Comparison of the Alkalizing Effects of Bicarbonate Precursors in Calves with Experimentally Induced Metabolic Acidosis

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NOTE Pharmacology

Sodium bicarbonate is very effective in treating acute and severe metabolic acidosis because it has a rapid effect and induces greater changes in base excess (BE) [10, 12–15, 18, 20]. However, a rapid infusion or overdosage of sodium bicarbonate has been associated with extracellular fluid hyperosmolarity, cerebrospinal fluid acidosis, intracranial hemorrhage, and a decrease in the availability of cellular oxygen [10]. Therefore, bicarbonate precursors such as sodium lactate and acetate should be used to correct mild metabolic acidosis [3]. Kasari et al. [14] demonstrated that 50 mM of sodium acetate has a superior alkalizing effect compared with 50 mM of sodium lactate because it induces its alkalizing effect more rapidly than sodium lactate did. However, commercial acetated Ringer’s solution has a superior alkalizing effect compared with commercial lactated Ringer’s solution contain only 28 mM of bicarbonate precursor. Therefore, the present study was designed to confirm whether commercial acetated Ringer’s solution has a superior alkalizing effect compared with commercial lactated Ringer’s solution in treatment of mild metabolic acidosis in calves.

All procedures were in accordance with the Guide for Care and Use of Laboratory Animals approved by the National Research Council Guidelines for the Care and Use of Laboratory Animals [17]. Twenty healthy Holstein male calves, 50.0 ± 4.1 day-old weighing 58.3 ± 4.9 kg, were enrolled in this study. All calves were induced into mild metabolic acidosis by the following acidification procedure. The calves were primed with cold milk, which was prepared by adding 400 g of commercial milk replacer (Mo-toku milk 02 for calf, Kagakusiryou CO., Tokyo) to 3 l of cold water (below 4°C) and given twice a day for 2 days using a feeding tube. For the next 2 days, calves were fed warm milk with stearic acid, which was prepared by adding 200 g of commercial milk replacer and 100 g of stearic acid to 1.5 l of warm water (approximately 36°C), twice a day. The acidification procedure in this study significantly decreased venous HCO3− and base excess (BE) concentration, from 2.9 ± 1.5 to −8.9 ± 2.8 mM (p<0.001). In general, a calf with a BE<−10 mM is diagnosed with severe metabolic acidosis [3]. Therefore, the acidification procedure used in this study was a suitable method of inducing mild acidosis model.

After completion of these procedures, all calves were intravenously (IV) administered one of four commercial fluids at a dose of 80 ml/kg BW and a flow rate of 40 ml/kg/hr (5 calves per fluid). The commercial fluids used in this study were as follows (table 1): isotonic saline (ISS, Nippon Zenyaku Kogyo, Co., Ltd, Fukushima, Japan), DL-lactated Ringer’s solution (DLR, Nippon Zenyaku Kogyo), L-lactated Ringer’s solution (LR, Terumo Co., Tokyo, Japan) and acetated Ringer’s solution (AR, Terumo Co.). Berchtold [3] described the algorithm for initial on-farm fluid therapy of calves with dehydrate and mild acidosis. The fluid volume for calves (average weight: 50 kg) with dehydrate and mild acidosis calf is 4 l (80 ml/kg) in this algorithm.

Venous blood samples were anaerobically collected into heparinized 1-ml syringes from the left jugular vein immediately before (Pre), at 15, 30, 45, 60, 90 and 120 min after and a day after initiation of fluid infusion. The blood samples were analyzed for venous pH and blood gases using an automatic gas analyzer at 37°C (model 248, Bayer Medical, Tokyo, Japan), and the values were automatically corrected...
Some venous blood samples were used to determine hemoglobin concentrations (Hb) and hematocrit values (Ht) using an automatic cell counter (MEK-6248, Nihon Koden, Tokyo, Japan) in order to calculate the relative plasma volume (rPV) using accepted formulas [9, 20].

Data are expressed as means ± standard deviation. Measured dependent variables were compared among groups for each sample collection period using repeated-measures ANOVA. Within groups, mean values for each dependent
variable were compared with the pre values, using the Bonferroni test after analysis of ANOVA as a post-hoc test. Differences were considered significant at p<0.05.

Clinical signs, such as moist rales on auscultation, moist cough, jugular vein congestion, ophthalmoptosis, salivation and arrhythmia, were not observed throughout fluid infusion and remained constant throughout the experimental period for all the groups. The rPV in the ISS, DLR, LR and AR groups were significantly increased during the fluid infusion period, reaching 136.8 ± 9.9%, 136.3 ± 7.7%, 144.0 ± 21.4% and 140.4 ± 9.4% at t=90 min, respectively (p<0.05).

No significant differences were observed in the rPV values among the different fluids.

Figure 1 shows the sequential changes in the venous HCO₃⁻ and BE concentrations in the calves that received alkalizing fluid. ISS induced significant decreases in the HCO₃⁻ and BE concentrations during the infusion period, from 17.0 ± 2.9 at Pre to 15.2 ± 2.0 mM at t=120 (p<0.05) and from -8.9 ± 2.6 at Pre to -11.1 ± 2.3 mM at t=120 (p<0.05), respectively. The average decrement of BE from the Pre value was 2.5 ± 1.0 mM at t=90 min (p<0.05) in the calves that received ISS. This result indicates that IV infusion of ISS might cause dilution acidosis.

In the DLR group, the above parameters were not affected by DLR infusion and remained constant throughout the experiment. The BE and HCO₃⁻ concentrations in the calves that received LR were also unaffected until t=60 min, but slight increases in these parameters were observed after t=90. Although the metabolism of D-lactate is slower than that of L-lactate in calves because calves have a negligible quantities of D-lactate dehydrogenase [11, 12], both DLR and AR are inappropriate as an alkalinizing fluids in calves with metabolic acidosis.

In contrast, AR induced significant increases in the HCO₃⁻ and BE concentrations 90 min after initiation of fluid infusion (p<0.05, respectively). During the fluid infusion period, the average accrual in BE was 2.4 ± 0.9 mM at t=120 min compared with the Pre value. The sequential changes in the HCO₃⁻ and BE concentrations in the AR group were significantly higher than those in the ISS and DLR groups during the fluid infusion period (p<0.05, respectively). Acetate can be metabolized more quickly than lactate by calves [14, 16] because metabolism of acetate acid takes place in muscle [1, 2, 19], whereas metabolism of lactic acid takes place mainly in the liver [5–8]. In addition, the blood lactate concentrations of acidic calves may have already increased, and lactate metabolism may have decreased simultaneously [4, 14, 19]. Our results show that acetate induced a significantly greater increase in the BE concentration than lactate. Therefore, commercial acetated Ringer’s solution has a superior alkalinizing effect compared with commercial DL- and L-lactated Ringer’s solutions in treatment of mild metabolic acidosis in calves. In addition, bicarbonate precursors such as sodium acetate should be useful as a riskless therapy for mild metabolic acidosis in calves.

REFERENCES