Clinical Efficacy of Intravenous Hypertonic Saline Solution or Hypertonic Bicarbonate Solution in the Treatment of Inappetent Calves with Neonatal Diarrhea

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Background: The clinical efficacy of IV administered hypertonic saline solution and hypertonic bicarbonate solution (HBS) in the treatment of inappetent diarrheic calves has not been compared yet.

Hypothesis: HBS is more advantageous than hypertonic saline in the treatment of calves with severe metabolic acidosis.

Methods: In 2 consecutive clinical studies, calves were initially treated with saline (5.85%; 5 mL/kg body weight [BW] over 4 minutes; study I: N = 16) or bicarbonate solution (8.4%; 10 mL/kg BW over 8 minutes; study II: N = 12), respectively, followed by oral administration of 3 L isotonic electrolyte solution 5 minutes after injection. Clinical and laboratory variables were monitored for 72 hours.

Results: Treatment failed in 6 calves of study I and in 1 calf of study II as indicated by a deterioration of the general condition. All treatment failures had more severe metabolic acidosis compared with successfully treated calves before treatment. In the latter, rehydration was completed within 18 hours after injection; metabolic acidosis was corrected within 24 hours (study I) and 6 hours (study II) after injection.

Conclusions and Clinical Importance: Diarrheic calves with slight metabolic acidosis (base excess [BE] > –10 mM) can be treated successfully with hypertonic saline. HBS is appropriate in calves without respiratory problems with more severe metabolic acidosis (BE up to –20 mM). Intensive care of the calves is required to ensure a sufficient oral fluid intake after the initial IV treatment.

Key words: Dehydration; Hypertonic rehydration; Metabolic acidosis; Suckling reflex.
to 12 Holstein Friesian calves (7 females, 5 males). All clinical assessments were carried out following a standardized protocol by the same person.

**Animals**

Both studies were carried out with calves admitted to the Clinic for Cattle. Calves were chosen based on the following selection criteria: age < 15 days, neonatal diarrhea (defined as soupy or watery consistency of the feces), dehydration (distance between the medial canthus and the eyeball at least 2 mm), no sucking reflex, and no clinical symptoms indicating moderate to severe secondary organ diseases.

**Initial Clinical Examination and Collection of Samples**

Immediately after admission, each calf was weighed. The general condition was assessed using a score system (1 = agile, physiologic; 2 = slight depression, able to stand; 3 = moderate depression, sternal recumbency; 4 = severe depression, lateral recumbency). A nipple bottle filled with milk was offered to the animal to assess the sucking reflex. The extent of enophthalmus was quantified by estimating the distance between the medial canthus and the eyeball (mm). Respiratory rate, heart rate, and rectal temperature were assessed. Lung auscultation and navel as well as joints' examination were carried out to exclude secondary diseases.

After checking by clinical investigation that all selection criteria were fulfilled, blood was collected from the jugular vein to assess PCV, serum variables, and blood gases. Centrifugation of the blood (3,000 x g, 4°C, 12 minutes) took place within 60 minutes after withdrawal. Finally, a grab sample of feces was taken from the *Anaspula recti*, which was tested for *rotavirus, coronavirus, Cryptosporidium parvum*, and *E. coli F 5*, and for *salmonellae* by fecal culture.

**Initial Treatment**

The initial treatment was conducted after introducing a venous catheter into the jugular vein. In study I, each calf received 5 mL/kg body weight (BW) saline solution (5.85%) over 4 minutes (study I: NaCl) corresponding to 5 mmol NaCl/kg BW. In study II, each calf received 10 mL/kg BW bicarbonate solution (8.4%) over 8 minutes (study II: NaHCO₃) corresponding to 10 mmol NaHCO₃/kg BW.

Immediately after injection, calves were allowed to suckle 3 L ORS. If calves refused to drink, they were administered fluid with a drencher 10 minutes after injection. ORS contained per liter 4 g NaCl, 0.5 g KCl, 2.5 g NaHCO₃, and 20 g glucose (calculated osmolarity 321 mOsmol/L). Procain-penicillin (20,000 IU/kg BW) SC q24h was administered for 5 days.

