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Treatment of acute rumen lactic acidosis with intravenous hypertonic sodium chloride or bicarbonate solutions followed by intraruminal water

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ABSTRACT

The effectiveness of 7% hypertonic saline solution (HSS) and 6% hypertonic bicarbonate solution (HBS) followed by intraruminal water administration for the treatment of acute rumen lactic acidosis (ARLA) has not been evaluated yet. The hypothesis of the study is that treatment with HBS causes a faster correction of imbalances and clinical recovery than treatment with HSS. ARLA was induced in six healthy mature female sheep with sucrose twice. The sheep received both treatment regimens in a cross over design. After 18 h of induction, rumen lavage was performed and IV infusion of 7% HSS (4 mL/kg BW) or 6% HBS (6.7 mL/kg BW) was done over 5 min, followed by intraruminal administration of water (8% BW). The solutions provided 4.8 mmol/kg BW of sodium. Physical and laboratory tests were performed for 168 h. Both treatments increased plasma volume. After HSS treatment, pH and HCO_3^- returned to baseline values at 144 h and BE at 168 h. With HBS treatment, pH returned to baseline at 24 h, and HCO_3^- and BE at 48 h. In both treatments, the ruminal motility and the maximum hay intake were restored at 96 and 120 h, respectively. In conclusion, administration of HSS or HBS followed by intraruminal water corrects dehydration and mild-to-moderate metabolic acidosis in sheep with ARLA. Treatment with HBS promoted a faster correction of metabolic acidosis and could be indicated for the most severe cases.

1. Introduction

Acute rumen lactic acidosis (ARLA) generates economic losses because it is the main cause of morbidity and mortality in intensive ruminant production systems (Snyder and Credille, 2017). The accumulation of lactic acid due to fermentation of excessive amounts of carbohydrates in the rumen causes metabolic acidosis, dehydration, and hypovolemia. Besides, endotoxins and histamines are released and may cause secondary complications. The treatment of ARLA involves the removal of ruminal content and the correction of water and acid-base imbalances (Snyder and Credille, 2017). Conventionally, the treatment of metabolic acidosis caused by ARLA is performed with IV administration of isotonic sodium bicarbonate solution (1.3% $NaHCO_3$), obtaining the required amount of HCO_3^- for the correction from the value of the base deficit. For rehydration, continuous IV infusion of isotonic electrolyte solution is used and the volume is defined according to the estimated degree of dehydration (Jones and Navarre, 2014; Snyder and Credille, 2017).

This treatment requires time for animal monitoring, which makes it impractical to be executed in the field. The efficacy of rapid administration of hypertonic saline solution (HSS) followed by oral electrolyte solution (OES) to reverse dehydration and electrolyte imbalance was confirmed in neonatal calves with induced osmotic diarrhea (Constable et al., 1996; Leal et al., 2012; Walker et al., 1998) and naturally occurring diarrhea (Aydogdu et al., 2018; Koch and Kaske, 2008; Trefz et al., 2017). Moreover, the effectiveness and safety of this procedure were also proved with the use of IV hypertonic sodium bicarbonate solution (HBS) followed by OES in acidotic calves (Koch and Kaske, 2008; Trefz et al., 2017). To date, only one study has evaluated the efficacy of rapid HSS infusion for the treatment of adult ruminants affected by ARLA (Rodrigues et al., 2011).

The aim of this study was to compare the efficacy of IV

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administration of 7% HSS and 6% HBS followed by intraruminal water administration, for the treatment of ARLA in sheep. The hypothesis is that HBS promotes a faster correction of imbalances and clinical recovery than HSS because HSS does not have an alkalinizing capacity.

2. Materials and methods

The methods used in this study were approved by the Commission of Ethics in the Use of Animals of the Universidade Estadual de Londrina (protocol n° 5909.2017.43). Six crossbred adult (3 to 6 years old) sheep were used. The animals were healthy, non-pregnant and non-lactating, with a mean body weight of 50.62 ± 5.62 kg. The ewes were housed in collective stalls where they underwent a period of diet adaptation for 30 days before being submitted to induction. During this period they were fed with commercial ration for adult sheep in the amount corresponding to 1% of body weight (BW) divided into two portions daily, and with coast-cross grass hay and water at will.

After the adaptation period, the sheep were submitted to 18 h of solid fasting and ARLA induction, which was performed with 15 g/kg BW sucrose (Kezar and Church, 1979) diluted in two liters of warm water (39 °C) and administered into the rumen via a stomach tube. During the fasting period, the animals had free access to the water. Each sheep was submitted to induction twice, with the second induction done at least 30 days after full recovery from the first induced disease.

Treatment started 18 h after sucrose administration, consisting of removal of the ruminal fluid contents through the stomach tube and rumen lavage, infusion of hypertonic solution intravenously, and intraruminal water administration. Rumen lavage was performed with 4 L of warm water and siphoning with the help of manual compression of the abdomen in the ventrocaudal position. This procedure was repeated five times, with a total lavage volume of 20 L of water in order to remove the largest possible volume of ruminal content composed of liquid and smaller particles.

Immediately after rumen lavage, the animals were catheterized (catheter 18G) in the left jugular vein and a 20 cm extender tube was attached for the infusion of the hypertonic solutions. After catheter fixation, IV administration of one of the two hypertonic solutions was started: HSS – 7% sodium chloride solution (Cloreto de Sódio 7%, Laboratório Prado S.A., Curitiba, PR) at a dosage of 4 mL/kg BW; and HBS – 6% sodium bicarbonate solution (Solução de Bicarbonato de Sódio 6%, Laboratório Prado S.A., Curitiba, PR) at a dosage of 6.7 mL/kg BW. Regardless of the volume administered, the infusion was performed over five minutes. The cross-over design was used, and all the sheep received both solutions, one during each ARLA induction. Treatment assignments were randomly established. Both solutions provided 4.8 mmol of sodium/kg BW. These hypertonic solutions were selected because they are commercially available for veterinary use in the Brazilian market.

Immediately after the infusion of the hypertonic solution, water was supplied in a volume corresponding to 8% of the BW in a bucket that the animals were accustomed to. The volume of water ingested voluntarily was measured and the remaining water was administered into the rumen via the stomach tube. This procedure was completed ten minutes after the end of IV administration of the hypertonic solutions.

Physical examinations, including measurements of rectal temperature, heart and respiratory rates, and ruminal movements (RM), clinical assessment of mucosal color, capillary refill time, turgor of eyelid skin, presence of enophthalmia, feces characteristics, and behavior and posture were performed at −36 h (before fasting) and at other times intended for blood collection, except 5 min after starting IV infusion. Subjective appetite assessment was performed, from the time hay and water were supplied (moment 2 h), through the behavior exhibited by interest towards food. Objective appetite assessment was performed by measuring the difference between the weights of the hay offered and the surplus in the trough every 24 h. The volume of water ingested was also measured every 24 h.

Venous blood samples were collected at the following moments: before induction (−18 h), before starting IV infusion (0 h), at the end of IV infusion (5 min), at the end of intraruminal water administration (15 min) and 30 min, 1 h, 2 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h after the treatment. Blood was collected directly from the catheter with a syringe and needle from 0 h to 24 h. At other times, including the 5 min mark at the end of IV infusion, blood was collected directly from the right jugular vein. The samples were conditioned in vacuum tubes containing EDTA anticoagulant without sodium fluoride for the determination of the total plasma protein concentration (TPP) and with sodium fluoride for L-lactate and creatinine determinations. Fluorinated plasma was obtained by centrifugation (1500 × *g* for 10 min) within 10 min after collection and frozen at −20 °C until the time of the analysis within 6 months. For the blood gas analysis, the venous blood samples were collected under anaerobic conditions using 3 mL heparinized (Hemofol, Cristália, Itapira, SP) syringes.

Urine samples were obtained by spontaneous urination or induced by brief manual obstruction of the nostrils and mouth at times: −18 h, 0 h, 1 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h. The urine specific gravity was determined shortly after collection. For the other analyzes, the samples were kept frozen (−20 °C).

The ruminal fluid was collected via the stomach tube with the aid of suction at the following times: −36 h, −18 h, 0 h, 24 h, 48 h, 72 h, 120 h, and 168 h for fresh analysis.

TPP concentrations were measured by refractometry (Refratômetro manual portátil, Atago Brasil Ltda., Ribeirão Preto, SP). Plasma concentrations of creatinine and L-lactate were measured by kinetic and colorimetric spectrophotometric methods, respectively (Dimension Xpand Plus, Siemens Ltda., São Paulo, SP). The blood measurements of pH, partial pressure of carbon dioxide (pCO_2), bicarbonate concentration (HCO_3^-), base excess (BE), sodium (Na^+), potassium (K^+), and chloride (Cl^-) concentrations, and osmolality were performed in a blood gas analyzer (RAPIDpoint 500, Siemens Ltda., São Paulo, SP) within 15 min after collection.

The urine specific gravity was measured by refractometry (Refratômetro manual portátil, Atago Brasil Ltda., Ribeirão Preto, SP). Urine creatinine concentrations were determined using the kinetic method while the Na^+, K^+, and Cl^- concentrations were determined using the ion-selective electrodes method (Dimension Xpand Plus, Siemens Ltda., São Paulo, SP).

Ruminal fluid analyses were performed within 30 min after collection, and consisted of pH measurements with the electronic potentiometer (PG1800, Gehaka, Indústria e Comércio Eletro Eletrônica Gehaka Ltda, São Paulo, SP), evaluation of color, odor and consistency, and determining methylene blue reduction time (MBRT) (Dirksen, 1993). Protozoans were evaluated for viability (live or dead). The ratio between Gram-positive and Gram-negative bacteria was established on smears after Gram staining.

