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Comparison of the alkalizing abilities between 1.35% sodium bicarbonate solutions with and without dextrose in healthy calves

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ABSTRACT. The present study aimed to clarify the alkalizing ability of 1.35% isotonic sodium bicarbonate solution (ISBS), which did not contain dextrose, compared with that of 1.35% isotonic bicarbonate sodium solution containing 4.03% dextrose (ISBD) in healthy calves. The calves were intravenously administered with 20.7 mL/kg of the solutions for 30 min as the volume required to correct base deficit of 10 mM. ISBS increased the blood pH, HCO_3^-, and base excess from 7.44 ± 0.02, 29.6 ± 1.9 mM, and 5.3 ± 2.1 mM to 7.49 ± 0.02, 36.9 ± 2.3 mM, and 13.5 ± 2.6 mM respectively (P<0.05). These factors for the ISBD group increased from 7.41 ± 0.02, 29.0 ± 1.1 mM, and 4.5 ± 1.3 mM to 7.43 ± 0.02, 33.5 ± 1.9 mM, and 9.5 ± 1.7 mM (P<0.05), respectively. Furthermore, in the ISBD group, the relative plasma volume and blood glucose level increased while the K^+ level decreased, which did not occur in the ISBS group. Therefore, the results revealed that ISBS had better alkalizing ability in calves than ISBD.

KEYWORDS: calf, dextrose, hyperkalemia, isotonic sodium bicarbonate, metabolic acidosis

Metabolic acidosis is a common consequence of diarrhea in calves [3, 6, 8, 10, 18, 20]. The main causes are loss of bicarbonate ions (HCO_3^-) from the intestinal tract due to diarrhea and impaired excretion of hydrogen ions (H^+) in the kidney [24]. In severe acidosis, buffering of the acid-base balance in the blood is impaired, and H^+ accumulates in the cells, which can lead to the death of animals [4]. Thus, alkalinization of the blood is an important treatment for this disease [1, 2]. For moderate or severe acidosis, sodium bicarbonate ($NaHCO_3$) is administered intravenously after the dose is calculated from the determination of blood gas and clinical symptoms [4]. It is recommended that 1.35% isotonic $NaHCO_3$ solution (ISBS) is administered intravenously at a rate of 30–40 mL/kg/hr because there is a risk of paradoxical acidosis of the cerebrospinal fluid caused by rapid administration of hypertonic $NaHCO_3$ solution [1, 2, 5]. In clinical practice, if the veterinarians do not have ISBS, a solution of hypertonic $NaHCO_3$ and 5% glucose solution is used instead [16, 27]. However, few studies have evaluated the effects of this combination. Even if the amount of $NaHCO_3$ is the same as ISBS, the components and osmotic pressure are different, so it is unclear whether these solutions have the same effects on cows. The present study aimed to clarify the alkalizing ability of ISBS without dextrose compared with solutions containing 4.03% dextrose (ISBD) in healthy calves.

MATERIALS AND METHODS

All procedures were performed in accordance with the standards outlined by the Good for the Care and Use of Laboratory Animals and the Clinical Practice of the Central Research Institute, Nippon Zenyaku Kogyo Co., Ltd., Koriyama, Japan (NZ66). Four healthy Holstein calves were studied, with an average body weight of 98.5 ± 39.4 kg. ISBS was used as an alkalinization fluid (isotonic sodium bicarbonate solution, Nippon Zenyaku Kogyo Co., Ltd.) (Table 1). Additionally, for comparison with ISBS, the combination of 7% hypertonic $NaHCO_3$ (sodium bicarbonate solution, Nippon Zenyaku Kogyo Co., Ltd.) and 5% dextrose (vitamin B_1 added 5% dextrose solution, Nippon Zenyaku Kogyo Co., Ltd.) was used for ISBD (Table 1).