Additional blood samples were withdrawn from 9 randomly chosen calves of each study 0, 10, and 60 minutes after injection for determination of acid-base status. Fecal grab samples (approximately 10 mL) were taken after each clinical investigation and kept frozen at −20°C for subsequent dry matter (DM) determination.

**Feeding**

Milk replacer (MR; 125 g/L) corresponding to 10% of BW per day was offered divided into 4 meals (7:00 AM, 12:00 AM, 3:00 PM, 9:00 PM). ORS was available in nipple buckets from 9:00 to 11:00 AM, 1:00 to 2:00 PM, 5:00 to 9:00 PM, and 11:00 PM to 6:00 AM, respectively. Recumbent calves were encouraged to drink ORS at least 10 minutes at each time. Intake of MR and ORS was recorded.

**Treatment Failure**

A treatment failure was defined as a deterioration of the general condition between 2 consecutive clinical investigations during the 72-hour monitoring period. After the exclusion from the study, calves were treated by an established protocol, ie, a continuous infusion of an isotonic solution in the ear vein (8 L of 0.9% saline solution, 2 L of 5% glucose solution, 0.25 L of 8.4% bicarbonate solution).

**Analyses**

PCV was measured with a hemogram analyzer. Venous blood pH, base excess (BE), partial pressure of carbon dioxide (PCO₂), and standard bicarbonate (sHCO₃⁻) were determined with a blood gas analyzer. Serum concentrations of total protein (TP), urea, sodium, chloride, and potassium were determined with an automatic analyzing system. The concentration of i-lactate in plasma was measured by a quantitative enzymatic test. After thawing of the fecal samples, their DM content was assessed by weighing the sample twice before and after the drying process (93°C, 36 hours).

**Calculations**

Anion gap (AG) was calculated as
\[
AG(\text{mM}) = (\text{Na}^+ [\text{mM}] + K^+ [\text{mM}]) - (\text{Cl}^- [\text{mM}] + s\text{HCO}_3^- [\text{mM}]).
\]

Strong ion gap (SIG) was calculated according to Constable et al:
\[
SIG(g/L) = \frac{0.343}{1 + 10^{7.2-\text{pH}}} - AG(\text{mM}).
\]

**Statistics**

Signmagst at 2.0th was used for statistical analysis of the results. Results not differing significantly from a normal distribution as indicated by the Kolmogorov-Smirnov test are presented as means and standard deviations; otherwise, they are depicted as medians with 25/75 quartiles. The significance of differences between the treatment studies I and II was tested by a t-test and a rank-sum test, respectively. Differences between points of time within a study group were checked by one-way repeated-measures analysis of variance (ANOVA) and one-way repeated-measures ANOVA on ranks, respectively. The significance of differences between proportion of treatment failures in studies I and II was tested by Fisher's exact test. Differences were classified as significant if \( P < .05 \).

**Results**

**Infectious Agents**

Infectious agents were found in the fecal smear of all calves investigated. *E. coli (F 5)* were detected in 6 calves (21%); mixed infections with either *rotavirus* and *C. parvum* or *coronavirus* and *C. parvum* were evident in 8 calves (29%) and in 3 calves (11%), respectively. Exclusively, *C. parvum* were found in 11 calves (39%). *Salmonellae* were found in the feces of none of the calves. Patients infected with *E. coli (F 5)* were younger and the
metabolic acidosis was not as severe as compared with the calves suffering from neonatal diarrhea caused by viral or cryptosporidium infections, or both (Fig 1).

**Basal Conditions and Treatment Failures**

The status of the calves before hypertonic rehydration indicated profound diarrhea, moderate to severe dehydration, moderate to severe depression, and a pronounced metabolic acidosis.