Subsequent variables were calculated using the following formulas:

a) Strong Ion Difference (SID_3) (Constable, 1997):

$$SID_3 = (Na^+ + K^+) - (Cl^-)$$

b) Anion Gap (AG) (Constable, 2014):

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

c) Strong Ion Gap (SIG) (Constable, 2002):

$$SIG = ([3.6 \times PPT]/[1 + 10^{7.06-pH}]) - AG$$

d) Total Concentration of Nonvolatile Buffers (A_{tot}) (Constable, 2002):

$$A_{tot} = 3.6 \times PPT\ (g/dL)$$

e) Percent change in plasma volume (%PV) (Carlson and Bruss, 2008):

$\%PV = [(TPP^1/TPP^2)–1] \times 100$

Where TPP^1 is the TPP value observed prior to induction and TPP^2 are the TPP values of the subsequent times.

f) Fractional excretion of electrolytes (Garry et al., 1990):

FE (a)
= (urinary concentration of (a) × plasma creatinine
/plasma concentration of (a)×urine creatinine) × 100

Where (a) is the excreted substance.

2.1. Statistical analysis

Two way repeated measures analysis of variance was used to test the effects of time (before and after solution infusion and water administration), the effects of the treatment (i.e., the type of hypertonic solution), and to evaluate the interaction between these two factors (time and treatment). When the F statistic was significant, the Tukey test was used for multiple comparisons. The volume of water ingested voluntarily after the infusion of hypertonic solution was compared between treatments by t-test. The SigmaPlot package for Windows 13.1 was used for all analysis (Systat Software Inc., San Jose, California) and P-values < 0.05 were considered statistically significant.

3. Results

The induction protocol was effective in causing ARLA and the observed changes were the same on both occasions after disease induction. All of the sheep had lethargy, watery diarrhea, mild-to-moderate dehydration, and rumen atonia, with ruminal pH < 5.0 (HSS: 4.37 ± 0.13; HBS: 4.43 ± 0.16) at moment 0 h (Fig. 1). The heart rate increased, but no changes in the respiratory rate and body temperature were observed. The following changes were seen in ruminal fluid before treatment (0 h): brown color, acid odor, watery consistency, increase in MBRT > 20 min (Fig. 1), the predominance of Gram-positive bacteria (from 80 to 95%) and small amounts of dead protozoans.

With the induction of ARLA (0 h), reductions in blood pH (HSS: 7.201 ± 0.087; HBS: 7.245 ± 0.084), HCO_3^- (HSS: 14.63 ± 2.37 mmol/L; HBS: 17.18 ± 2.64 mmol/L), and BE (HSS: −13.37 ± 3.76 mmol/L; HBS: −10.15 ± 3.90 mmol/L) were observed, while pCO_2 remained unchanged (Fig. 2, Table 1). There was an increase in blood concentrations of Na^+ (HSS: 151.50 ± 1.23 mmol/L; HBS: 150.10 ± 3.39 mmol/L) and Cl^- (HSS: 118.50 ± 1.52 mmol/L; HBS: 117.17 ± 2.32 mmol/L); no changes in K^+ concentrations were observed while SID_3 was decreased (HSS: 37.12 ± 1.27 mmol/L; HBS: 37.22 ± 1.83 mmol/L) (Fig. 3, Table 2). The plasma concentration of L-lactate remained unchanged as did the A_{tot} (Fig. 4, Table 3). There was an increase in AG (HSS: 22.47 ± 1.89 mmol/L; HBS: 20.07 ± 2.28 mmol/L) and plasma osmolality (HSS: 305.78 ± 2.38 mOsm/kg; HBS: 302.80 ± 7.13 mOsm/kg), and a decrease in SIG (HSS: −7.13 ± 2.56 mmol/L; HBS: −3.40 ± 3.13 mmol/L). Plasma volume decrease was observed (HSS: −3.84 ± 6.83%; HBS: −8.23 ± 4.70%) although it did not differ from the values observed before induction (−18 h). Fractional excretion of electrolytes and urine specific gravity did not vary with disease induction (Fig. 5, Table 5).

The infusion of HSS (5 min) caused a higher pH drop (7.098 ± 0.060) that reverted, in 15 min, to the value observed before treatment (0 h). The values of HCO_3^- (11.38 ± 1.53 mmol/L) and BE (−18.28 ± 2.47 mmol/L) also decreased at the end of the infusion although they did not differ from the values observed at time 0 h. The pCO_2 showed a gradual reduction, reaching the lowest value 12 h after treatment (31.35 ± 2.80 mmHg). The pH and HCO_3^- values returned to their baselines 144 h after treatment; the BE values returned to baseline 168 h after treatment and the pCO_2 48 h after treatment (Fig. 2, Table 1). The Na^+ (161.25 ± 2.98 mmol/L) and Cl^- (134.0 ± 3.69 mmol/L) concentrations increased; K^+ (3.29 ± 0.27 mmol/L) and SID_3 (33.54 ± 2.37 mmol/L) were reduced with HSS infusion (5 min). The Na^+ and K^+ concentrations returned to their original values at 2 h and 30 min, respectively (Fig. 3, Table 2). The Cl^- concentration, and SID_3 did not return to their original values throughout the observation period (168 h).

With HSS administration (5 min), there was an increase in plasma osmolality (325.83 ± 5.78 mOsm/kg) and %PV (26.58 ± 9.76%) that returned to baseline values after 1 and 6 h, respectively. There was also a reduction of the A_{tot} (20.16 ± 1.20 mmol/L) which returned to the original value after 12 h. The plasma concentration of L-lactate and the AG and SIG did not change with infusion. The AG returned to the baseline value after 30 min, while the SIG gradually increased before return to the original value after 6 h (Fig. 4, Table 3).

HBS infusion (5 min), on the other hand, caused immediate elevations of pH (7.596 ± 0.036), HCO_3^- (41.92 ± 3.39 mmol/L), and BE (20.03 ± 3.70 mmol/L). The pH values were gradually reduced to values lower than the baseline values between 6 h and 12 h, and then returning to them after 24 h. The reductions of HCO_3^- and BE were more pronounced, reaching pre-treatment values (0 h) between 2 h and 24 h, and returning to baseline values from 48 h after treatment. The pCO_2 (44.12 ± 4.04 mmHg) showed no significant increase immediately after infusion, then it gradually decreased up to 12 h and returned to the original value after 24 h (Fig. 2, Table 1). The concentration of Na^+ (155.37 ± 4.40 mmol/L) and SID_3 (53.72 ± 3.03 mmol/L) increased with infusion, decreased and maintained lower values between 6 h and 24 h, and then returned to their baseline values from 48 h after treatment. The Cl^- concentration, increased with the disease, was corrected at the end of the infusion. The K^+ concentration remained reduced between 15 min and 48 h (Fig. 3, Table 2).

With HBS administration (5 min), the plasma L-lactate concentration increased (5.85 ± 1.90 mmol/L) before returning to its original value from 2 h. There was an increase in plasma osmolality (314.28 ± 8.78 mOsm/kg), SIG (3.63 ± 1.25 mmol/L), and %PV (27.43 ± 9.17%), and a reduction in the AG (11.78 ± 2.02 mmol / L) and A_{tot} (19.92 ± 1.42 mmol/L). The osmolality decreased over the first 24 h before returning to baseline at 48 h. The %PV, A_{tot}, and SIG returned to their original values at 1 h while the AG returned to its original value from 15 min (Fig. 4, Table 3 and Table 4).

Urinary variables exhibited the same behavior with the two types of treatment tested. The FE of Na^+ increased only at the 1 h point while the FE of K^+ and Cl^- did not change over the study duration. Finally, the urinary specific gravity remained lowered between 1 h and 24 h (Fig. 5, Table 5).

The differences observed between the two types of treatment studied were significant for pH, HCO_3^-, BE, SID_3 and SIG, which were always higher, and for Cl^-, which was always lower, after HBS treatment (i.e., from the end of the infusion; Figs. 2, 3 and 4, Table 1, Table 2 and Table 3). Na^+ concentration was higher with HSS treatment, at the end of the infusion and between 6 h and 24 h. The K^+ concentration was higher between 1 h and 12 h. The L-lactate concentration remained lowered from the end of HSS infusion until 2 h. AG was higher with HSS treatment at the end of infusion and at 24 h, 48 h, 96 h, and 120 h. The osmolality was higher at the end of the HSS infusion and between 6 h and 24 h. In the HBS treatment, %PV was lower and A_{tot} was higher at 1 h and 2 h after infusion.

The volumes of water ingested voluntarily after hypertonic solutions infusions varied between sheep (200 to 1096 mL after HSS and 400 and 700 mL after HBS) but were not significantly different between treatments (P = 0.282). Two sheep did not drink water after receiving HSS and four did not drink after receiving HBS.