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Table 1. Median (minimum–maximum) of osmolarity and pH of each solution

Solution	Osmolarity	pH
1.35% isotonic $NaHCO_3$ solution (ISBS)	292 (291–294)	7.71 (7.57–7.74)
7% hypertonic $NaHCO_3$ solution	1,414 (1,407–1,421)	7.88 (7.84–7.92)
5% dextrose solution	301 (300–302)	3.90 (3.83–3.94)
1.35% isotonic $NaHCO_3$ solution with 4.03% dextrose (ISBD)	541 (540–544)	8.18 (8.16–8.21)

The median (minimum–maximum) of osmolarity and pH was determined by measurement of 5 products of each solution.

Assuming a base deficit of 10 mM, the dose of ISBS for each calf was calculated as follows.

Base needed (mmol)=BW (kg) × 10 mM × 1/3 [13, 18]

ISBS (mL)=Base needed (mmol)/161 (mmol) × 1,000 (mL)

ISBS (mL/kg)≈20.7 (mL/kg)

The dose of ISBD was first calculated by the following with the amount of 7% $NaHCO_3$ solution so that the amount of $NaHCO_3$ was the same as that of ISBS.

7% hypertonic $NaHCO_3$ (mL)=ISBS (mL) × 161 (mmol)/ 833 (mmol)

Furthermore, the total volume of 5% dextrose solution mixed with 7% hypertonic $NaHCO_3$ calculated above was adjusted to be the same as that of ISBS. The ratio of 5% dextrose / 7% hypertonic $NaHCO_3$ was 4.17, so ISBD contained 4.03% dextrose.

Each solution was administered intravenously to the calves using the cross-over method with a one-week interval between the first and second tests by 2 × 2 cross-over method (n=4 in each group). In particular, 16-gauge catheters were placed in the bilateral jugular veins 15 min before administration. The solution was administered via the right jugular vein for 30 min.

The venous blood was collected from the left jugular vein using a heparinized 1-mL syringe before administration (0 min), 15, 30, 45, 60, 90, 120, 180, and 240 min after administration. The blood samples were analyzed for Na^+, K^+, Cl^-, pH, HCO_3^-, base excess (BE), total carbon dioxide (TCO_2), carbon dioxide pressure (PCO_2), glucose (GLU), hematocrit value (Ht), and hemoglobin (Hb) using an automatic analyzer (i-STAT 200A, Abbott Japan LLC., Matsudo, Japan) at 37°C within 5 min of collection. The changes in relative plasma volume (rPV) were calculated from Hb and Ht, using the accepted formulas [19].

Statistical software was used for all the statistical analyses (StatLight, version 2.0, Yukms Co., Ltd., Tokyo, Japan). First, Bartlett's test was performed to confirm equal variances within each group. Then, the data were analyzed by one-way ANOVA to confirm significant changes after administration. Finally, the Dunnett's test was used to analyze whether the data of each point differed from pre-administration. In the comparison between the ISBS and ISBD group, F test was performed to confirm the variance at each point, and then the data were compared using the Student's *t*-test or Welch's *t*-test based on the results. *P*-values <0.05 were considered significant. Herein, the data is reported as the means ± standard deviation (SD).

RESULTS

The blood pH of the ISBS and ISBD groups were 7.44 ± 0.02 and 7.41 ± 0.02 before administration and increased to 7.49 ± 0.02 and 7.43 ± 0.02 after 30 min, respectively. The pH due to ISBS was maintained at significantly higher values than ISBD from 45 to 90 min (Fig. 1). The HCO_3^- levels of the ISBS and ISBD groups were 29.6 ± 1.9 and 29.0 ± 1.1 mM at 0 min and increased to 36.9 ± 2.3 and 33.5 ± 1.9 mM at 30 min, respectively (Fig. 1). The ISBS group showed significantly higher HCO_3^- levels than the ISBD group at 30, 45 and 90 min (Fig. 1). The BE levels of the ISBS and ISBD groups were 5.3 ± 2.1 and 4.5 ± 1.3 mM at 0 min and increased to 13.5 ± 2.6 and 9.5 ± 1.7 mM at 30 min, respectively (Fig. 1). The ISBS group showed significantly higher BE levels than the ISBD group at 30, 45, 90, and 240 min (Fig. 1).