Hypertonic rehydration using saline (study I) was successful in 10 of 16 calves (63%). Six calves had to be removed between 6 and 30 hours after injection. These treatment failures were on average 5 days older and exhibited before treatment a more severe acidemia (pH: 6.96 ± 0.10; sHCO₃⁻: 8 ± 1 mM; BE: −22.6 mM [−24.5/−19.5]) compared with successfully treated calves (pH: 7.17 ± 0.12; sHCO₃⁻: 17 ± 6 mM; BE: −9.4 mM [−17.9/−3.2]); no further differences between successfully treated calves and treatment failures were found (Table 1).

Hypertonic rehydration using bicarbonate solution (study II) was successful in 11 of 12 calves (92%). The sole calf that was not successfully resuscitated with hypertonic sodium bicarbonate was removed 60 hours after application of the hypertonic solution. This calf had severe metabolic acidosis (pH: 6.88; BE: −28 mM) before treatment despite only slight dehydration (4% of BW, PCV 0.29 L/L; urea 7.2 mM).

The proportion of treatment failures was 36, 48, and 60 hours after injection significantly higher in study I (NaCl) compared with study II (NaHCO₃) (P = .024) after injection.

**Initial treatment**

No clinically important adverse effects occurred during the administration of hypertonic solutions. Roughly 75% of the calves exhibited signs of discomfort and moderate to severe restlessness during the injection of the hypertonic solutions as indicated by twitching of the limbs, general shivering, and occasionally groaning. No obvious differences with respect to the extent of these clinical signs were observed between calves of study I (NaCl) and study II (NaHCO₃); however, during application of HBS, the respiratory rate increased more profoundly up to roughly 60 breaths per minute compared with the calves treated with hypertonic saline. These signs disappeared gradually within 5 minutes after the injection in all calves. Nine calves (56%) of study I (NaCl) and 6 calves (50%) of study II (NaHCO₃) drank voluntarily 3 L ORS within 10 minutes after the injection of hypertonic solutions; the remaining calves received the ORS by drenching.

### Table 1. Age, body weight (BW), clinical variables, and results of blood analysis before initial IV treatment of diarrheic calves with saline (5.85%; 5 mL/kg BW over 4 minutes; study I) and sodium bicarbonate (8.4%; 10 mL/kg BW over 8 minutes; study II), respectively, followed by administration of 3 L of oral rehydration solution.

| Study I (NaCl) | Successfully Treated | Therapy Failures |
|---------------|----------------------|------------------|
| Age (days)    | 5.2 ± 0.40           | 10.3 ± 3.3       |
| BW (kg)       | 37.2 ± 6.1           | 36.8 ± 6.5       |
| General condition (score 1–4) | 3.0 (3.0 / 3.5) | 3.0 (2.5 / 3.5) |
| Heart rate (1/min) | 120 ± 32          | 117 ± 15         |
| Respiratory rate (1/min) | 46 ± 16          | 34 ± 9           |
| Enophthalmus (mm) | 4.0 (3.0 / 5.5) | 3.3 (2.0 / 4.0)  |
| Dehydration (% of BW) | 7.0 (6.0 / 10.0) | 6.0 (4.0 / 7.0)  |
| PCV (L/L)     | 0.38 ± 0.07          | 0.35 ± 0.09      |
| TP (g/L)      | 59.0 ± 10.7          | 61.5 ± 12.5      |
| Urea (mM)     | 14.6 (8.8 / 6.0)     | 14.5 (10.3 / 18.4) |
| t-Lactate (mM) | 4.0 ± 2.3            | 3.2 ± 2.4        |
| Sodium (mM)   | 135 ± 10             | 134 ± 9          |
| Potassium (mM) | 7.6 ± 2.0            | 7.8 ± 2.6        |
| Chloride (mM) | 92 ± 8               | 98 ± 10          |
| pH            | 7.17 ± 0.12          | 6.96 ± 0.10      |
| PCO₂ (mmHg)   | 56 ± 11              | 42 ± 17          |
| PO₂ (mmHg)    | 22 ± 4               | 34 ± 8           |
| BE (mM)       | −9.4⁻ (−17.9 / −3.2) | −22.6⁻ (−24.5 / −19.5) |
| sHCO₃⁻ (mM)   | 17⁺ ± 6              | 8⁺ ± 1           |
| AG (mM)       | 34.6 ± 5.7           | 36.5 ± 8.4       |
| SIG (mM)      | −23.5 ± 6.1          | −27.5 ± 9.3      |
| Glucose (mM)  | 5.8 ± 1.8            | 5.0 ± 1.7        |
| Fecal dry matter (%) | 7.7 ± 3.9         | 8.3 ± 0.5        |

