Viçosa (CEUA/UFV process number 88/2018) following the guidelines of Brazilian legislation edited by the National Council of Animal Experimentation Control (CONCEA/MCTI).

3.1 Study design

The study was carried out at the Veterinary Hospital of the Federal University of Viçosa, Brazil. Six healthy Saanen x Pardo-alpine crossbred female dairy goats aged between two and five years, with a body weight between 52–72 kg, non-pregnant and non-lactating, were used. During the study, the goats were kept in individual masonry

bays, 2 × 2 m ($4m^2$) with a shavings bed and fed with hay, water, and a mineral supplement *ad libitum*, and a concentrate (2% of body weight) mixed with chopped elephant grass (*Pennisetum purpureum*), divided into two portions a day before and after water and food restriction. The animals were submitted to 24 hours of water and food restriction before the beginning of the fluid therapy period.

The animals were randomly included in the experiment in a crossover design with six animals × two treatments (6 × 2), where each animal received all treatments with an interval of seven days between them. The treatments with maintenance hydroelectrolytic solution were named and composed of solution 1 (SEE1): 4.5 g sodium chloride; 1 g potassium chloride; 0.5 g magnesium chloride; 1 g calcium chloride in 1000 mL of water (measured osmolarity: 202 mOsmol L^{-1}; SID = 0); solution 2 (SEE2): 4.5 g of sodium chloride; 1 g of potassium chloride; 0.5 g of magnesium chloride; 2 g of calcium acetate in 1000 mL of water (measured osmolarity: 212 mOsmol L^{-1}; SID = 22.6). The solutions were administered naso-ruminally at a dose rate of 15 ml kg^{-1} h^{-1}, for 12 hr.

Immediately before fluid therapy started, the animals were contained in trunks suitable for small ruminants and were probed naso-ruminally with a silicone, non-toxic PVC probe, 5 × 7 mm thick and 1.5 m long. The probe was attached to a halter and connected to the enteral fluid therapy system, a 20L water gallon, with a spiral tube containing a flow regulator.

3.2 Collection of biological samples and laboratory evaluations

Biochemical, blood gas, and urinary analyses were performed. The evaluations were carried out in the following moments: T−24: beginning of water and food restriction (control); T0: end of water and food restriction and the start of the fluid

therapy phase; T4: four hours after fluid therapy started; T8: eight hours after fluid therapy started; T12: twelve hours of fluid therapy and end of the fluid therapy period; T24: twelve hours after the fluid therapy phase ended.

After antisepsis, blood samples were collected by jugular venipuncture, using a vacuum system for multiple collections with 25 × 8 mm (21 G 1) needles (BD Vacutainer®, Becton and Dickinson, São Paulo. Brazil). Blood was collected in vials (BD Vacutainer®, Becton and Dickinson, São Paulo. Brazil) without anticoagulant to obtain serum, containing sodium fluoride to obtain plasma, and ethylenediamine tetraacetic acid (EDTA) to measure the packed cell volume (PCV) using the microhematocrit technique.

The samples were centrifuged and the serum and plasma aliquots frozen for further analysis. Serum osmolarity (Osm) was measured in an osmometer (model 3320, Advanced Instruments, USA) by the freezing point depression method. Serum elements: total plasma proteins (TPP), magnesium (Mg2+), phosphorus (P) and creatinine (Creat) and plasma elements: glucose (Gluc) and lactate (Lac) were obtained with an automatic device HumaStar 300 (Human, In Vitro diagnóstica Ltda, Itabira, MG, Brazil) using a measurement kit (Bioclin – Quibasa Clínica Básica Ltda, Belo Horizonte, MG, Brazil). In a selective ion analyzer (Humalyte plus 5 – In Vitro Diagnóstica, Brazil) ionic calcium (Ca^{2+}), chloride (Cl^{-}), sodium (Na^{+}), potassium (K^{+}) were measured in the serum.

For the blood gas evaluation, 2 mL of blood was collected in syringes (Vacuette, Centerlab Ltda, Belo Horizonte, MG, Brazil) containing lithium heparin. The sample was processed using a blood gas analyzer (Radiometer ABL 5, Copenhagen, Denmark). The values of venous blood potential of hydrogen (pH), partial pressure of carbon dioxide (pCO_2), bicarbonate concentration ($cHCO_3^{-}$),

concentration of titratable bases (BE) were determined, and the anion gap (AG) and strong ions difference (SID) were calculated according to the formulas proposed by Constable (2000):

$$AG = (Na^+ + K^+) - (Cl^- + HCO_3^-) \qquad SID = (Na^+ + K^+) - (Cl^-)$$

In the urine obtained by spontaneous urination at moments: T−24 (samples collected in an interval of two hours), during the entire fluid therapy period, and at time T24 (samples collected in an interval of two hours), the total volume of the produced urine was measured, and biochemical analysis and filtered load (FL) calculations were made. Urine specific gravity (USG), performed by refractometry (Master-20T, Atago Brazil Ltda, São Paulo, SP, Brazil), and urinary pH (upH), verified in a pH meter (DLA – PH, Del Lab, Araraquara, SP, Brazil), were measured immediately after urine collection, and then an aliquot was taken to measure sodium (uNa^+) and potassium (uK^+) by flame photometry (Photometry B462 Micronal, Brasil), urinary creatinine (uCreat), chloride (uCl^-), total calcium (uCa^{2+}), and magnesium (uMg^{2+}) were made with an automatic device HumaStar 300 (Human, In Vitro diagnóstica Ltda, Itabira, MG, Brazil) using a measurement kit (Bioclin – Quibasa Clínica Básica Ltda, Belo Horizonte, MG, Brazil).