The TCO_2 levels of ISBS group was 30.8 ± 1.7 mM at 0 min and increased to 38.3 ± 2.2 mM at 30 min. These levels increased significantly from 15 to 60 min. In ISBD group, the TCO_2 levels were higher than pre-administration at 15, 180 and 240. This increased to the highest level of 35.3 ± 2.2 mM at 180 min (Fig. 2). The PCO_2 level of ISBS group increased to 48.8 ± 1.4 mmHg at 30 min (Fig. 2).

The rPV of the ISBS group increased to 115.0 ± 6.7% at 15 min. In the ISBD group, the rPV increased to 118.0 ± 5.4% at 30 min, and tended to be higher than the maximum level of the ISBS group (Fig. 3). The GLU levels increased from 88.8 ± 12.0 mg/dL to 356.8 ± 32.0 mg/dL in the ISBD group (Fig. 3).

No significant changes were confirmed in the Na^+ levels of either group (Fig. 4). The K^+ level of the ISBS group tended to decrease with the administration, but no significant difference was observed (Fig. 4). In the ISBD group, the K^+ level decreased significantly from 4.08 ± 0.31 to 3.18 ± 0.29 mM after 45 min, and the level at 120 min remained lower than that at 0 min. The Cl^- levels of both groups decreased 30 min after administration (Fig. 4).

DISCUSSION

The present study compared the alkalizing abilities of ISBS and ISBD in healthy calves. In the ISBS group, we observed that the pH, HCO_3^-, and BE increased, as expected. The BE increased by about 10 mM compared with the concentration before administration. In contrast, the ISBD data did not increase as much as those of ISBS. Therefore, it was revealed that ISBS had better alkalizing ability than ISBD.