Means and standard deviations or medians and 25–75-quartiles are depicted, respectively, for calves successfully treated and those for calves excluded from the study because of treatment failure. Within a row, different superscripts indicate significant differences (P < .05) between the basal values of successfully treated calves and treatment failures in study I (NaCl).

TP, total protein; PCO₂, partial pressure of carbon dioxide; PO₂, partial pressure of oxygen; BE, base excess; sHCO₃⁻, standard bicarbonate; AG, anion gap.
minutes later the plasma pH reached the upper limit of 7.39. However, this was a transient effect; already 10 minutes after the saline injection, the pH decreased again (Table 3).

Table 2. General condition, rectal temperature, enophthalmus, heart rate, respiratory rate, and fecal dry matter before and after initial IV treatment of diarrheic calves with saline (5.85%; 5 mL/kg BW over 4 minutes; study I) and sodium bicarbonate (8.4%; 10 mL/kg BW over 8 minutes; study II), respectively, followed by administration of 3 L of oral rehydration solution.

| Number of calves in the study | Study          | 0 h a. inj. | 12 h a. inj. | 24 h a. inj. | 36 h a. inj. | 48 h a. inj. | 60 h a. inj. | 72 h a. inj. |
|------------------------------|----------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
|                              | NaCl           | 16          | 14          | 12          | 12          | 12          | 12          | 12          |
|                              | NaHCO3         | 12          | 12          | 12          | 12          | 12          | 12          | 11          |
| General condition (score 1–4)| NaCl           | 3.0 (2.8 / 3.5) | 2.0 (2.0 / 3.0) | 2.3 (1.5 / 2.5) | 2.0 (1.0 / 2.0) | 1.5 (1.0 / 2.0) | 1.0 (1.0 / 1.5) | 1.0 (1.0 / 1.0) | 1.0 (1.0 / 1.0) |
|                              | NaHCO3         | 3.0 (2.5 / 3.3) | 2.0 (1.3 / 2.5) | 1.8 (1.0 / 2.5) | 1.5 (1.0 / 2.3) | 1.3 (1.0 / 2.3) | 1.0 (1.0 / 1.5) | 1.0 (1.0 / 1.0) | 1.0 (1.0 / 1.0) |
| Rectal temperature (°C)      | NaCl           | 38.6 ± 1.1 | 39.0 ± 0.9 | 39.4 ± 0.5 | 39.3 ± 0.4 | 39.5 ± 0.4 | 39.5 ± 0.4 | 39.5 ± 0.4 | 39.5 ± 0.4 |
|                              | NaHCO3         | 38.8 ± 1.4 | 39.3 ± 0.6 | 39.3 ± 0.4 | 39.1 ± 0.4 | 39.4 ± 0.4 | 39.4 ± 0.4 | 39.4 ± 0.4 | 39.5 ± 0.4 |
| Enophthalmus (mm)            | NaCl           | 3.8 (3.0 / 5.5) | 2.0 (0.8 / 3.5) | 0.3 (0.0 / 2.0) | 0.0 (0.0 / 1.5) | 0.0 (0.0 / 1.0) | 0.0 (0.0 / 1.0) | 0.0 (0.0 / 0.0) | 0.0 (0.0 / 0.0) |
|                              | NaHCO3         | 4.8 (3.0 / 6.5) | 2.5 (1.5 / 3.5) | 1.5 (0.5 / 2.3) | 0.8 (0.0 / 1.5) | 0.0 (0.0 / 0.8) | 0.0 (0.0 / 1.0) | 0.0 (0.0 / 1.0) | 1.0 (0.0 / 1.5) |
| Heart rate (1/min)           | NaCl           | 120 (100 / 138) | 124 (106 / 139) | 108 (96 / 128) | 116 (104 / 128) | 110 (94 / 122) | 112 (108 / 120) | 108 (98 / 112) | 106 (96 / 116) |
|                              | NaHCO3         | 122 (86 / 134) | 120 (106 / 146) | 100 (100 / 128) | 104 (104 / 120) | 114 (98 / 130) | 114 (104 / 124) | 108 (100 / 122) | 112 (97 / 120) |
| Respiratory rate (1/min)     | NaCl           | 41 ± 5   | 40 ± 22   | 34 ± 15   | 33 ± 15   | 32 ± 10   | 27 ± 5   | 32 ± 10   | 37 ± 13   |
|                              | NaHCO3         | 43 ± 20  | 39 ± 22   | 34 ± 13   | 33 ± 11   | 37 ± 19   | 39 ± 18   | 39 ± 19   | 40 ± 19   |
| Fecal dry matter [%]         | NaCl           | 7.9 ± 3.1 | 6.0 ± 3.2 | 5.1 ± 3.1 | 5.2 ± 3.7 | 5.8 ± 2.9 | 6.8 ± 4.9 | 4.8 ± 2.7 | 6.5 ± 4.4 |
|                              | NaHCO3         | 7.3 ± 3.0 | 3.9 ± 2.0 | 6.9 ± 4.9 | 7.9 ± 2.7 | 6.0 ± 4.3 | 6.8 ± 5.2 | 11.0 ± 7.0 | 10.5 ± 8.0 |