The FL calculation was performed per animal using the urinary electrolyte [uE (mEq/L) or uE (mg/dL)] value and multiplied by the volume of urine [V (L) or V (dL)] produced in the same sample:

$$FL(uE) = uE(mEq/L) \times V(L)$$

$$FL(uE) = uE(mg/dL) \times V(dL)$$

Then, the results were grouped in time (GT) according to the serum collections. The entire FL (uE) calculation obtained during T−24 and T24 was added and divided by two (duration in hours of collection) to determine a single result:

$$GTFLuE = [FL(uE)1 + FL(uE)2 + FL(uE)3] \div 2$$

The results obtained during the fluid therapy period (T0 to T12), were grouped into four stages so that a comparison could be made with the serum samples. For this, four periods of three hours were used: T0–3 (first three hours of fluid therapy); T3–6 (from the third hour of fluid therapy to the sixth hour of fluid therapy); T6–9 (from the sixth hour of fluid therapy to the ninth hour of fluid therapy); and T9–12 (from the ninth hour of fluid therapy to the end of fluid therapy). The FL (uE) obtained during these times were added in their proper grouping and divided by three (duration in hours of collection) with a single result being determined:

$$GTFLuE = [FL(uE)1 + FL(uE)2 + FL(uE)3] \div 3$$

3.3 Statistical analysis

Percentage data were submitted to the arc-sine transformation ($Y'=arcsen\sqrt{Y}$); the other variables were subjected to the Kolmogorov–Smirnov and Bartlett tests, to verify the normality of errors and homogeneity of variances, respectively. When necessary, the variables were subjected to transformations according to the relationship between the means and variances (Barbosa, 1983) so that: the variables GTFL(uNa$^+$), GTFL(uK$^+$), GTFL(uMg^{2+}), GTFL(uCl$^-$), and GTFL(uCreat) were submitted to logarithmic transformation ($Y'=\log(Y+1)$); the variables K$^+$, Osm, Gluc, and Lac were subjected to the root-square transformation ($Y'=\sqrt{Y}+0.5$); and the USG variable was submitted to transformation $Y' = Y - 96$.

For analysis of the data, the Mixed Procedure of the Statistical Analysis System (SAS, version 9.4) was used. The experiment was conducted in a crossover (6 × 2) design with repeated measures over time, according to the model:

$$Yijk = \mu + Si + Tj + (ST)ij + eijk$$

where: $Yijk$, observed response; μ, constant; Si, effect of the solution; Tj, effect of time; $(ST)\ ij$, interaction; $eijk$, random error.

The factor of repeated measures was the time (animal) for each level of animal (treatment) (subject) and a covariance matrix with a compound symmetry structure was used. The data were then submitted to analysis of variance and the means (LS-means) compared by t test (Littell et al., 2006). The level of significance adopted was $\alpha = 0.05$.

4. Results

In the SEE1 animals, there was an increase ($P < 0.05$) in the PCV values at time T4 and in the TPP values at T0. In SEE1, Osm increased at T4, T8, and T12, while in SEE2 there was an increase only at T8 and T12. There was a difference between treatments at T8 (Table 1).

There was a significant increase in the amount of Na^+ in the SEE1 animals at T12 and in the SEE2 animals at T8 and T12. In turn, an increase in K^+ values was recorded in both treatments at T12. The values of Cl^- showed similar behavior in the treatments, with an increase at T8, T12, and T24, however only in the SEE1 treatment was there a decrease at T0 (Table 2).

Mg^{2+} in SEE1 showed a significant decrease at T4 and T−24. In SEE2, the concentration of Mg^{2+} increased significantly at T8 and decreased ($P < 0.05$) at T24 (Table 2). A significant difference was observed between treatments at T−24 and T0. Ca^{2+} values decreased at T8 and T12 in SEE1 and at T4, T8, and T12 in SEE2, while phosphorus values increased at T12 in SEE1 and at T8 in SEE2 (Table 2).

Table 1

Mean ± standard deviations for parameters of goats submitted to treatments with two enteral electrolytic solutions: Packed cell volume (PCV), Total plasma proteins (TPP) and Osmolarity (Osm).