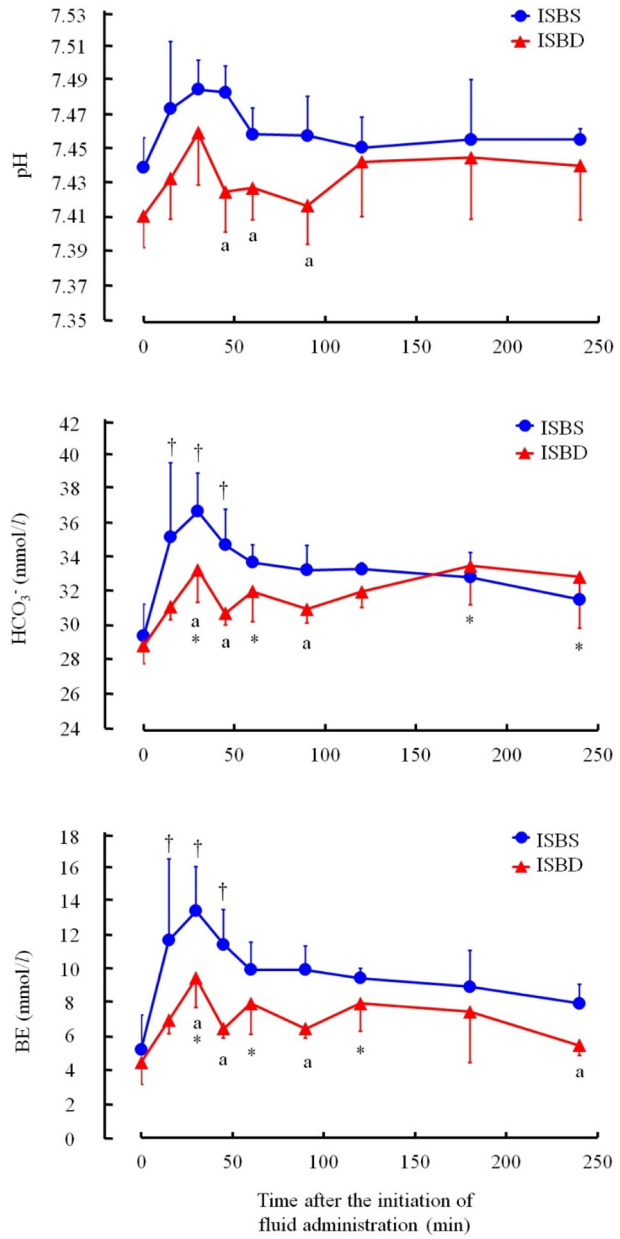

Fig. 1. Graphs depicting the blood pH, HCO_3^- and base excess (BE) levels in calves given ISBS and ISBD. The alphabet (a) indicates the data were significantly different at each time point between ISBS and ISBD groups using the Student's *t*-test or Welch's *t*-test. ISBS: isotonic $NaHCO_3$ solution, ISBD: ISBS with 4.03% dextrose. Daggers (†) and asterisks (*) indicate the data was significantly different from the pre-value (Time=0 hr) at each measurement time point after the administration of ISBS and ISBD using Dunnett's test.

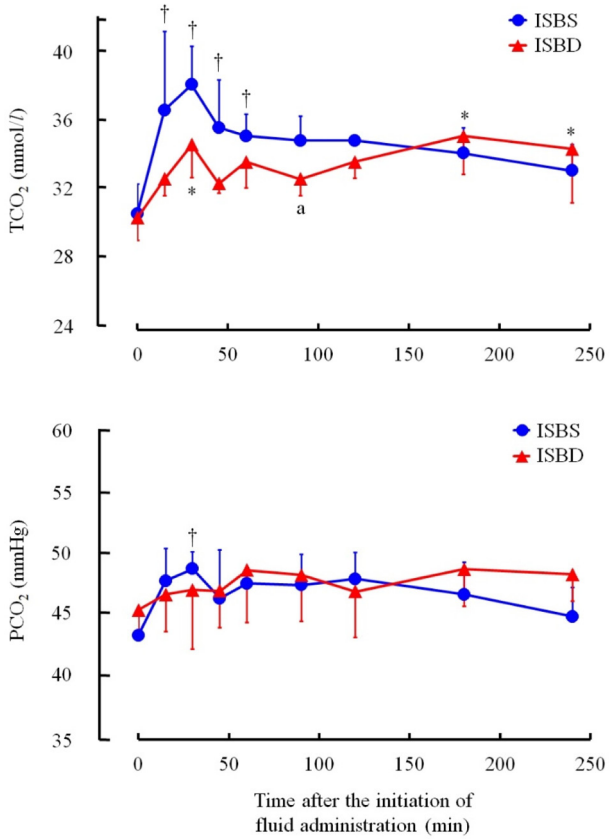

Fig. 2. Graphs depicting the blood TCO_2 and PCO_2 levels in calves given ISBS and ISBD. The alphabet (a) indicates the data were significantly different at each time point between ISBS and ISBD groups using the Student's *t*-test or Welch's *t*-test. ISBS: isotonic $NaHCO_3$ solution, ISBD: ISBS with 4.03% dextrose. Daggers (†) and asterisks (*) indicates the data was significantly different from the pre-value (Time=0 hr) at each measurement time point after the administration of ISBD using Dunnett's test.

ISBS is known to be safe and slowly improve acidosis and rPV [5, 11]. In this study, the TCO_2 increased significantly in ISBS and ISBD group. Especially, TCO_2 of ISBS group changed according to the levels of HCO_3^- and BE. It was considered that the carbonic acid-bicarbonate buffer system acted by administration of ISBS. However, PCO_2 increased only slightly at 30 min in the ISBS group. These changes were not considered to affect severely. Therefore, similar to previous studies, we observed that ISBS increased HCO_3^-, BE, and rPV without significantly affecting PCO_2 and electrolytes. The results suggest that ISBS was a suitable fluid solution for the improvement of calves presenting dehydration and acidosis.