Means and standard deviations or medians and 25%/75-quartiles are depicted, respectively. Asterisks indicate significant differences (P < 0.05) between the results in studies I and II. a inj., after injection; BW, body weight; h, hours.
Table 3. PCV, total protein (TP), urea, t-lactate, sodium, potassium, chloride, pH, partial pressure of carbon dioxide (PCO₂), partial pressure of oxygen (PO₂), base excess (BE), standard bicarbonate (sHCO₃), anion gap (G), and strong ion gap (SIG) before and after initial IV treatment of diarrheic calves with saline (5.85%; 5 mL/kg body weight [BW] over 4 minutes; study I) and sodium bicarbonate (8.4%; 10 mL/kg BW over 8 minutes; study II), respectively, followed by administration of 3 L of oral rehydration solution:

| Study     | 0h a. inj. | 6h a. inj. | 12 h a. inj. | 18 h a. inj. | 24 h a. inj. | 30 h a. inj. | 36 h a. inj. | 48 h a. inj. | 60 h a. inj. | 72 h a. inj. |
|-----------|------------|------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| NaCl      | NaHCO₃     | NaCl       | NaHCO₃       | NaCl         | NaHCO₃       | NaCl         | NaHCO₃       | NaCl         | NaHCO₃       | NaCl         |
| PCV (L/L) |            | 0.37 ± 0.08| 0.31 ± 0.06  | 0.31 ± 0.06  | 0.30 ± 0.07  | 0.29 ± 0.06  | 0.29 ± 0.07  | 0.28 ± 0.06  | 0.27 ± 0.05  | 0.27 ± 0.05  |
|           |            | 0.38 ± 0.07| 0.32 ± 0.05  | 0.31 ± 0.05  | 0.29 ± 0.06  | 0.28 ± 0.05  | 0.28 ± 0.05  | 0.27 ± 0.05  | 0.26 ± 0.04  | 0.27 ± 0.05  |
| TP (g/L)  |            | 59.9 ± 11.0| 50.8 ± 7.8   | 49.2 ± 8.7   | 46.4 ± 7.6   | 47.6 ± 7.2   | 46.8 ± 7.8   | 45.9 ± 6.6   | 44.5 ± 6.3   | 45.1 ± 6.8   |