			Fluid therapy phase				
	Group	**T-24**	**T0**	**T4**	**T8**	**T12**	**T24**
PCV	SEE1	36.0 ± 3.4 ^{cA}	38.8 ± 2.7 ^{abA}	39.8 ± 4.0 ^{aA}	37.2 ± 1.9 ^{bcA}	35.2 ± 2.6 ^{cA}	36.3 ± 2.9 ^{bcA}
	SEE2	38.0 ± 1.8 ^{aA}	37.8 ± 1.2 ^{aA}	37.8 ± 1.2 ^{aA}	36.7 ± 1.8 ^{aA}	35.5 ± 3.4 ^{aA}	37.5 ± 3.1 ^{aA}
TPP	SEE1	6.9 ± 0.3 ^{bcA}	7.3 ± 0.4 ^{aA}	7.1 ± 0.4 ^{abA}	6.9 ± 0.3 ^{bcA}	6.7 ± 0.3 ^{cA}	6.9 ± 0.4 ^{bcA}
	SEE2	7.0 ± 0.2 ^{abA}	7.2 ± 0.4 ^{aA}	7.1 ± 0.3 ^{abA}	6.9 ± 0.3 ^{bA}	6.8 ± 0.3 ^{bA}	6.9 ± 0.4 ^{bA}
Osm	SEE1	297.5 ± 1.0 ^{cA}	297.5 ± 5.0 ^{cA}	300.5 ± 3.4 ^{bA}	302.2 ± 7.1 ^{bB}	306.8 ± 5.0 ^{aA}	297.5 ± 4.0 ^{cA}
	SEE2	298.3 ± 4.4 ^{bcA}	296.8 ± 2.8 ^{cA}	302.2 ± 2.2 ^{bA}	309.2 ± 4.7 ^{aA}	310.2 ± 7.2 ^{aA}	299.8 ± 3.7 ^{bcA}

The mean values followed by different lowercase letters on the same line and different uppercase letters in the same column differ from each other ($P \leq 0.05$).

USG showed a significant reduction in its values in both treatments at T0–3, T6–9, and T9–12. The upH showed a difference between treatments at T24, while in SEE1 a decrease was recorded at T9–12 and T24. In SEE2, a decrease was detected at T24 (Table 3).

The variable uCreat increased at T0–3 and decreased at T3–6, T6–9, and T24 in SEE1 and increased at T0–3 and decreased at T3–6, T9–12, and T24 in SEE2 (Table 3).

The concentrations of uNa^+ showed similar behavior in both treatments. The values increased from T3–6, remaining until T24. The uK^+ and uCl^- showed similar behavior in both treatments, there was a reduction at T0–3 and an increase in their values from T6–9 to T24. The concentrations of uCa^{2+} decreased at T0–3 and T3–6 and increased at T24. The concentration of uMg^{2+} decreased at T0–3, T3–6, T6–9, and T9–12 in SEE1, while in SEE2 the decrease was observed only at T3–6 (Table 3).

There was a decrease ($P < 0.05$) in the pH values in SEE1 from T4 to T24. In SEE2, the decrease was recorded only at T8. In both treatments, pCO_2 showed an increase ($P > 0.05$) at T0 and T4 in relation to T24. The values of HCO_3^- and BE

showed similar behavior in both treatments. They decreased from T8 to T24. At those times, there was also a difference between treatments (Table 4).

Table 2

Mean ± standard deviations for biochemical parameters of goats subjected to treatments with two enteral electrolytic solutions: Sodium (Na^+), Potassium (K^+), Chloride (Cl^-), Magnesium (Mg^{2+}), Calcium (Ca^{2+}), Phosphate (P), Glucose (Gluc), Lactate (Lac), Urea and Creatinine (Creat).