On the other hand, ISBD tended to have a lower alkalinizing ability than ISBS. Furthermore, ISBS and ISBD contained the same amount of $NaHCO_3$ but did not have the same effects on the calves. For example, the effects of ISBD on rPV, GLU, and electrolytes

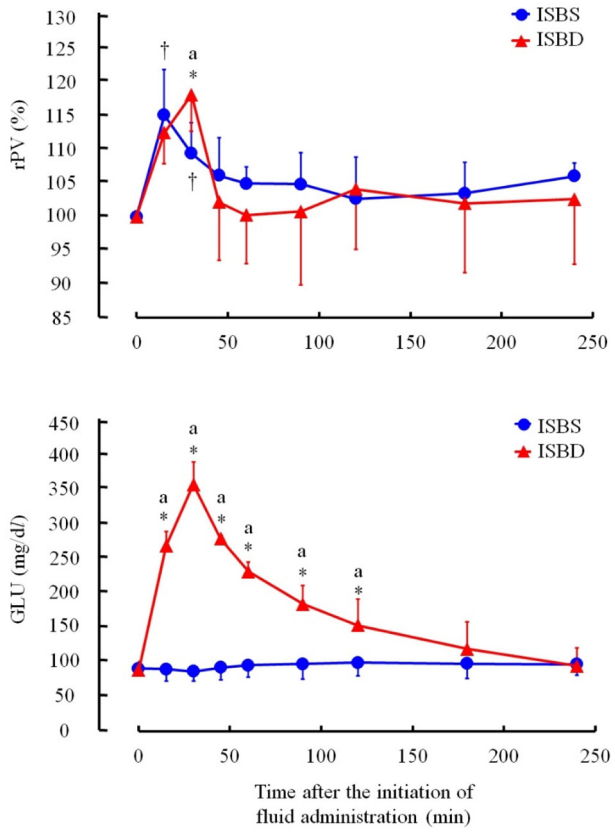

Fig. 3. Graphs depicting the rPV and glucose (GLU) levels in calves given ISBS and ISBD. The alphabet (a) indicates the data were significantly different at each time point between ISBS and ISBD groups using the Student's *t*-test or Welch's *t*-test. ISBS: isotonic $NaHCO_3$ solution, ISBD: ISBS with 4.03% dextrose. Daggers (†) and asterisks (*) indicate the data was significantly different from the pre-value (Time=0 hr) at each measurement time point after the administration of ISBS and ISBD using Dunnett's test.