All sheep clinically recovered after treatment with HSS and HBS, demonstrating a similar pattern of evolution over time. There were no

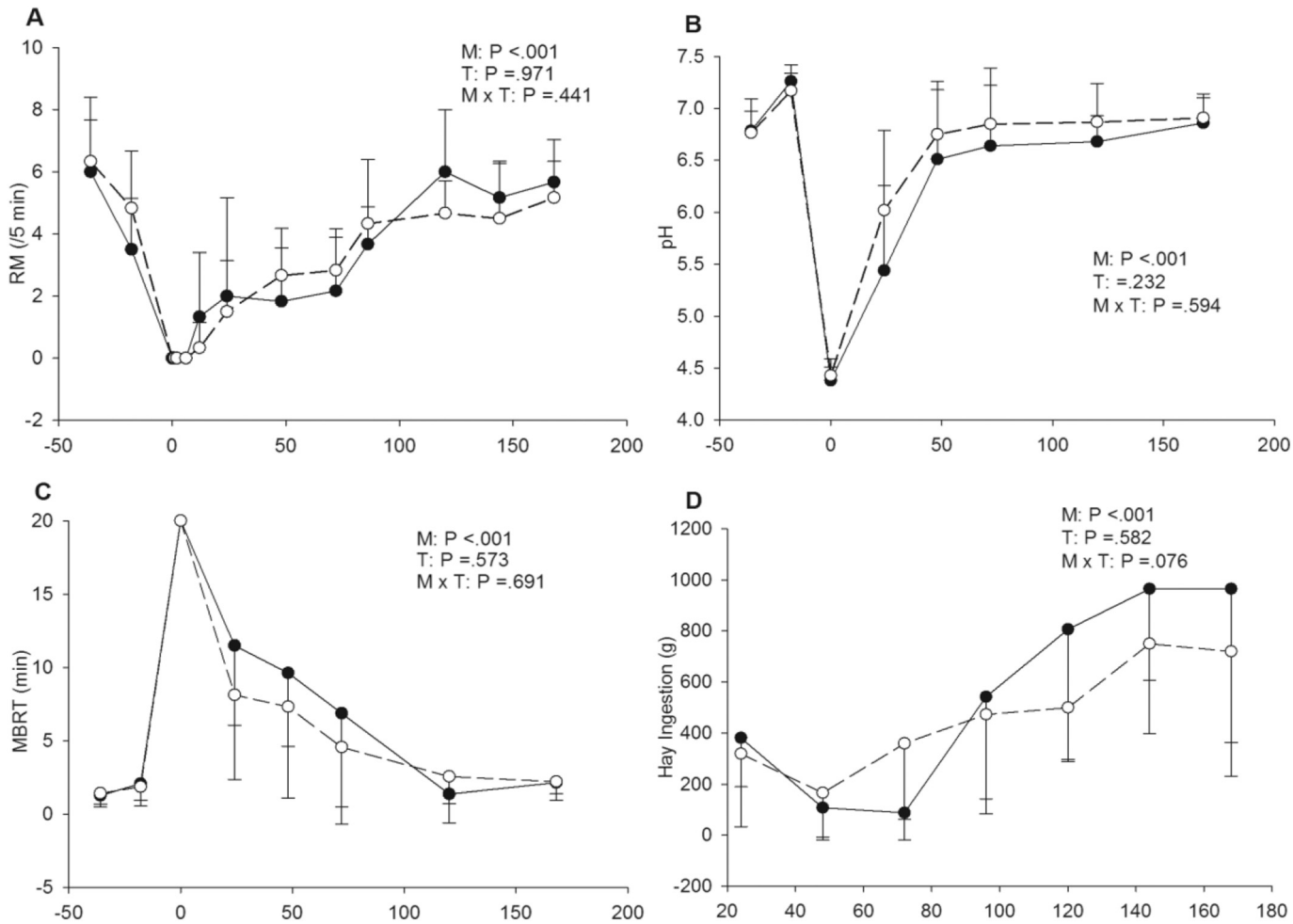

Fig. 1. Variation of ruminal movements, pH, and methylene blue reduction time (MBRT) of the ruminal fluid of sheep with induced ARLA. Measurements were done before fasting (−36 h), before induction (−18 h), and before (0 h) and after treatment (24 h, 48 h, 72 h, 120 h, and 168 h). Hay ingestion was measured after treatment (24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h). The animals were treated with IV hypertonic saline solution (—●—) or hypertonic sodium bicarbonate solution (–○–), followed by intraruminal administration of water. M = moment; T = treatment; M × T = moment × treatment interaction.

apparent side effects during or after the administration of the hypertonic solutions. Regardless of the treatment, ruminal fluid pH, MBRT, and RM frequency gradually returned to their pre-fasting values (−36 h) from 48, 72, and 96 h, respectively. The predominance of Gram-negative bacteria and the presence of live protozoans returned at 48 and 24 h after infusion, respectively. The daily intake of roughage and water gradually increased and remained at a maximum from 120 h after infusion (Fig. 1), without any distinction between treatments ($P = 0.582$ for roughage; $P = 0.317$ for water).

4. Discussion

The results confirmed that rumen lavage and IV administration of 7% HSS or 6% HBS followed by intraruminal water administration is effective for the treatment of ARLA induced in sheep. Some researchers have proven the efficacy of hypertonic solutions followed by oral electrolyte solution (OES) for the treatment of dehydrated diarrheal calves (Aydogdu et al., 2018; Constable et al., 1996; Koch and Kaske, 2008; Leal et al., 2012; Trefz et al., 2017; Walker et al., 1998). In the case of ARLA, only one study had previously evaluated the dehydration correction in cattle using 7.5% HSS. However, hydration was performed with IV infusion of isotonic saline solution (0.9% NaCl) combined with the administration of water into the rumen (Rodrigues et al., 2011). The study reported here is the first to use a small volume of 7% HSS or 6% HBS rapidly administered by IV followed by intraruminal water administration for the treatment of water and acid-base imbalances due to ARLA.

The two tested solutions induced immediate and transient iatrogenic metabolic imbalances; HSS exacerbated already-established metabolic acidosis, while HBS induced metabolic alkalosis. Both solutions provoked hypernatremia, but hyperchloremia was induced only with HSS administration. By providing equivalent amounts of Na^+ and Cl^-, the HSS induced hyperchloremic acidosis with a reduction in plasma SID_3. Despite the animal's hydration and clinical improvement, the Cl^- concentration remained elevated and the SID_3 remained lowered at the end of the observation period. Although the decrease in blood pH after HSS infusion was on average 0.103 units (i.e., more pronounced than observed and described by other researchers) (Constable, 1999; Rodrigues et al., 2011), there were no apparent clinical changes. Similar to other observations in sheep, acidemia caused by ARLA was not accompanied by compensatory hypocapnia (Flaiban, 2010). However, after HSS administration, the pCO_2 declined, reaching its lowest value at 12 h, indicating that the compensatory response depends on the severity of the acidosis. Transient hypokalemia observed after HSS infusion supports previous results (Trefz et al., 2017) and can be attributed to the plasma volume expansion and K^+ entry into the cells to reverse the increase in intracellular Na^+ concentration (Aronson and Giebisch, 2011; Constable, 1999). The transient reduction of K^+ can, therefore, be considered a disadvantage of HSS use. However, this alteration was mild in the studied sheep and did not determine changes in heart rate.

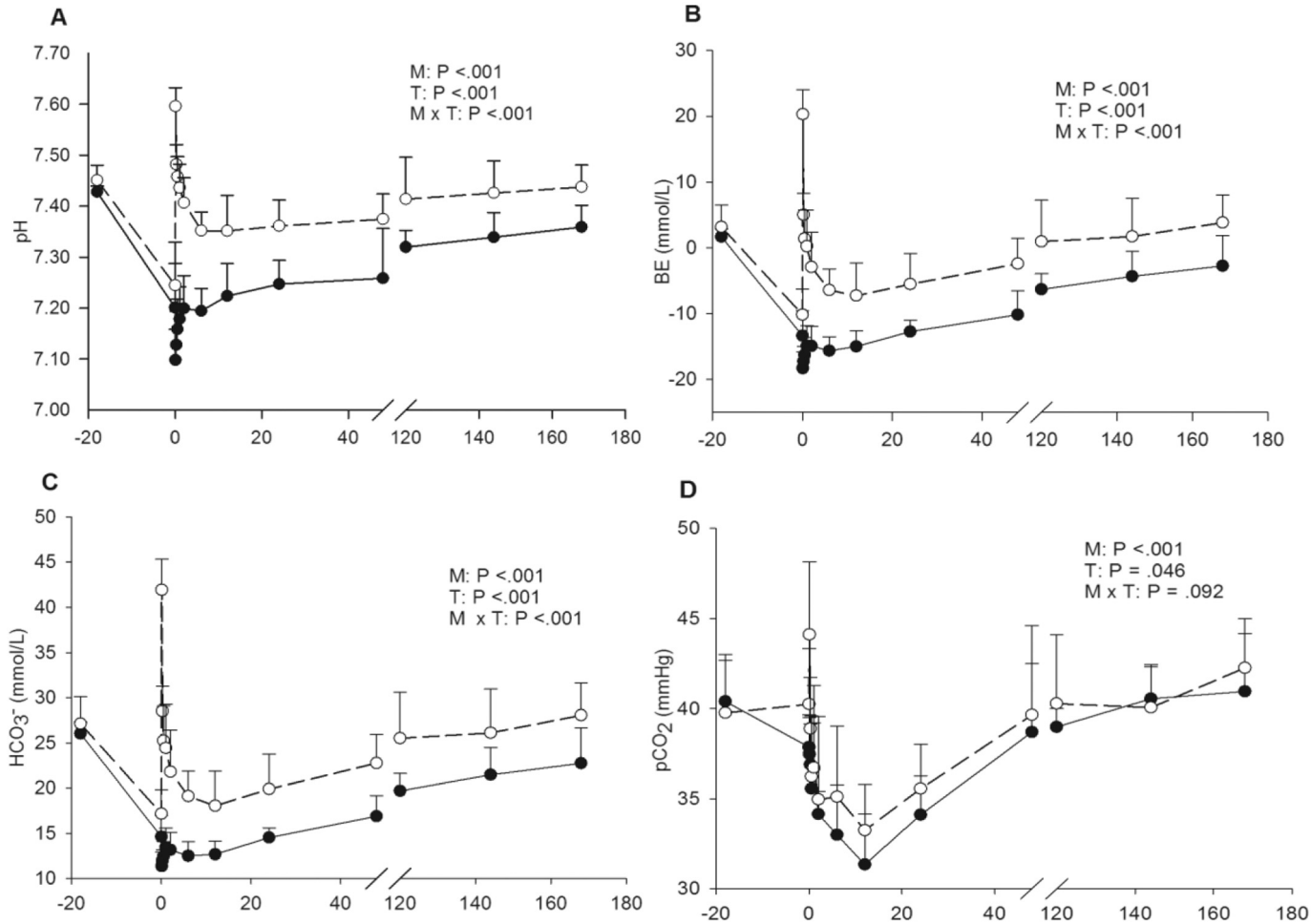

Fig. 2. Variation of pH, pCO_2, HCO_3-, and base excess (BE) of venous blood of sheep with induced ARLA. Measurements were done before induction (−18 h) and before (0 h), during (5 min and 15 min) and after treatment (30 min, 1 h, 2 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h) with IV hypertonic saline solution (—●—) or hypertonic sodium bicarbonate solution (–○–), followed by intraruminal administration of water. M = moment; T = treatment; M × T = moment × treatment interaction.