			Fluid therapy phase				
	Group	**T-24**	**T0**	**T4**	**T8**	**T12**	**T24**
Na^+	SEE1	141.1 ± 1.5 ^{cA}	140.4 ± 1.5 ^{cA}	142.5 ± 1.8 ^{bcA}	144.4 ± 2.7 ^{bA}	147.1 ± 2.5 ^{aA}	143.8 ± 1.4 ^{bA}
	SEE2	141.6 ± 1.5 ^{bcA}	140.2 ± 0.9 ^{cA}	143.1 ± 1.5 ^{bA}	146.9 ± 2.8 ^{aA}	148.5 ± 4.0 ^{aA}	143.6 ± 2.2 ^{bA}
K^+	SEE1	4.16 ± 0.35 ^{cA}	3.84 ± 0.25 ^{cA}	4.19 ± 0.27 ^{bcA}	4.55 ± 0.18 ^{abA}	4.72 ± 0.23 ^{aA}	4.14 ± 0.52 ^{cA}
	SEE2	4.11 ± 0.40 ^{abA}	4.06 ± 0.37 ^{bA}	4.23 ± 0.11 ^{abA}	4.39 ± 0.12 ^{abA}	4.48 ± 0.36 ^{aA}	4.28 ± 0.55 ^{abA}
Cl^-	SEE1	105.6 ± 1.6 ^{cA}	103.0 ± 1.0 ^{dA}	105.7 ± 1.7 ^{cA}	109.4 ± 2.0 ^{bB}	113.6 ± 2.0 ^{aA}	110.8 ± 1.0 ^{bA}
	SEE2	106.3 ± 1.8 ^{cdA}	104.5 ± 2.0 ^{dA}	106.8 ± 1.1 ^{cA}	112.1 ± 2.2 ^{bA}	114.3 ± 4.1 ^{aA}	110.5 ± 2.5 ^{bA}
Mg^{2+}	SEE1	2.88 ± 0.24 ^{aA}	2.68 ± 0.42 ^{abA}	2.57 ± 0.28 ^{bA}	2.67 ± 0.19 ^{abA}	2.70 ± 0.11 ^{abA}	2.48 ± 0.34 ^{bA}
	SEE2	2.45 ± 0.34 ^{abcB}	2.25 ± 0.31 ^{cdB}	2.30 ± 0.29 ^{bcdA}	2.55 ± 0.18 ^{aA}	2.50 ± 0.15 ^{abA}	2.20 ± 0.37 ^{dA}
Ca^{2+}	SEE1	1.27 ± 0.05 ^{aA}	1.24 ± 0.07 ^{abA}	1.22 ± 0.08 ^{bcA}	1.18 ± 0.07 ^{cA}	1.20 ± 0.04 ^{cA}	1.25 ± 0.05 ^{abA}
	SEE2	1.23 ± 0.06 ^{aA}	1.21 ± 0.07 ^{aA}	1.17 ± 0.09 ^{bA}	1.14 ± 0.09 ^{bA}	1.17 ± 0.08 ^{bA}	1.23 ± 0.04 ^{aA}
P	SEE1	4.82 ± 0.53 ^{dA}	5.48 ± 1.13 ^{cdA}	5.88 ± 1.58 ^{bcA}	6.43 ± 1.29 ^{abA}	7.08 ± 0.71 ^{aA}	5.63 ± 0.84 ^{bcdA}
	SEE2	4.70 ± 1.26 ^{dA}	5.43 ± 0.99 ^{cdA}	5.83 ± 1.63 ^{bcA}	6.77 ± 1.70 ^{aA}	6.58 ± 1.49 ^{abA}	5.40 ± 1.26 ^{cdA}
Gluc	SEE1	61.8 ± 6.5 ^{aA}	58.0 ± 8.7 ^{aA}	61.0 ± 7.6 ^{aA}	60.7 ± 10.4 ^{aA}	62.5 ± 9.5 ^{aA}	68.5 ± 20.6 ^{aA}
	SEE2	58.2 ± 12.5 ^{aA}	53.5 ± 11.4 ^{aA}	62.2 ± 13.6 ^{aA}	64.7 ± 18.9 ^{aA}	70.2 ± 37.5 ^{aA}	56.2 ± 19.8 ^{aA}
Lac	SEE1	5.93 ± 2.09 ^{aA}	6.77 ± 6.19 ^{aA}	6.62 ± 2.20 ^{aA}	6.00 ± 1.17 ^{aA}	4.75 ± 1.43 ^{aA}	6.72 ± 7.26 ^{aA}
	SEE2	6.97 ± 6.44 ^{aA}	4.92 ± 3.11 ^{aA}	6.55 ± 3.10 ^{aA}	7.10 ± 5.78 ^{aA}	7.45 ± 2.94 ^{aA}	5.88 ± 3.59 ^{aA}
Urea	SEE1	28.3 ± 16.4 ^{aA}	35.0 ± 21.5 ^{aA}	32.1 ± 15.8 ^{aA}	30.7 ± 10.9 ^{aA}	24.8 ± 13.0 ^{aA}	20.5 ± 12.9 ^{aA}
	SEE2	26.6 ± 11.6 ^{aA}	40.7 ± 28.7 ^{aA}	40.0 ± 20.6 ^{aA}	32.9 ± 14.6 ^{aA}	29.9 ± 11.6 ^{aA}	22.8 ± 12.5 ^{aA}
Creat	SEE1	1.14 ± 0.10 ^{aA}	1.20 ± 0.26 ^{aA}	1.05 ± 0.35 ^{aA}	1.10 ± 0.31 ^{aA}	1.11 ± 0.17 ^{aA}	1.20 ± 0.16 ^{aA}
	SEE2	0.88 ± 0.27 ^{aA}	1.15 ± 0.23 ^{aA}	0.89 ± 0.31 ^{aA}	0.90 ± 0.18 ^{aA}	0.88 ± 0.13 ^{aA}	1.14 ± 0.39 ^{aA}

The mean values followed by different lowercase letters on the same line and different uppercase letters in the same column differ from each other ($P \leq 0.05$).

Table 3

Mean ± standard deviations for urinary parameters of goats submitted to treatments with two enteral electrolytic solutions: Urine specific gravity (USG), Urinary hydrogen potential (upH), Urinary creatinine (uCreat), Urinary sodium (uNa^+), Urinary chloride (uCl^-), Urinary potassium (uK^+), Urinary calcium (uCa^{2+}) and Urinary magnesium (uMg^{2+}).