|           |            | 59.4 ± 11.2| 51.4 ± 7.4   | 50.8 ± 7.0   | 45.5 ± 6.1   | 45.9 ± 6.4   | 45.8 ± 4.8   | 45.5 ± 4.9   | 46.1 ± 5.3   | 47.3 ± 5.8   |
| Urea (mM) |            | 14.5 ± 9.5/16.2| 13.1 ± 6.8/17.8| 8.3 ± 5.8/16.2| 7.1 ± 5.8/12.3| 6.3 ± 5.4/12.9| 6.6 ± 4.7/11.9| 5.2 ± 3.7/7.0| 4.8 ± 3.3/8.4| 3.8 ± 2.1/4.9|
|           |            | 14.8 ± 8.6/24.2| 14.6 ± 8.6/22.6| 14.7 ± 7.9/20.5| 11.7 ± 7.8/15.6| 9.2 ± 6.0/11.5| 6.7 ± 5.0/9.3| 4.9 ± 4.0/8.2| 3.9 ± 3.4/5.2| 3.6 ± 2.9/5.4|
| t-Lactate (mM) | 3.4 ± 2.2| 2.6 ± 2.4| 1.8 ± 1.3| 1.4 ± 0.9| 1.3 ± 0.8| 1.1 ± 0.5| 1.1 ± 0.5| 1.3 ± 0.3| 1.4 ± 0.9| 1.3 ± 0.6|
| Sodium (mM) | 134 ± 8 | 139 ± 6| 137* ± 7 | 136 ± 7 | 134* ± 7 | 134 ± 7 | 133* ± 7 | 132* ± 7 | 135 ± 5 | 135 ± 7 |
| Potassium (mM) | 7.6 ± 2.2| 6.5 ± 1.7| 6.0 ± 1.5| 5.5 ± 1.4| 6.0 ± 1.3| 5.8 ± 0.9| 5.4* ± 1.0| 5.6 ± 1.0| 5.3 ± 0.8| 5.4 ± 0.9 |
| Chloride (mM) | 94 ± 9 | 99 ± 8| 99 ± 9 | 98 ± 8| 95 ± 8| 95 ± 8| 94 ± 7| 93 ± 7| 95 ± 6| 95 ± 6 |
| pH | 7.09 ± 0.15| 7.18 ± 0.15| 7.24 ± 0.12| 7.27 ± 0.14| 7.28 ± 0.15| 7.28 ± 0.14| 7.33 ± 0.09| 7.34 ± 0.08| 7.31 ± 0.10| 7.35 ± 0.09 |
| PCO₂ (mmHg) | 50 ± 15| 46 ± 11| 43 ± 11| 44 ± 9| 45 ± 8| 46 ± 10| 50 ± 6| 50 ± 10| 52 ± 9| 50 ± 7 |
| PO₂ (mmHg) | 27 ± 8| 28 ± 5| 28 ± 7| 28 ± 8| 30 ± 9| 27* ± 8| 24* ± 5| 27* ± 8| 22* ± 5| 28 ± 10 |
| BE (mM) | -18.1(−21.7/−6.5)| -12.4*(−19.5/−2.7)| -3.2(−16.2/0.7)| -0.4(−15.6/2.4)| 1.6(−14.4/4.0)| 2.3(−13.6/6.5)| 3.4(−1.7/5.9)| 5.9(−5.8/7.3)| 4.0(−7.0/6.7)| 6.5(−7.7/8.9) |
| sCHO₃ (mM) | 13 ± 7| 16* ± 8| 18 ± 7| 20 ± 8| 20 ± 7| 21 ± 8| 24 ± 6| 25 ± 6| 24 ± 6| 25 ± 9 |
| AG (mM) | 35 ± 7| 29 ± 7| 26 ± 3| 24 ± 4| 24 ± 5| 23 ± 5| 21 ± 4| 20 ± 5| 21 ± 4| 21 ± 8 |
| SIG (mM) | -25 ± 7| -20 ± 8| -16 ± 4| -15 ± 5| -14 ± 6| -13 ± 6| -11 ± 5| -10 ± 5| -12 ± 4| -11 ± 7 |