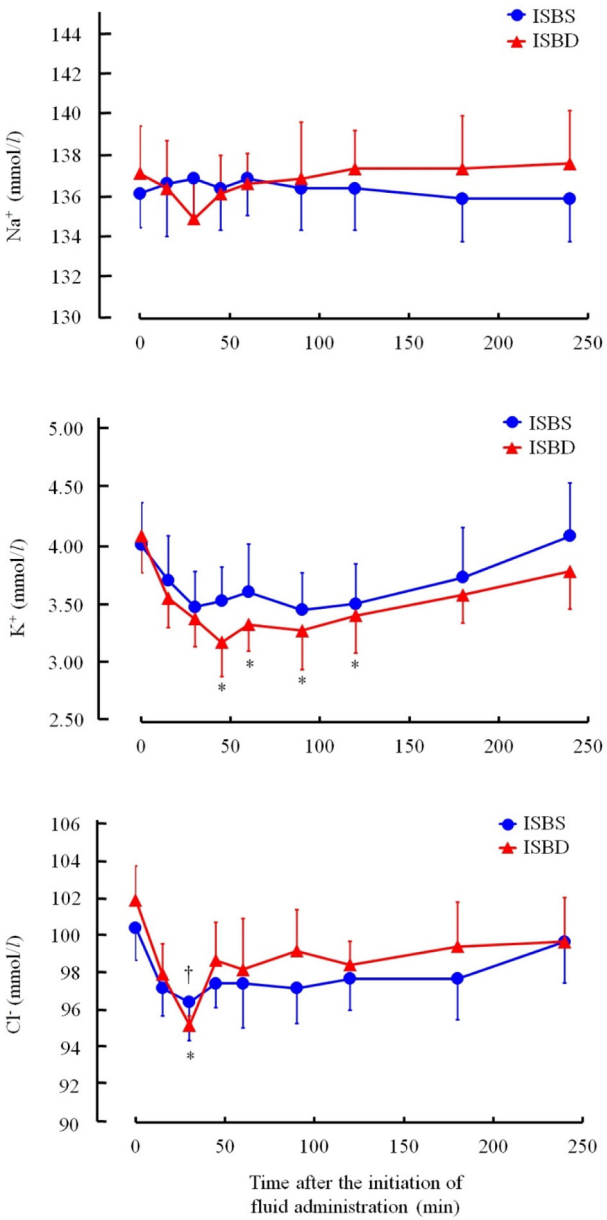

Fig. 4. Graphs depicting the blood Na^+, K^+ and Cl^- levels in calves given ISBS and ISBD. ISBS: isotonic $NaHCO_3$ solution, ISBD: ISBS with 4.03% dextrose. Dagger (†) and asterisks (*) indicate the data was significantly different from the pre-value (Time=0 hr) at each measurement time point after the administration of ISBS and ISBD using Dunnett's test.

were different from those of ISBS. The osmolarity ratio of ISBS was 1, whereas that of ISBD was about 2. When a solution with a high osmolarity ratio is administered intravenously, the intracellular and interstitial fluid temporarily move to blood vessels, increasing rPV [21]. An increase in the rPV was one of the factors that suppressed the rise of blood pH caused by dilutional acidemia. When $NaHCO_3$ is administered into the blood vessel, it moves H^+ from the intracellular to the extracellular fluid, and K^+ is pulled into the cells [4, 25]. The K^+ level decreased when both solutions were administered; however, the level is significantly lower for ISBD than for ISBS. When blood glucose is absorbed into the cell, K^+ also moves into the cell [9, 15, 25]. The transport of K^+ and H^+ accompanying the absorption of blood glucose was also considered to be the second factor that prevented the increase in blood pH. In diarrhea of calves, not only dehydration and metabolic acidosis but also hyperkalemia is one of the serious pathological conditions [7, 12, 22, 25]. In addition, it has been reported that hypoglycemia often occur in calf diarrhea and administration of intravenous dextrose is effective for the condition [23, 26]. Although the alkalinizing ability is lower compared with ISBS, ISBD may be a suitable fluid solution for diarrhea of calves with hyperkalemia and hypoglycemia.

Moreover, ISBD is a combination of 7% hypertonic $NaHCO_3$ and 5% dextrose solutions, which has a pH slightly higher than the ISBS and 7% $NaHCO_3$ solutions (Table 1). When acidic dextrose or saline solutions are mixed with alkaline $NaHCO_3$ solution, CO_2 gas is generated, and the pH of the solution changes [14, 28]. However, only minimal amounts of gas are generated, and the concentration of HCO_3^- in the solution is almost unchanged [14, 28]. The pH standard of $NaHCO_3$ solution is 7.0–8.5 [17], and the pH of ISBD is in this range. Therefore, the amounts of HCO_3^- contained in ISBS and ISBD are believed to be similar.

In conclusion, ISBS and ISBD contain the same concentration of $NaHCO_3$, but the solutions with or without dextrose in them have different effects on the blood of calves. The solution containing dextrose enhances the increase of rPV and decrease of blood K^+ level but reduces the alkalizing ability compared with ISBS. Thus, we observed that ISBS had better alkalizing ability than ISBD.

CONFLICT OF INTEREST. The authors declare no conflicts of interest.

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