			Fluid therapy phase				
	Group	**T-24**	**T0-3**	**T3-6**	**T6-9**	**T9-12**	**T24**
USG	SEE1	1022.2 ± 6.9 ^{aA}	1019.5± 6.0 ^{abA}	1008.0 ± 4.8 ^{cA}	1004.4 ± 2.8 ^{dA}	1003.6 ± 0.5 ^{dA}	1014.4 ± 5.6 ^{bA}
	SEE2	1024.6 ± 8.8 ^{aA}	1018.0± 7.0 ^{abA}	1005.4 ± 3.3 ^{cA}	1003.2 ± 1.0 ^{cA}	1003.5 ± 0.9 ^{cA}	1013.8 ± 3.0 ^{bA}
upH	SEE1	7.5 ± 0.5 ^{aA}	7.4 ± 0.4 ^{aA}	7.3 ± 0.3 ^{abA}	7.0 ± 0.3 ^{abA}	6.8 ± 0.6 ^{bA}	4.9 ± 0.6 ^{cB}
	SEE2	7.7 ± 0.4 ^{aA}	7.1 ± 0.7 ^{aA}	7.3 ± 0.5 ^{aA}	7.2 ± 0.3 ^{aA}	7.3 ± 0.4 ^{aA}	6.2 ± 1.0 ^{bA}
uCreat	SEE1	75.6 ± 30.6 ^{abA}	112.7 ± 64.5 ^{aA}	47.9 ± 12.4 ^{bA}	58.4 ± 22.5 ^{bA}	72.0 ± 22.5 ^{abA}	61.6 ± 28.1 ^{bA}
	SEE2	48.2 ± 22.2 ^{bA}	91.9 ± 59.0 ^{aA}	46.3 ± 16.1 ^{bA}	65.5 ± 21.3 ^{abA}	48.7 ± 13.9 ^{bA}	49.8 ± 16.8 ^{bA}
uNa^+	SEE1	1.5 ± 2.1 ^{dA}	1.7 ± 1.7 ^{dA}	6.2 ± 5.5 ^{cA}	20.9 ± 9.1 ^{bA}	48.0 ± 17.7 ^{aA}	21.2 ± 6.9 ^{bA}
	SEE2	0.9 ± 0.9 ^{dA}	2.0 ± 2.3 ^{dA}	8.5 ± 8.1 ^{cA}	34.1 ± 11.8 ^{aA}	43.2 ± 10.9 ^{aA}	16.5 ± 9.5 ^{bA}
uCl^-	SEE1	21.0 ± 7.4 ^{cA}	5.8 ± 4.6 ^{eA}	11.8 ± 9.0 ^{dA}	37.8 ± 22.4 ^{bcA}	82.3 ± 31.3 ^{aA}	56.3 ± 20.2 ^{abA}
	SEE2	12.5 ± 9.5 ^{bA}	6.4 ± 4.7 ^{cA}	14.5 ± 16.9 ^{bA}	59.2 ± 29.0 ^{aA}	75.6 ± 25.2 ^{aA}	51.9 ± 22.7 ^{aA}
uK^+	SEE1	14.5 ± 7.3 ^{aA}	5.0 ± 1.9 ^{cA}	3.1 ± 1.8 ^{cA}	4.6 ± 1.8 ^{cA}	8.3 ± 3.0 ^{bA}	9.9 ± 7.1 ^{abA}
	SEE2	8.8 ± 6.7 ^{abA}	3.0 ± 2.2 ^{cA}	3.5 ± 3.6 ^{cA}	5.1 ± 2.4 ^{bA}	6.7 ± 2.7 ^{abA}	9.4 ± 5.2 ^{aA}
uCa^{2+}	SEE1	39.5 ± 40.8 ^{abA}	27.6 ± 30.5 ^{bA}	13.1 ± 20.9 ^{bA}	40.9 ± 62.7 ^{abA}	37.0 ± 47.0 ^{abA}	71.8 ± 93.6 ^{aA}
	SEE2	21.5 ± 26.6 ^{aA}	28.2 ± 40.2 ^{aA}	23.4 ± 32.5 ^{aA}	34.0 ± 32.3 ^{aA}	36.1 ± 47.7 ^{aA}	56.0 ± 44.1 ^{aA}
uMg^{2+}	SEE1	34.9 ± 19.0 ^{aA}	13.1 ± 11.8 ^{bcA}	5.9 ± 3.4 ^{cA}	11.0 ± 3.4 ^{bcA}	15.9 ± 4.3 ^{bA}	22.8 ± 20.7 ^{abA}
	SEE2	21.3 ± 12.0 ^{aA}	17.4 ± 19.9 ^{abA}	8.5 ± 7.5 ^{bA}	13.8 ± 4.1 ^{abA}	16.3 ± 4.2 ^{abA}	19.5 ± 9.3 ^{aA}

The mean values followed by different lowercase letters on the same line and different uppercase letters in the same column differ from each other ($P \leq 0.05$).

The AG increased ($P < 0.05$) in SEE1 at T8 and T24, and showed a difference between treatments at T8 and T24 (Table 4). SID values increased in SEE1 at T0 and decreased at T24, while values in SEE2 increased at T4 and decreased at T12 and T24 (Table 4).

Table 4

Mean ± standard deviations for blood gas parameters of goats submitted to treatments with two enteral electrolytic solutions: Potential of hydrogen (pH), Partial pressure of carbon dioxide concentration (pCO2), Bicarbonate concentrations ($cHCO_3^-$), Bases excess (BE), Anion gap (AG) and Strong ions difference (SID).