The administration of HBS caused immediate alterations distinct from those observed with HSS infusion. It induced hypernatremia and marked SID_3 elevation, since the Cl^- plasma concentration was reduced due to hemodilution, and marked iatrogenic alkalosis should be understood as a consequence of these electrolytic changes (Constable, 2014). The sheep experienced a sudden change in the acid-base state from acidosis to metabolic alkalosis, and the mean increases in pH and BE values were 0.351 units and 30 mmol/L, respectively. These effects were quickly reversed and the alkalemia was resolved ten minutes after the infusion had ended. These results supported previously observed results in acidotic diarrheic calves that received a rapid IV infusion of 8.4% HBS (Coskun et al., 2010; Koch and Kaske, 2008; Trefz et al., 2017). Furthermore, hypercapnia in response to alkalemia or as a result of rapid buffering was not observed in our animals. This observation contrasts with only one previous study in calves (Koch and Kaske, 2008). As previously demonstrated in calves (Trefz et al., 2017), HBS administration resulted in more pronounced and lasting hypokalemia than that caused by HSS infusion, which may be due to the plasma volume expansion added to K^+ cellular influx due to the Na^+ K^+-ATPase activation (Grünberg et al., 2011; Trefz et al., 2015). The sudden reversal of acid-base imbalances and hypokalemia were not accompanied by any apparent clinical manifestation in the studied animals.

Variations of L-lactate, AG, and SIG were not influenced by HSS infusion. At the end of HBS administration, however, L-lactate and SIG elevations and AG reduction were observed. The effect on SIG and AG was brief and was reversed after 10 min. The effect on L-lactate concentration was longer and hyperlactatemia was maintained for two hours. The alterations in the AG was similar to that reported in calves (Koch and Kaske, 2008), but the variations in SIG cannot be compared with observations from previous studies because there was no measurement immediately after HBS infusion. The increase in L-lactate plasma concentration supports previous evidence in calves, in which its elevation was also maintained for up to two hours after starting treatment (Trefz et al., 2017), in ponies with endotoxemia (Gossett et al., 1990) and in high-performance athletes (Egger et al., 2014). This probably occurs as a consequence of the L-lactate output from muscle cells in response to extracellular medium alkalinization, as shown in in vitro studies (Seo, 1984; Spriet et al., 1986).

The Na^+ excess caused by HSS and HBS infusions was corrected by renal elimination, as evidenced by the increase in Na^+ FE one hour after starting treatment. The same was not observed for Cl^- excess triggered by HSS administration and this may justify why plasma concentrations remained elevated until the end of the follow-up period with this treatment. The ovine species presents a renal capacity for the correction of hyperchloremic acidosis, as observed after 4 h of HCl continuous infusion in a volume corresponding to 10% BW in normovolemic sheep (Romão et al., 2019). Fluid excess facilitated Na^+ and Cl^- excretion present in excess amounts and, in addition, the amount of Cl^- supplied was greater than that of the present study, which may explain the difference in results.

Table 1
Mean ± standard deviations for venous blood pH, pCO_2, HCO_3^- and BE of sheep with induced ARLA before induction (−18 h) and before (0 h), during (0.08 h and 0.25 h) and after treatment (0.50 h, 1 h, 2 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h) with IV infusion of hypertonic saline or hypertonic sodium bicarbonate solution, followed by intraruminal administration of water.

Hour	pH		pCO_2 (mmHg)		HCO_3^- (mmol/L)		BE (mmol/L)	
	7% HSS	6% HBS	7% HSS	6% HBS	7% HSS	6% HBS	7% HSS	6% HBS
−18	7.428 ± 0.011^{Aa}	7.451 ± 0.029^{Abcd}	40.40 ± 2.61^{Aab}	39.77 ± 2.92^{Aabc}	26.03 ± 1.30^{Aa}	27.13 ± 2.98^{Abc}	1.68 ± 1.24^{Aa}	3.17 ± 3.32^{Abc}
0	7.201 ± 0.087^{Adefg}	7.245 ± 0.084^{Af}	37.87 ± 1.78^{Aabcd}	40.25 ± 3.08^{Aabc}	14.63 ± 2.37^{Adef}	17.18 ± 2.64^{Ag}	−13.37 ± 3.76^{Adef}	−10.15 ± 3.90^{Ag}
0.08	7.098 ± 0.060^{Bh}	7.596 ± 0.036^{Aa}	37.48 ± 2.03^{Babcd}	44.12 ± 4.04^{Aa}	11.38 ± 1.53^{Bf}	41.92 ± 3.39^{Aa}	−18.28 ± 2.47^{Bf}	20.30 ± 3.70^{Aa}
0.25	7.128 ± 0.065^{Bgh}	7.482 ± 0.039^{Ab}	36.90 ± 2.26^{Aabcde}	38.88 ± 2.85^{Aabc}	11.97 ± 1.22^{Bf}	28.52 ± 2.78^{Ab}	−17.23 ± 2.23^{Bf}	5.03 ± 3.26^{Ab}
0.50	7.158 ± 0.059^{Bfgh}	7.458 ± 0.039^{Abc}	35.57 ± 0.64^{Abcde}	36.23 ± 3.36^{Acd}	12.45 ± 1.65^{Bef}	25.25 ± 3.84^{Abcd}	−16.28 ± 2.62^{Bf}	1.38 ± 4.35^{Abcd}
1	7.178 ± 0.063^{Befgh}	7.436 ± 0.046^{Abcde}	36.70 ± 2.52^{Aabcde}	36.73 ± 4.55^{Abcd}	13.47 ± 2.11^{Bef}	24.45 ± 4.81^{Abcde}	−14.93 ± 3.08^{Bef}	0.23 ± 5.49^{Abcde}
2	7.199 ± 0.064^{Bdefg}	7.407 ± 0.049^{Abcde}	34.15 ± 1.26^{Acde}	34.97 ± 4.60^{Acd}	13.17 ± 1.94^{Bef}	21.82 ± 4.61^{Adefg}	−14.92 ± 2.98^{Bef}	−2.92 ± 5.33^{Adef}
6	7.194 ± 0.044^{Bdefg}	7.353 ± 0.036^{Ae}	33.00 ± 2.76^{Ade}	35.12 ± 3.90^{Acd}	12.50 ± 1.57^{Bef}	19.12 ± 2.80^{Afg}	−15.65 ± 2.15^{Bef}	−6.42 ± 3.22^{Afg}
12	7.224 ± 0.064^{Bdef}	7.351 ± 0.069^{Ae}	31.35 ± 2.80^{Ae}	33.25 ± 2.54^{Ad}	12.68 ± 1.46^{Bef}	18.05 ± 3.85^{Ag}	−15.00 ± 2.37^{Bef}	−7.27 ± 5.00^{Afg}
24	7.247 ± 0.046^{Bcdef}	7.361 ± 0.050^{Ade}	34.12 ± 2.17^{Acde}	35.57 ± 2.46^{Acd}	14.53 ± 1.09^{Bdef}	19.92 ± 3.86^{Aefg}	−12.73 ± 1.76^{Bdef}	−5.50 ± 4.64^{Aefg}
48	7.259 ± 0.097^{Bcde}	7.375 ± 0.049^{Acde}	38.70 ± 5.92^{Aabc}	39.65 ± 2.85^{Aabc}	16.90 ± 2.31^{Bcde}	22.77 ± 3.15^{Acdef}	−10.17 ± 3.68^{Bcde}	−2.40 ± 3.86^{Acdef}
72	7.286 ± 0.060^{Bbcd}	7.372 ± 0.081^{Acde}	39.17 ± 1.36^{Babc}	43.55 ± 5.74^{Aa}	18.42 ± 2.93^{Bbcd}	24.85 ± 3.54^{Abcd}	−8.20 ± 3.88^{Bbcd}	−0.38 ± 4.60^{Abcde}
96	7.279 ± 0.055^{Bbcd}	7.417 ± 0.047^{Abcde}	41.18 ± 5.36^{Aa}	39.98 ± 2.06^{Aabc}	18.88 ± 2.45^{Bbcd}	25.27 ± 2.54^{Abcd}	−7.85 ± 3.01^{Bbcd}	0.75 ± 3.24^{Abcd}
120	7.320 ± 0.032^{Bbc}	7.414 ± 0.082^{Abcde}	38.98 ± 1.01^{Aabc}	40.28 ± 3.82^{Aabc}	19.70 ± 1.93^{Bbc}	25.53 ± 5.08^{Abcd}	−6.30 ± 2.40^{Bbc}	0.95 ± 6.29^{Abcd}
144	7.338 ± 0.048^{Babc}	7.426 ± 0.062^{Abcde}	40.55 ± 1.90^{Aab}	40.07 ± 2.25^{Aabc}	21.48 ± 3.03^{Babc}	26.13 ± 4.83^{Abc}	−4.32 ± 3.80^{Bbcd}	1.73 ± 5.80^{Abcd}
168	7.359 ± 0.042^{Bab}	7.438 ± 0.043^{Abcde}	40.95 ± 3.22^{Aab}	42.27 ± 2.72^{Aab}	22.75 ± 3.90^{Bab}	28.07 ± 3.54^{Ab}	−2.72 ± 4.58^{Babc}	3.85 ± 4.15^{Ab}

pCO_2, partial pressure of carbon dioxide; HCO_3^-, bicarbonate; BE, base excess. Different letters indicate significant ($p < 0.05$) differences among the treatments (A-B) or among the time (a-h); while shared letters indicate no significant difference.