			Fluid therapy phase				
	Group	**T-24**	**T0**	**T4**	**T8**	**T12**	**T24**
pH	SEE1	7.41 ± 0.02 ^{aA}	7.39 ± 0.03 ^{abA}	7.37 ± 0.02 ^{bcA}	7.35 ± 0.02 ^{cdA}	7.33 ± 0.03 ^{dB}	7.33 ± 0.07 ^{dB}
	SEE2	7.41 ± 0.03 ^{aA}	7.38 ± 0.05 ^{abA}	7.39 ± 0.03 ^{abA}	7.38 ± 0.04 ^{bA}	7.39 ± 0.04 ^{abA}	7.39 ± 0.03 ^{abA}
pCO_2	SEE1	44.7 ± 4.0 ^{abA}	47.9 ± 4.5 ^{aA}	48.2 ± 3.2 ^{aA}	46.3 ± 3.8 ^{abA}	46.2 ± 4.0 ^{abA}	43.7 ± 4.2 ^{bA}
	SEE2	45.1 ± 5.1 ^{abA}	48.2 ± 8.0 ^{aA}	47.3 ± 4.9 ^{aA}	46.3 ± 5.8 ^{abA}	45.3 ± 5.1 ^{abA}	43.4 ± 3.7 ^{bA}
$cHCO_3^-$	SEE1	27.7 ± 1.0 ^{abA}	28.0 ± 1.1 ^{aA}	26.5 ± 0.6 ^{bA}	24.4 ± 1.0 ^{cB}	23.4 ± 1.4 ^{cB}	21.8 ± 1.7 ^{dB}
	SEE2	28.0 ± 2.1 ^{aA}	27.6 ± 1.1 ^{abA}	27.5 ± 1.7 ^{abA}	26.3 ± 1.3 ^{bcA}	25.8 ± 1.1 ^{cA}	25.2 ± 1.7 ^{cA}
BE	SEE1	3.15 ± 0.78 ^{aA}	2.92 ± 1.36 ^{aA}	1.65 ± 0.54 ^{aA}	-0.45 ± 1.03 ^{bA}	-1.98 ± 1.54 ^{bcB}	-3.17 ± 3.25 ^{cB}
	SEE2	3.47 ± 2.02 ^{aA}	2.45 ± 1.27 ^{abA}	2.52 ± 1.61 ^{aA}	0.83 ± 1.13 ^{bA}	0.92 ± 0.90 ^{bA}	1.07 ± 2.10 ^{bA}
AG	SEE1	12.0 ± 1.7 ^{cA}	13.3 ± 1.8 ^{bcA}	14.5 ± 1.1 ^{abA}	15.2 ± 1.4 ^{aA}	14.8 ± 1.4 ^{abA}	15.3 ± 2.2 ^{aA}
	SEE2	11.3 ± 2.4 ^{aA}	12.2 ± 0.5 ^{aA}	13.0 ± 1.9 ^{aA}	12.9 ± 1.9 ^{aB}	12.9 ± 1.7 ^{aA}	12.1 ± 2.0 ^{aB}
SID	SEE1	39.7 ± 1.0 ^{bA}	41.3 ± 1.0 ^{aA}	41.0 ± 1.3 ^{aA}	39.6 ± 1.2 ^{bA}	38.1 ± 1.2 ^{cA}	37.1 ± 1.2 ^{cA}
	SEE2	39.4 ± 1.5 ^{abA}	39.8 ± 1.3 ^{abB}	40.5 ± 1.5 ^{aA}	39.2 ± 1.1 ^{bA}	38.7 ± 1.2 ^{bA}	37.3 ± 1.3 ^{cA}

The mean values followed by different lowercase letters on the same line and different uppercase letters in the same column differ from each other ($P \leq 0.05$).

5. Discussion

Throughout the experiment, the animals remained alert, responsive, and active, showing no signs of discomfort or changes in attitude or behavior with the probe and the naso-ruminal probe for 12 hours, nor with the infusion of the enteral electrolyte solution at the dose of 15ml kg^{-1} h^{-1}. It is noteworthy that this therapeutic modality has already been used in different animal species (Alves et al., 2019; Monteiro et al., 2020; Ribeiro Filho et al., 2017, 2015). Its use is a minimally stressful practice for animals, as described by other authors (Alves et al., 2019; Gomes et al., 2014).

The water and food restriction protocol caused a discreet change in some variables, such as PCV and TPP, demonstrating that 24 hours of water–food restriction is not enough to cause accentuated hydroelectrolytic and acid–base imbalances in this

animal species, as the rumen functions as an important reservoir of water and goats are extremely adept at maintaining water balance and using the rumen as a water reserve for longer periods (Alves et al., 2019; Dahlborn and Karlberg, 1985; Silanikove, 2000).

Serum sodium and osmolarity did not show significant changes at T0, but increased in both treatments during the fluid therapy phase, reaching the highest values 12 hours after the start of hydration ($P < 0.05$; Tables 1 and 2). This result demonstrates that, despite the hypotonicity of the enteral electrolyte solutions, the values of the variables mentioned above do not decrease, in contrast, there was an increase. Serum or plasma hyponatremia can occur when electrolyte solutions with low sodium are administered; this type of solution can also increase its intensity in patients who already have this type of electrolytic imbalance. However, the electrolytic solutions tested in the present study, by not having this type of adverse effect proved to be safe, and may even be used in patients with mild hyponatremia. Similar results to the present trial have been described in calves (Ribeiro Filho et al., 2017) and cattle (Alves et al., 2019).

Urinary sodium corroborates this statement, as during the fluid therapy period there was an increase in its excretion into the urine after three hours post-fluid therapy (T3–6), reaching the highest rates at 12 hours of fluid therapy (T9–12) ($P < 0.05$; Table 3) and despite that, the animals did not present serum hyponatremia. It is noteworthy that this increase, in addition to the composition of the electrolytic solution, also had the contribution of decreasing aldosterone, because, with the increase in volume resulting from the action of enteral fluid therapy, there is a decrease in aldosterone, resulting in an increase in urinary sodium excretion (DiBartola, 2012a). However, as mentioned by Ribeiro Filho et al. (2017), it should be emphasized that the use of

hypotonic enteral electrolytic solutions should be done with caution, especially in cases of more pronounced hyponatremia, and with constant monitoring of the patient.