The two hypertonic solutions followed by intraruminal water administration were efficient to correct dehydration, which was verified with physical examinations and confirmed with the plasma osmolality, %PV, A_{tot} and urinary density curves (Figs. 4 and 5, Table 3, Table 4 and Table 5). Although the same amount of Na^+ (4.8 mmol/kg BW) was supplied in both treatments, HSS caused immediate elevation of osmolality greater than HBS, with mean increments of 20 mOsm/kg and 11 mOsm/kg at the end of HSS and HBS infusions, respectively. Probably this is due to the sum of the osmotic actions of Na^+ and Cl^- in the HSS treatment. However, this difference does not characterize the HSS superiority for the plasma volume expansion. In the studied sheep, the intensity of the osmotic effect and, consequently, the degree of expansion of the plasma volume can be considered equivalent in the two types of treatment tested.

The efficacy of HSS or HBS rapid infusion followed by OES has already been shown to correct dehydration in diarrheic calves (Constable et al., 1996; Koch and Kaske, 2008; Leal et al., 2012; Walker et al., 1998). Even in severe conditions of dehydration, the therapeutic effect was observed within a few hours after treatment. It should be noted that the success of hydration depends on the adequate volume of OES after HSS or HBS infusion because the hypertonic solution's effect on the volemia is transient and it is unable to correct dehydration if administered alone (Constable et al., 1996; Leal et al., 2012).

The volume of water ingested voluntarily after infusion of hypertonic solutions was insufficient to promote rehydration, and some sheep were not interested in drinking water after hypertonic solutions infusion. This observation is consistent with previous experiences in calves, noting that only half of the animals voluntarily ingested the full volume of the OES provided within ten minutes after hypertonic solutions infusion (Koch and Kaske, 2008; Trefz et al., 2017). All these results show that the thirst behavior after the administration of hypertonic solutions in sick animals is variable and that the efficiency of voluntary intake is questionable. In the case of ewes affected by ARLA, it is clear that the indicated procedure is water administration via stomach tube at the end of IV hypertonic solution infusion.

Although dehydration correction occurred similarly in both treatments, reversal of metabolic acidosis was faster with HBS administration. When treated with this solution, the sheep returned to equilibrium at 48 h, whereas HSS treatment promoted the same effect only after 144 h (i.e., 4 days later). The faster correction of metabolic acidosis indicates that HBS treatment is more advantageous and proves part of our hypothesis right. Contrary to expectations, however, a faster return to acid-base balance was not accompanied by a faster clinical recovery. In both types of treatment, the reticulum-rumen motor function and the maximum intake of hay were recovered at 96 and 120 h, respectively. It must be emphasized, however, that the studied ewes presented just a mild-to-moderate imbalances. It is reasonable to expect that animals with a more severe acidosis would likely benefit more from HBS treatment.

Some researchers have used this same protocol for ARLA induction in sheep and goats, provoking a degree of imbalances very similar to that observed in our study (Flaiban, 2010; Pereira, 2016). They performed two rumen lavages at different times and treated the animals with IV alkalinizing isotonic electrolyte solutions in a volume corresponding to 10% BW, totaling 4 h of continuous infusion. The metabolic acidosis correction was already observed in the middle of the infusion and reversal of dehydration was successful. Even so, the sheep only recovered appetite and forestomach motor activity at 96 h after the start of treatment (Flaiban, 2010), and the goats had ruminal motility restored at 72 h, and hay intake at 96 h (Pereira et al., 2018). These results support the statement that the treatment protocols tested in the present study are efficient because there is no distinction in the time necessary for the clinical recovery of the animals when compared with conventional treatments using a continuous infusion of alkalinizing solutions.

This work aimed to test low-cost, easy, and fast protocols for ARLA

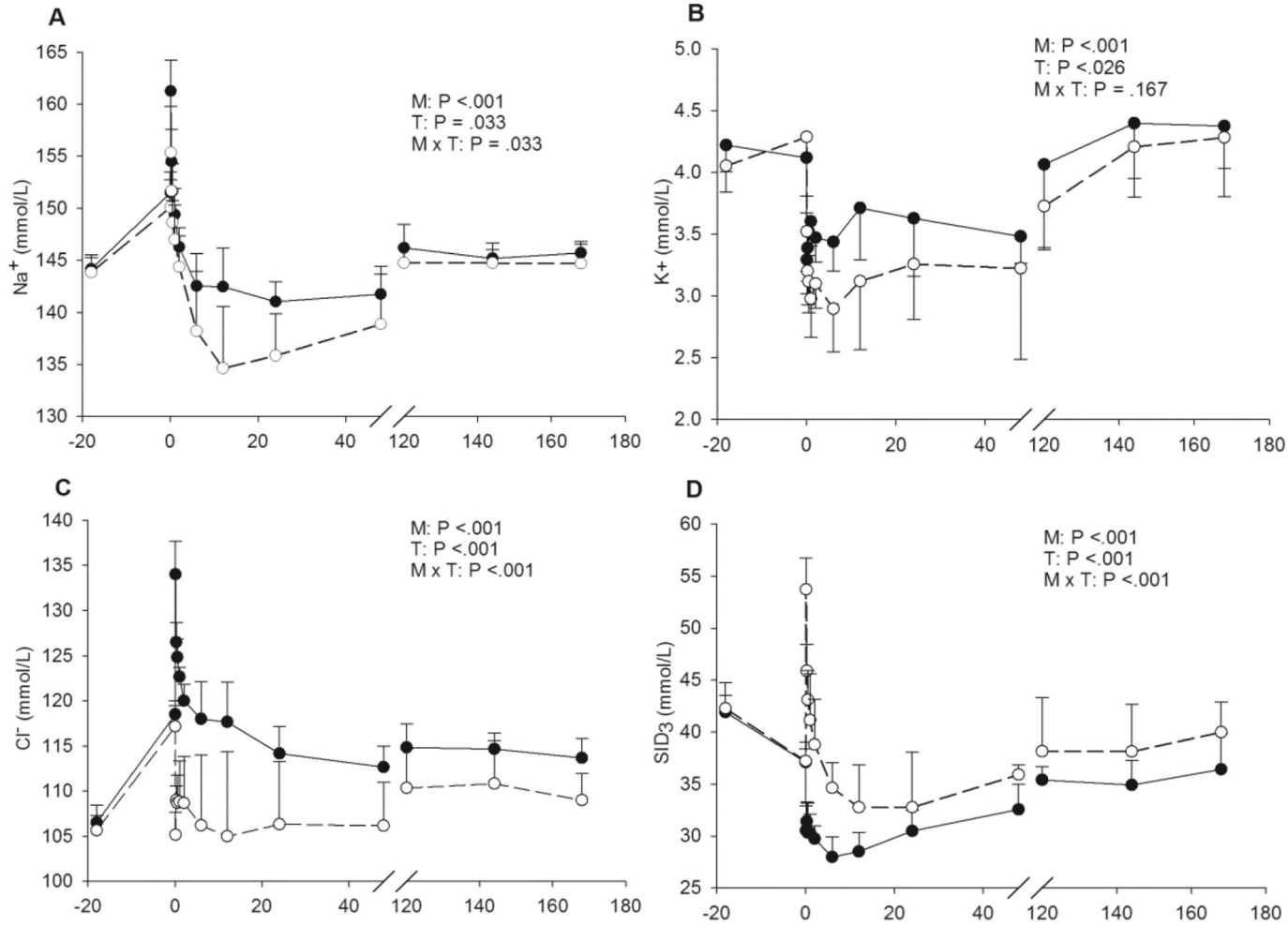

Fig. 3. Variation of Na^+, K^+, and Cl^- concentrations and strong ion difference (SID_3) of venous blood of sheep with induced ARLA. Measurements were done before induction (−18 h) and before (0 h), during (5 min and 15 min), and after treatment (30 min, 1 h, 2 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h) with IV hypertonic saline solution (—●—) or hypertonic sodium bicarbonate solution (–○–), followed by intraruminal administration of water. M = moment; T = treatment; M × T = moment × treatment interaction.

Table 2
Mean ± standard deviations for plasma concentration of Na^+, K^+, Cl^- and the SID_3 of sheep with induced ARLA before induction (−18 h) and before (0 h), during (0.08 h and 0.25 h) and after treatment (0.50 h, 1 h, 2 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h) with IV infusion of hypertonic saline or hypertonic sodium bicarbonate solution, followed by intraruminal administration of water.