Serum potassium showed a slight change during the fluid therapy phase. This result demonstrates that electrolyte solutions were able to maintain potassium homeostasis in adult goats, confirming the results obtained by Atoji-Henrique et al. (2012). However, when evaluating the potassium excreted in the urine, it was noticed that from T0 there was a decrease in its values in animals in both treatments, maintaining this characteristic until the end of the fluid therapy phase. Aldosterone is the main modulator of potassium excretion in urine, increasing sodium absorption and potassium excretion (DiBartola and De Morais, 2012). With rehydration and increased blood volume in the animals, there was a decrease in aldosterone, with an increase in uNa^+ excretion and a decrease in uK^+ (Table 3). This decrease may also have been contributed to by the imposed fasting during the experimental phase (T−24 to T12), because, as mentioned by Ward (1966), the main source of potassium for ruminants is fodder. That said, in patients who are experiencing serum or plasma hypokalemia, as in diarrhea and metabolic alkalosis associated with lack of appetite or anorexia, the enteral electrolyte solution may contain more than 1g of KCl per liter.

The serum chloride showed a small decrease at T0 in the animals of both treatments. Then, there was a gradual increase over time, reaching the highest values at T12 in both treatments ($P < 0.05$; Table 3). The increase during the fluid therapy phase was similar to Na^+, being related to the composition of the enteral electrolyte solutions. Both electrolytic solutions had salts that contained Cl^- in their composition, thus, providing significant amounts of this electrolyte to the animals.

The animals of both treatments, at T12, presented a low serum chloride value above the reference range (Jerry Kaneko et al., 2008). Although SEE1 contained more

chloride in its composition (111.1 mmol/L) than SEE2 (93.2 mmol/L), unexpectedly, there was no difference between them at T12 ($P > 0.05$; Table 3). Despite the absence of a statistical difference, SEE1 promoted a 10.29% increase in serum chloride at the end of the hydration phase (T12), while in SEE2, the increase was 9.37%. Perhaps the decrease in chloride in SEE2 may make it more suitable for use in prolonged treatment of animals that are not presenting hypochloremia.

As with urinary sodium excretion, urinary chloride excretion also increased. This increase occurs because most of the filtered chloride in the renal glomeruli is passively reabsorbed due to the reabsorption of sodium, therefore, because of the greater excretion of sodium there is also a greater excretion of chloride, justifying the findings of the present trial. (Waldrop, 2008).

Serum Ca^{2+} and Mg^{2+} values showed a small decrease in SEE1 and SEE2 (Table 2). These decreases signal the possibility of an increase in Ca^{2+} and Mg^{2+} in the electrolyte solutions, since the urinary excretion of these two electrolytes also decreased, especially in animals treated with SEE1. When there is an increase in renal tubular flow, promoted by plasma expansion, there may be a decrease in the process of tubular reabsorption of some substances, among them calcium and magnesium (Riella, 2012), causing greater excretion of these elements. However, what was observed was a decrease in uCa^{2+} and uMg^{2+} concentrations. Therefore, these results point to the possibility of increasing the amount of Ca^{2+} and Mg^{2+} in the electrolytic solution, especially for patients who have serum or plasma hypocalcemia and hypomagnesemia.

The concentration of serum phosphorus increased in the fluid therapy phase in the animals of both treatments. Despite this increase, the values remained within the

normal range mentioned by Jerry Kaneko et al. (2008), making them without clinical significance.

Plasma glucose is not a better energy indicator in ruminants. They keep their blood concentrations low in relation to other species due to the use of fats and volatile fatty acids as an energy substrate (Kozloski, 2011). It can be seen that during the whole experimental phase there were no changes in their values in both treatments ($P > 0.05$). Plasma lactate is a good indicator of cellular respiratory activity (Jerry Kaneko, 2008). However, its behavior was similar to that of glucose; there were no significant changes ($P > 0.05$) in the animals of the two treatments during the entire experimental phase (Table 2).

Serum creatinine did not show significant changes during the entire experimental phase in animals from both treatments ($P > 0.05$). The urinary excretion of creatinine showed a small decrease during the fluid therapy period in both treatments. This decrease was caused by hemodilution resulting from the expansion of blood volume (Tables 2 and 3).

Urine specific gravity is considered a good marker of dehydration and volume expansion in animals. In the goats in the present trial, there was a significant decrease in USG in both treatments, reaching the lowest values at T9–12 ($P < 0.05$, Table 3). The results of the present trial demonstrated the effective and mainly early effect of enteral fluid therapy in the expansion of blood volume, confirming the results obtained by Dias et al. (2019), Alves et al. (2019) and Monteiro et al. (2020).

The blood pH of the animals that received SEE1 showed a slight decrease during the fluid therapy phase, reaching the lowest value at T12, maintaining the values at T24 ($P < 0.05$). In those that were infused with SEE2, the pH remained unchanged during the fluid therapy phase, remaining so until the moment of final

evaluation. The decrease in pH from T8 observed in SEE1 animals reveals the presence of mild acidemia, which was maintained until the final 24 hours of observation. Bicarbonate and cBase showed similar behavior to blood pH, reaching the lowest values in SEE1 animals at T12 and T24. The cBase showed negative rates, −3.7 mmol/L at T24, indicating the presence of mild metabolic acidosis (Table 4). The persistence of these changes at T24 was due to the volume of the electrolyte solution that remained in the rumen and that was absorbed after the end of the electrolyte solution administration (T12 to T24).

Solutions with SID less than 25 mEq/L have an acidifying potential (Constable, 2014). The administration of this type of solution causes the appearance of metabolic acidosis, emphasizing that the intensity of the acidosis will depend on the amount of chloride, the volume, and the time of infusion of the solution. The composition of SEE1, presenting the same amount of cations and anions, that is, SID = zero, makes it acidifying. This characteristic translated into a decrease in the pH, $cHCO_3^-$, and cBase of the animals, confirming low-intensity metabolic acidosis. Electrolyte solutions with this peculiarity have a specific indication, patients with hypochloremic metabolic alkalosis. According to Roussel (2014), more than 50% of adult ruminants that arrive sick to hospitals for treatment have metabolic alkalosis, usually caused by changes in abomasal emptying causing hypochloremia. Electrolytic solutions such as SEE1 are indicated for the correction of these imbalances. Regarding SEE2, despite having caused a small decrease in cBase at T8, T12, and T24, the values remained in the normal range for goats (Redlberger et al., 2017).

The presence of mild metabolic acidosis caused by SEE1 was confirmed by the urinary pH of the animals at T9–12 and T24 ($P < 0.05$, Table 3). Goats feeding with a higher proportion of roughage have alkaline urinary pH like all herbivores (Jones et

al., 2012). The most intense aciduria recorded at T24 occurred 12 hours after the end of hydration; it came from the effect of the residual volume of the electrolyte solution. The supply of the diet shortly after the end of fluid therapy may also have contributed to the decrease in urinary pH observed at T24. In turn, SEE2 did not change the urinary pH during the administration of the electrolytic solution, which registered a decrease in urinary pH only at T24, also signaling the contribution of the diet to this clinical observation.

A small increase in the pressure of carbon dioxide (pCO_2) was recorded at T0 and T4 in the animals of both treatments (Table 4). However, despite this increase, the values remained within the normal range mentioned by Stevens et al. (1994), who established the reference value for the variable in the caprine species between 34.6 and 48.8 mmHg.

Significant changes were observed in the AG values (Table 4) between treatments and in the SEE1 treatment over time ($P < 0.05$). The AG is used primarily to detect metabolic acidosis. This occurs when the values are above the reference range (DiBartola, 2012b). In SEE1 animals, the highest values of AG were detected at T8, T12, and T24, moments in which the lowest values of $cHCO_3^-$ and cBase were recorded. In metabolic acidosis, $cHCO_3^-$ and cBase decrease, as in the formula for calculating AG the value of $cHCO_3^-$ is used. This decrease caused by its use to neutralize H^+ ions will be reflected in the increase in the value of AG, expressing the presence of metabolic acidosis generated by the composition of SEE1. In animals that received SEE2, there was no variation in the AG over time ($P > 0.05$). The difference between treatments occurred at T8 and T24, times when the AG of SEE1 was higher than SEE2 ($P < 0.05$), confirming the mild acidifying effect of SEE1.

The values for difference of strong ions showed no difference between the experimental groups ($P > 0.05$). At T8, T12, and T24, the lowest SID values were recorded in SEE1 and SEE2 (Table 4). This decrease was caused by chloride, since it occurred in the respective times that the highest values of the chloride ion were detected (Table 2). Care should be taken with the amount of chloride, because if the amount is exacerbated and the patient is not presenting hypochloremia, a type of acidosis that is common in animals, called hyperchloremic metabolic acidosis, can be produced iatrogenically (Constable, 2003), which has as a cause solutions with high chloride content or solutions with low SID.

6. Conclusion

The studied enteral electrolytic solutions are effective in expanding blood volume. As it contains more chloride and a lower SID, Enteral Electrolytic Solution 1 demonstrated a low-intensity acidifying potential, which makes it a choice for patients with hypochloremic metabolic alkalosis, while Enteral Electrolytic Solution 2 can be used as a maintenance electrolytic solution for patients with discrete or no electrolyte and acid–base imbalances.

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Attachments

Annex 1 - Reference values for packed cell volume, biochemical and blood gas analysis in goats.

Parameter	**Reference value**	**Source**
Blood count		
Packed cell volume %	22-38	Pugh et al, 2012
Biochemical analysis		
Sodium mMol/L	142-155	Pugh et al, 2012
Potassium mMol/L	3.5-6.7	Pugh et al, 2012
Chloride mMol/L	99-110,3	Kaneko et al, 2008
Ionic calcium mMol/L	2.23-2.93	Kaneko et al, 2008
Magnesium mg/dL	2.8-3.6	Pugh et al, 2012
Phophorum mg/dL	4.2-9.1	Pugh et al, 2012
Creatinine mg/dL	1.0-1.82	Pugh et al, 2012
Glucose mg/dL	50-75	Pugh et al, 2012
Lactate mg/dL		
Proteínas plasmáticas g/dL	6.4-7.0	Pugh et al, 2012
Osmolarity mOsm/L		
Blood gas analysis		
pH	7.45±0.073	Nunes et al, 2014
Base excess mEq/L	0-5	Redlberger et al, 2017
Bicarbonate mEq/L	28.7±4.1	Nunes et al, 2014
pCO_2 mmHg	34.6-48.8	Stevens et al, 1994
Anion GAP mEq/L	11-20	Redlberger et al, 2017
SID mEq/L	41-46	Redlberger et al, 2017

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Annex 2 – Pictures