Hour	Na^+ (mmol/L)		K^+ (mmol/L)		Cl^- (mmol/L)		SID_3 (mmol/L)	
	7% HSS	6% HBS	7% HSS	6% HBS	7% HSS	6% HBS	7% HSS	6% HBS
−18	144.18 ± 1.10^{Aefg}	143.87 ± 1.68^{Acde}	4.22 ± 0.22^{Aab}	4.05 ± 0.21^{Aab}	106.50 ± 1.97^{Ag}	105.67 ± 1.63^{Ab}	41.90 ± 1.61^{Aa}	42.27 ± 2.47^{Abcd}
0	151.50 ± 1.23^{Abc}	150.10 ± 3.39^{Ab}	4.12 ± 0.44^{Aabc}	4.29 ± 0.48^{Aa}	118.50 ± 1.52^{Adef}	117.17 ± 2.32^{Aa}	37.12 ± 1.27^{Aab}	37.22 ± 1.83^{Aefgh}
0.08	161.25 ± 2.98^{Aa}	155.37 ± 4.40^{Ba}	3.29 ± 0.27^{Ad}	3.52 ± 0.32^{Aabcde}	134.00 ± 3.69^{Aa}	105.17 ± 2.48^{Bb}	30.54 ± 2.37^{Bcdef}	53.72 ± 3.03^{Aa}
0.25	154.52 ± 3.07^{Ab}	151.68 ± 2.66^{Aab}	3.39 ± 0.27^{Acd}	3.20 ± 0.27^{Acde}	126.50 ± 2.17^{Ab}	109.00 ± 1.55^{Bb}	31.41 ± 1.86^{Bcdef}	45.89 ± 2.55^{Ab}
0.50	151.65 ± 2.62^{Abc}	148.65 ± 2.12^{Abc}	3.52 ± 0.19^{Abcd}	3.12 ± 0.26^{Acde}	124.83 ± 2.04^{Abc}	108.67 ± 3.08^{Bb}	30.34 ± 2.86^{Bdef}	43.10 ± 2.83^{Abc}
1	149.38 ± 2.53^{Abcd}	147.00 ± 3.30^{Abcd}	3.60 ± 0.20^{Aabcd}	2.98 ± 0.31^{Bde}	122.67 ± 1.03^{Abcd}	108.83 ± 4.49^{Bb}	30.32 ± 1.81^{Bdef}	41.15 ± 4.48^{Abcde}
2	146.27 ± 1.10^{Adef}	144.37 ± 3.78^{Acd}	3.47 ± 0.20^{Abcd}	3.10 ± 0.20^{Acde}	120.00 ± 1.79^{Acde}	108.67 ± 5.20^{Bb}	29.74 ± 1.25^{Bef}	38.80 ± 4.38^{Acdefg}
6	142.53 ± 3.10^{Aefg}	138.20 ± 5.74^{Bf}	3.44 ± 0.23^{Abcd}	2.90 ± 0.35^{Be}	118.00 ± 4.15^{Adef}	106.20 ± 7.79^{Bb}	27.97 ± 1.94^{Bf}	34.64 ± 2.46^{Agh}
12	142.47 ± 3.73^{Aefg}	134.65 ± 5.92^{Bf}	3.71 ± 0.42^{Aabcd}	3.12 ± 0.56^{Bcde}	117.67 ± 4.41^{Aef}	105.00 ± 9.38^{Bb}	28.51 ± 1.85^{Bf}	32.77 ± 4.07^{Ah}
24	141.03 ± 1.94^{Ag}	135.85 ± 4.03^{Bf}	3.63 ± 0.47^{Aabcd}	3.26 ± 0.45^{Abcde}	114.17 ± 2.99^{Aef}	106.33 ± 6.95^{Bb}	30.50 ± 1.96^{Adef}	32.77 ± 5.30^{Ah}
48	141.75 ± 2.70^{Afg}	138.87 ± 4.82^{Aef}	3.48 ± 0.22^{Abcd}	3.22 ± 0.73^{Acde}	112.67 ± 2.34^{Af}	106.17 ± 4.83^{Bb}	32.56 ± 2.42^{Bbcdef}	35.92 ± 0.92^{Afgh}
72	144.62 ± 2.47^{Adefg}	143.40 ± 3.11^{Ade}	3.44 ± 0.25^{Abcd}	3.61 ± 0.82^{Aabcde}	113.67 ± 1.03^{Af}	107.50 ± 4.76^{Bb}	34.39 ± 3.74^{Bbcde}	39.51 ± 2.09^{Acdefg}
96	147.37 ± 3.18^{Acde}	144.12 ± 2.52^{Acd}	3.94 ± 0.59^{Aabcd}	3.88 ± 0.62^{Aabc}	116.33 ± 3.39^{Aef}	109.50 ± 5.89^{Bb}	34.97 ± 2.04^{Bbcd}	38.50 ± 3.42^{Acdefg}
120	146.18 ± 2.26^{Adefg}	144.77 ± 3.70^{Acd}	4.06 ± 0.67^{Aabcd}	3.73 ± 0.35^{Aabcd}	114.83 ± 2.64^{Aef}	110.33 ± 4.37^{Bb}	35.41 ± 1.27^{Bbc}	38.16 ± 5.13^{defg}
144	145.18 ± 0.87^{Adefg}	144.77 ± 1.89^{Acd}	4.40 ± 0.45^{Aa}	4.21 ± 0.41^{Aa}	114.67 ± 1.75^{Aef}	110.83 ± 4.75^{Ab}	34.91 ± 2.36^{Bbcd}	38.14 ± 4.53^{Adefg}
168	145.72 ± 1.09^{Adefg}	144.70 ± 1.87^{Acd}	4.38 ± 0.57^{Aa}	4.28 ± 0.25^{Aa}	113.67 ± 2.16^{Af}	109.00 ± 2.97^{Bb}	36.43 ± 3.43^{Bb}	39.98 ± 2.93^{Acdef}

SID_3, strong ion difference. Different letters indicate significant ($p < 0.05$) differences among the treatments (A-B) or among the time (a-h); while shared letters indicate no significant difference.

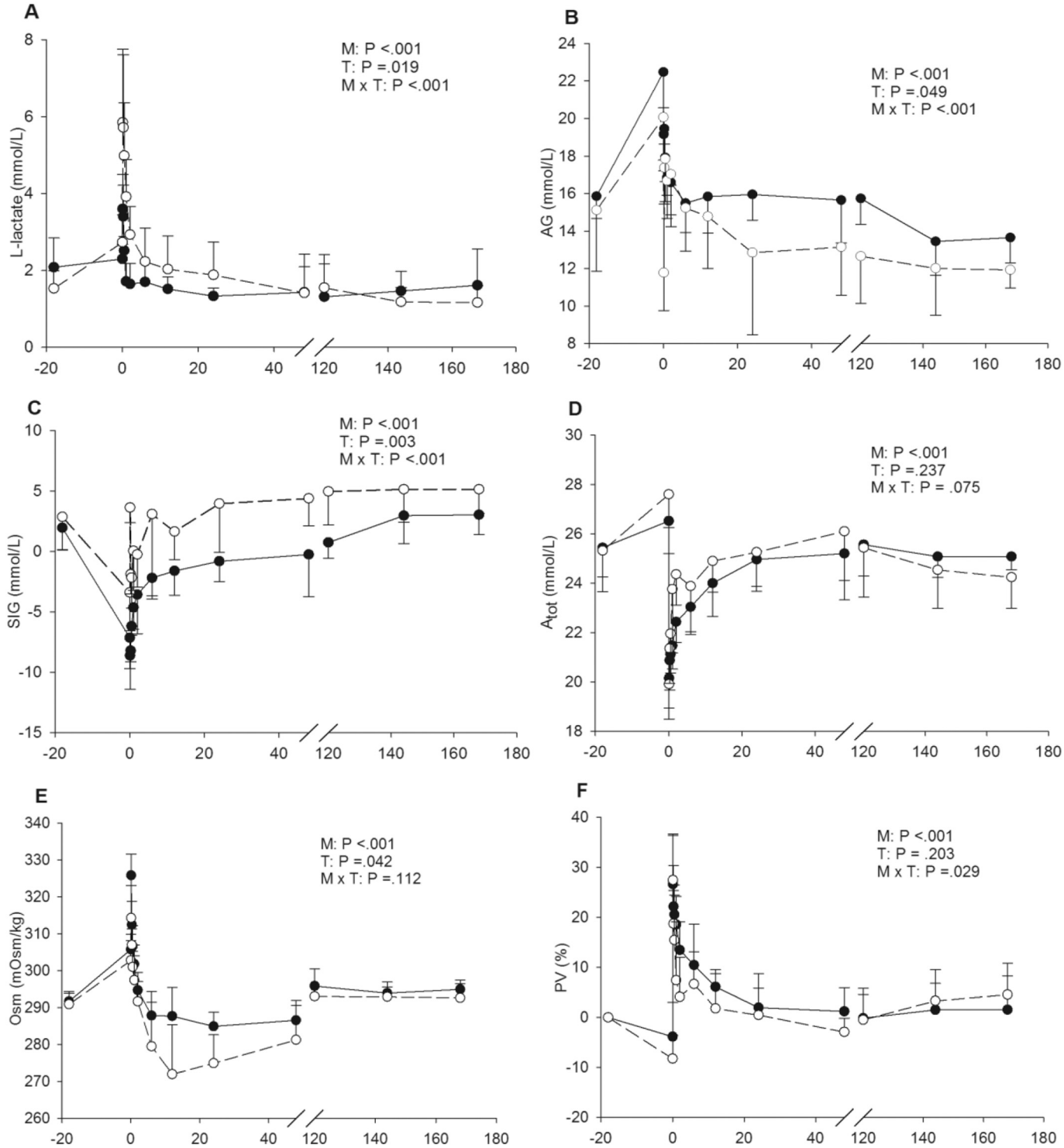

Fig. 4. Variation of plasma L-lactate, anion gap (AG), strong ion gap (SIG), total concentration of nonvolatile buffers (Atot), osmolality (Osm), and percentage change in plasma volume (%PV) of sheep with induced ARLA. Measurements were done before induction (−18 h) and before (0 h), during (5 min and 15 min) and after treatment (30 min, 1 h, 2 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h) with IV hypertonic saline solution (—●—) or hypertonic sodium bicarbonate solution (–○–), followed by intraruminal administration of water. M = moment; T = treatment; M × T = moment × treatment interaction.

treatment. The cost needed for the treatment of a 50 kg BW ewe considering diverse materials (volume of the solution, catheter, catheter extender tube, 60 mL syringes, and needle) is US $4.18 for 7% HSS (4 mL/kg) and US $11.50 for 6% HBS (6.7 mL/kg). The treatment with HBS is almost three times more expensive because of the higher cost of the hypertonic solution and the need to use a larger number of 60 mL syringes. The total time required for the execution of the therapeutic procedures, including rumen lavage, antisepsis, venous access, IV infusion of the hypertonic solution, and stomach intubation for intraruminal administration of water does not exceed 1 h.

Conventional treatment, on the other hand, is based on the IV administration of fluids for dehydration and metabolic acidosis correction. In ewes of the same weight (50 kg BW), with mild-to-moderate dehydration (8%) and moderate acidosis (BE = −10 mmol/L), the

Table 3
Mean ± standard deviations for plasma concentration of L-lactate and plasma AG, SIG and A_{tot} of sheep with induced ARLA before induction (−18 h) and before (0 h), during (0.08 h and 0.25 h) and after treatment (0.50 h, 1 h, 2 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h) with IV infusion of hypertonic saline or hypertonic sodium bicarbonate solution, followed by intraruminal administration of water.

Hour	L-lactate (mmol/L)		AG (mmol/L)		SIG (mmol/L) PT		A_{tot} (mmol/L)	
	7% HSS	6% HBS	7% HSS	6% HBS	7% HSS	6% HBS	7% HSS	6% HBS
−18	2.08 ± 0.77^{Aab}	1.53 ± 0.46^{Ade}	15.85 ± 1.17^{Acde}	15.12 ± 3.26^{Abcd}	1.95 ± 1.79^{Aab}	2.86 ± 2.75^{Aabc}	25.44 ± 1.18^{Aab}	25.32 ± 1.67^{Aab}
0	2.30 ± 0.38^{Aab}	2.73 ± 0.71^{Acde}	22.47 ± 1.89^{Aa}	20.07 ± 2.28^{Ba}	−7.13 ± 2.56^{Bfg}	−3.40 ± 3.13^{Ae}	26.52 ± 1.32^{Aa}	27.60 ± 1.34^{Aa}
0.08	3.60 ± 0.90^{Ba}	5.85 ± 1.90^{Aa}	19.15 ± 1.93^{Aabc}	11.78 ± 2.02^{Bd}	−8.61 ± 2.80^{Bg}	3.63 ± 1.25^{Aabc}	20.16 ± 1.20^{Af}	19.92 ± 1.42^{Ae}
0.25	3.40 ± 0.82^{Ba}	5.72 ± 1.89^{Aa}	19.45 ± 0.82^{Aab}	17.37 ± 1.91^{Aab}	−8.20 ± 0.91^{Bfg}	−1.89 ± 1.64^{Ade}	20.88 ± 1.20^{Aef}	21.36 ± 1.42^{Ade}
0.50	2.52 ± 0.38^{Bab}	4.98 ± 1.38^{Aab}	17.92 ± 1.28^{Abcd}	17.85 ± 2.29^{Aab}	−6.17 ± 0.76^{Befg}	−2.18 ± 2.50^{Ade}	21.12 ± 0.74^{Aef}	21.96 ± 0.87^{Acde}
1	1.72 ± 0.47^{Bb}	3.92 ± 0.97^{Abc}	16.85 ± 0.95^{Abcde}	16.68 ± 2.01^{Aabc}	−4.65 ± 1.77^{Bdefg}	0.05 ± 3.27^{Abcde}	21.48 ± 0.96^{Bef}	23.76 ± 2.58^{Abcd}
2	1.65 ± 0.53^{Bb}	2.93 ± 0.73^{Acd}	16.58 ± 2.35^{Abcde}	17.03 ± 2.18^{Aab}	−3.58 ± 3.21^{Bcdef}	−0.25 ± 2.70^{Acde}	22.44 ± 0.84^{Bdef}	24.36 ± 1.24^{Abc}
6	1.70 ± 0.49^{Ab}	2.23 ± 0.87^{Ade}	15.48 ± 1.56^{Ade}	15.24 ± 2.31^{Abcd}	−2.19 ± 1.73^{Bbcde}	3.09 ± 6.77^{Aabc}	23.04 ± 1.12^{Acde}	23.88 ± 1.85^{Abc}
12	1.52 ± 0.33^{Ab}	2.03 ± 0.87^{Ade}	15.83 ± 1.94^{Acde}	14.78 ± 2.76^{Abcd}	−1.61 ± 2.01^{Babcde}	1.64 ± 2.32^{Aabcd}	24.00 ± 1.34^{Abcd}	24.90 ± 1.26^{Ab}
24	1.33 ± 0.22^{Ab}	1.88 ± 0.86^{Ade}	15.95 ± 1.37^{Abcde}	12.85 ± 4.38^{Bd}	−0.82 ± 1.66^{Babcd}	3.96 ± 4.03^{Aabc}	24.96 ± 1.08^{Aabc}	25.26 ± 1.58^{Aab}
48	1.43 ± 0.99^{Ab}	1.42 ± 0.68^{Ade}	15.65 ± 2.28^{Acde}	13.15 ± 2.56^{Bd}	−0.25 ± 3.49^{Babcd}	4.39 ± 2.29^{Aabc}	25.20 ± 1.88^{Aabc}	26.10 ± 1.98^{Aab}
72	1.12 ± 0.26^{Ab}	1.92 ± 1.37^{Ade}	15.95 ± 1.82^{Abcde}	14.68 ± 2.63^{Abcd}	−0.16 ± 2.61^{Babcd}	2.85 ± 2.55^{Aabc}	25.20 ± 1.20^{Aabc}	26.10 ± 1.51^{Aab}
96	1.53 ± 0.73^{Ab}	1.93 ± 1.73^{Ade}	16.10 ± 1.10^{Abcde}	13.27 ± 2.02^{Bcd}	0.04 ± 1.36^{Babc}	4.66 ± 1.61^{Aab}	25.92 ± 1.64^{Aab}	25.80 ± 1.97^{Aab}
120	1.32 ± 0.85^{Ab}	1.55 ± 0.87^{Ade}	15.73 ± 1.38^{Acde}	12.65 ± 2.51^{Bd}	0.74 ± 1.31^{Babc}	4.97 ± 2.78^{Aa}	25.56 ± 2.12^{Aab}	25.44 ± 1.15^{Aab}
144	1.47 ± 0.51^{Ab}	1.18 ± 0.38^{Ae}	13.45 ± 1.80^{Ae}	12.02 ± 2.51^{Ad}	2.96 ± 2.33^{Aa}	5.14 ± 2.73^{Aa}	25.08 ± 0.84^{Aabc}	24.54 ± 1.55^{Ab}
168	1.62 ± 0.94^{Ab}	1.17 ± 0.44^{Ae}	13.65 ± 1.34^{Ae}	11.93 ± 0.97^{Ad}	3.03 ± 1.62^{Aa}	5.14 ± 1.99^{Aa}	25.08 ± 0.54^{Aabc}	24.24 ± 1.26^{Abc}

AG, anion gap; SIG, strong ion gap; A_{tot}, total concentration of nonvolatile buffers. Different letters indicate significant ($p < 0.05$) differences among the treatments (A-B) or among the time (a-g); while shared letters indicate no significant difference.

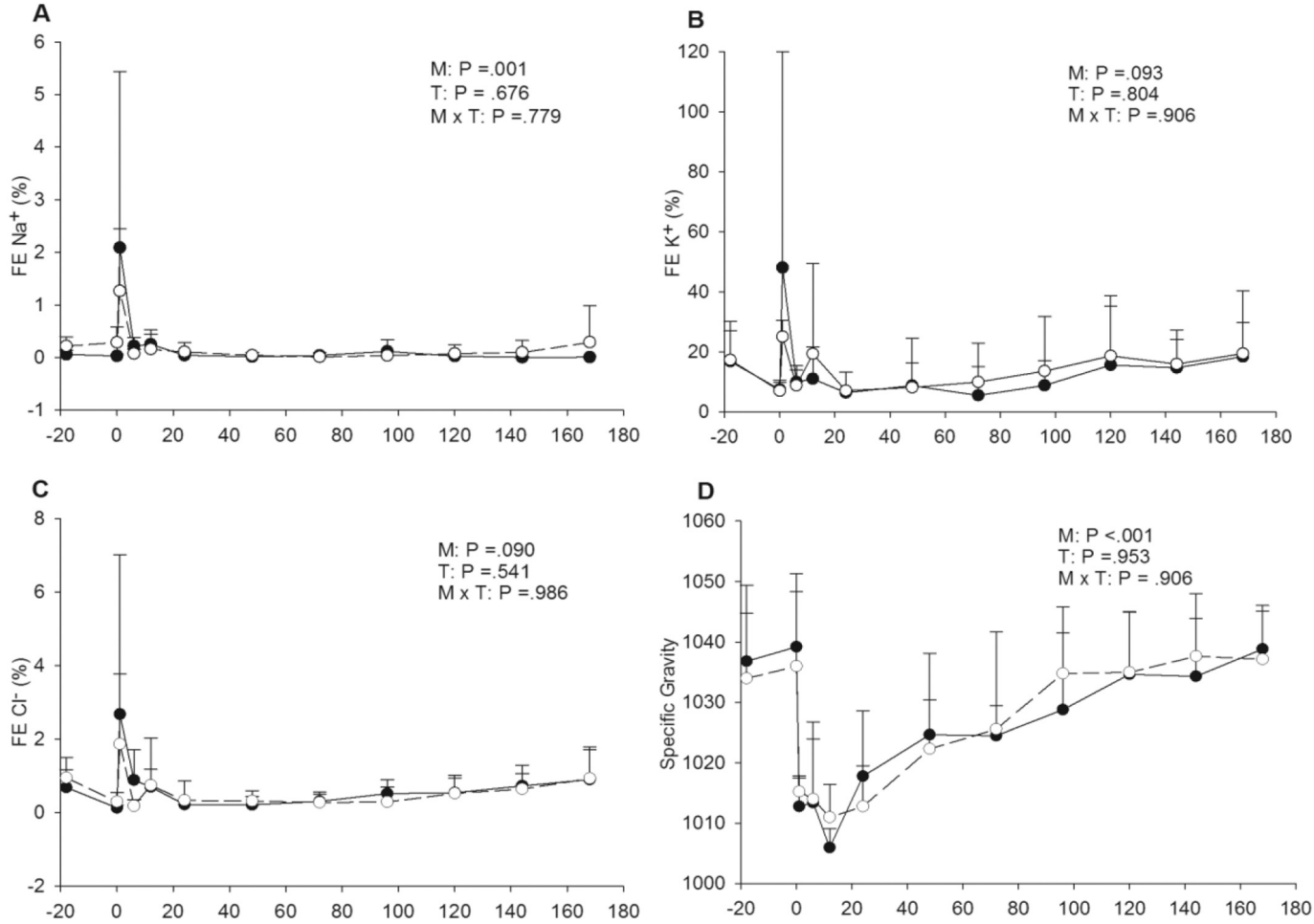

Fig. 5. Variation of fractional excretion of Na^+, K^+, and Cl^- and urinary specific gravity of sheep with induced ARLA. Measurements were done before induction (−18 h) and before (0 h) and after treatment (1 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h) with IV hypertonic saline solution (—●—) or hypertonic sodium bicarbonate solution (–○–), followed by intraruminal administration of water. M = moment; T = treatment, M × T = moment × treatment interaction.

Table 5
Mean ± standard deviations of fractional excretion of Na^+, K^+, and Cl^- and urinary specific gravity of sheep with induced ARLA before induction (−18 h) and before (0 h) and after treatment (1 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h) with IV infusion of hypertonic saline or hypertonic sodium bicarbonate solution, followed by intraruminal administration of water.

Hour	FE Na^+ (%)		FE K^+ (%)		FE Cl^- (%)		Specific gravity	
	7% HSS	6% HBS	7% HSS	6% HBS	7% HSS	6% HBS	7% HSS	6% HBS
−18	0.06 ± 0.07^{Ab}	0.22 ± 0.18^{Ab}	16.92 ± 13.25^{Aa}	17.38 ± 9.70^{Aa}	0.69 ± 0.49^{Aa}	0.95 ± 0.55^{Aa}	1036.83 ± 12.56^{Aab}	1034.00 ± 10.73^{Aab}
0	0.03 ± 0.03^{Ab}	0.29 ± 0.30^{Ab}	7.48 ± 2.40^{Aa}	7.04 ± 3,66^{Aa}	0.13 ± 0.07^{Aa}	0.30 ± 0.24^{Aa}	1039.20 ± 12.13^{Aab}	1036.00 ± 12.33^{Aa}
1	2.09 ± 3.34^{Aa}	1.27 ± 1.19^{Aa}	48.07 ± 71.90^{Aa}	25.13 ± 5.40^{Aa}	2.68 ± 4.33^{Aa}	1.87 ± 1.89^{Aa}	1012.80 ± 5.02^{Abc}	1015.25 ± 2.22^{Aab}
6	0.22 ± 0.17^{Ab}	0.08 ± 0.09^{Ab}	10.05 ± 5.43^{Aa}	8.93 ± 5.07^{Aa}	0.89 ± 0.82^{Aa}	0.19 ± 0.16^{Aa}	1013.40 ± 13.39^{Abc}	1014.00 ± 10.00^{Ab}
12	0.25 ± 0.27^{Ab}	0.16 ± 0.29^{Ab}	11.11 ± 10.65^{Aa}	19.38 ± 30.13^{Aa}	0.70 ± 0.48^{Aa}	0.75 ± 1.28^{Aa}	1006.00 ± 3.08^{Ac}	1011.00 ± 5.48^{Ab}
24	0.04 ± 0.03^{Ab}	0.11 ± 0.17^{Ab}	6.42 ± 6.97^{Aa}	7.09 ± 6.21^{Aa}	0.22 ± 0.11^{Aa}	0.34 ± 0.52^{Aa}	1017.80 ± 10.83^{Aabc}	1012.80 ± 6.72^{Ab}
48	0.02 ± 0.02^{Ab}	0.04 ± 0.05^{Ab}	8.82 ± 15.86^{Aa}	8.25 ± 8.16^{Aa}	0.22 ± 0.23^{Aa}	0.32 ± 0.28^{Aa}	1024.67 ± 5.72^{Aab}	1022.33 ± 15.82^{Aab}
72	0.04 ± 0.05^{Ab}	0.01 ± 0.01^{Ab}	5.55 ± 9.64^{Aa}	10.01 ± 13.04^{Aa}	0.31 ± 0.19^{Aa}	0.28 ± 0.29^{Aa}	1024.50 ± 17.22^{Aab}	1025.60 ± 3.85^{Aab}
96	0.12 ± 0.23^{Ab}	0.04 ± 0.06^{Ab}	8.90 ± 8.25^{Aa}	13.66 ± 18.22^{Aa}	0.52 ± 0.38^{Aa}	0.30 ± 0.40^{Aa}	1028.80 ± 12.77^{Aab}	1034.80 ± 11.01^{Aa}
120	0.03 ± 0.05^{Ab}	0.08 ± 0.17^{Ab}	15.72 ± 19.71^{Aa}	18.70 ± 20.03^{Aa}	0.54 ± 0.41^{Aa}	0.53 ± 0.50^{Aa}	1034.67 ± 10.25^{Aa}	1035.00 ± 10.00^{Aa}
144	0.00 ± 0.00^{Ab}	0.10 ± 0.23^{Ab}	14.82 ± 12.54^{Aa}	16.00 ± 8.23^{Aa}	0.73 ± 0.57^{Aa}	0.65 ± 0.42^{Aa}	1034.33 ± 9.52^{Aa}	1037.67 ± 10.31^{Aa}
168	0.01 ± 0.01^{Ab}	0.29 ± 0.70^{Ab}	18.48 ± 21.98^{Aa}	19.52 ± 10.35^{Aa}	0.91 ± 0.89^{Aa}	0.95 ± 0.77^{Aa}	1038.83 ± 7.22^{Aa}	1037.17 ± 7.96^{Aa}

FE, fractional excretion. Different letters indicate significant ($p < 0.05$) differences among the treatments (A-B) or among the time (a-c); while shared letters indicate no significant difference.

Table 4
Mean ± standard deviations for plasma osmolality and percentage of plasma volume (PV) of sheep with induced ARLA before induction (−18 h) and before (0 h), during (0.08 h and 0.25 h) and after treatment (0.50 h, 1 h, 2 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h, 144 h, and 168 h) with IV infusion of hypertonic saline or hypertonic sodium bicarbonate solution, followed by intraruminal administration of water.

Hour	Osmolality (mOsm/kg)		PV (%)	
	7% HSS	6% HBS	7% HSS	6% HBS
−18	291.73 ± 2.22^{Aefgh}	290.93 ± 3.52^{Aef}	0 ± 0^{Aef}	0 ± 0^{Ade}
0	305.78 ± 2.38^{Acd}	302.80 ± 7.13^{Abc}	−3.84 ± 6.83^{Af}	−8.23 ± 4.70^{Ae}
0.08	325.83 ± 5.78^{Aa}	314.28 ± 8.78^{Ba}	26.58 ± 9.76^{Aa}	27.43 ± 9.17^{Aa}
0.25	312.45 ± 6.33^{Ab}	307.02 ± 4.32^{Aab}	22.13 ± 8.21^{Aab}	18.71 ± 6.61^{Aab}
0.50	306.62 ± 5.63^{Abc}	301.02 ± 4.27^{Abcd}	20.53 ± 5.90^{Aabc}	15.44 ± 9.03^{Abc}
1	301.80 ± 5.18^{Acde}	297.45 ± 6.62^{Abcde}	18.54 ± 5.67^{Aabc}	7.42 ± 11.68^{Bcd}
2	294.75 ± 2.31^{Aefgh}	291.68 ± 7.87^{Adef}	13.45 ± 5.65^{Abcd}	4.12 ± 7.93^{Bd}
6	287.88 ± 6.50^{Afgh}	279.53 ± 11.93^{Bg}	10.45 ± 2.65^{Acde}	6.66 ± 12.02^{Acd}
12	287.73 ± 7.77^{Afgh}	271.98 ± 13.39^{Bg}	6.10 ± 3.42^{Adef}	1,81 ± 6.93^{Ade}
24	284.95 ± 3.82^{Ah}	274.95 ± 7.72^{Bg}	1.98 ± 3.90^{Aef}	0.49 ± 8.20^{Ade}
48	286.60 ± 5.36^{Agh}	281.28 ± 9.33^{Afg}	1.20 ± 4.77^{Aef}	−2.89 ± 2.74^{Ade}
72	292.60 ± 4.70^{Aefgh}	290.27 ± 6.25^{Aef}	1.07 ± 5.23^{Aef}	−3.01 ± 2.26^{Ade}
96	298.22 ± 6.41^{Adef}	291.85 ± 5.17^{Ade}	−1.68 ± 4.94^{Af}	−1.69 ± 5.02^{Ade}
120	295.90 ± 4.58^{Aefg}	293.08 ± 7.45^{Acde}	−0.14 ± 5.92^{Af}	−0.46 ± 5.04^{Ade}
144	293.97 ± 1.70^{Aefgh}	292.95 ± 3.99^{Acde}	1.51 ± 5.29^{Aef}	3.32 ± 6.23^{Ad}
168	295.00 ± 2.44^{Aefgh}	292.67 ± 3.84^{Acde}	1.55 ± 6.75^{Aef}	4.55 ± 6.29^{Ad}

Different letters indicate significant ($p < 0.05$) differences among the treatments (A-B) or among the time (a-h); while shared letters indicate no significant difference.

rational option would be to administer 1 L of 1.3% $NaHCO_3$ solution and 3 L of Lactated Ringer's Solution by continuous infusion. The total cost including all the necessary materials, would be US $10.52 and taking into account the infusion rate of 20 mL/kg/h, it will take 4 h for the administration of these solutions. There is practically no difference between the cost of conventional treatment and the protocol with 6% HBS. However, the practicality and the quickness of the treatment with 6% HBS are unquestionable advantages.

5. Conclusion

The two treatment protocols tested in this study are effective in correcting the imbalances in sheep with ARLA. Although HBS treatment promoted a more rapid correction of metabolic acidosis, clinical recovery, measured by appetite return and forestomach motor function restoration, occurred at the same rate in both treatments. Since it is cheaper, the protocol with 7% HSS can be used successfully as the protocol of choice in cases with mild-to-moderate acidosis. The protocol with 6% HBS could be indicated for the most severe cases of metabolic acidosis.

Declaration of Competing Interest

None.

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