Means and standard deviations or medians and 25-/75-quartiles are depicted, respectively. Asterisks indicate significant differences (P < .05) between results in studies I and II. a. inj., after injection; h, hours.
Table 4. Serum concentrations of electrolytes and pH, partial pressure of carbon dioxide (PCO₂), base excess (BE), and standard bicarbonate (sHCO₃) in venous blood and within 60 minutes after initial IV treatment of diarrheic calves with saline (5.85%; 5 mL/kg BW) over 4 minutes; study I) and sodium bicarbonate (8.4%; 10 mL/kg BW) over 8 minutes; study II), respectively, followed by administration of 3 L of oral rehydration solution.

| Study | Before Injection | 0 Minute after Injection | 10 Minutes after Injection | 60 Minutes after Injection |
|-------|------------------|-------------------------|---------------------------|---------------------------|
| Sodium (mM) | NaCl | 134 ± 8 | ND | ND | 140 ± 9 |
| Potassium (mM) | NaCl | 7.5 ± 2.2 | ND | ND | 7.7 ± 2.0 |
| Chloride (mM) | NaCl | 6.9 ± 2.1 | 5.4 ± 1.9 | 5.9 ± 1.9 | 5.6 ± 1.7 |
| pH | NaCl | 92 ± 7 | 93 ± 7 | 92 ± 11 | 92 ± 10 |
| PCO₂ (mmHg) | NaCl | 7.16 ± 0.13 | ND | ND | ND |
| PO₂ (mmHg) | NaCl | 7.08 ± 0.11 | 7.57 ± 0.04 | 7.43 ± 0.04 | 7.37 ± 0.07 |
| BE (mM) | NaCl | 51 ± 12 | ND | ND | ND |
| sHCO₃ (mM) | NaCl | 46 ± 16 | 63 ± 13 | 58 ± 15 | 55 ± 13 |
| AG (mM) | NaCl | 5 ± 17 | 38 ± 6 | 34 ± 9 | 33 ± 6 |

Means and standard deviations or medians and 25%-75-quartiles are depicted, respectively. Within a row, different superscripts indicate significant differences (P < .05) between different points of time in each study.

BW, body weight; PO₂, partial pressure of oxygen; AG, anion gap; SIG, strong ion gap; ND, not determined.

Rehydration of Diarrheic Calves

The reference range (pH: 7.43 ± 0.04) and decreased furthermore to 7.37 ± 0.07 60 minutes after injection. Six hours after injection, plasma pH averaged 7.32 ± 0.07; the mean BE was -5.0 mM (-2.8/8.3) (Table 3). Although the plasma pH tended to decrease during the subsequent 66 hours, no serious acidemia developed, as indicated by a pH of 7.26 ± 0.11 at the end of the investigation period (72 hours after injection). The basal serum concentration of l-lactate decreased linearly in both studies within 18 hours after injection by about 50% from 3.7 mM to approximately 1.6 ± 1.5 mM and remained at this level for the further investigation period (Table 3).

**Electrolyte Status**

For calves of study I (NaCl), serum sodium concentrations increased significantly from mean basal values of 134 ± 8 mM before saline application to 140 ± 9 mM measured 1 hour after injection. In calves of study II (NaHCO₃), a massive transient hypernatremia was evident from the results of short-interval collection of samples in 9 calves (Table 4). However, 6 hours after application of HBS, the mean sodium concentrations were again in the physiologic range (144 ± 9 mM). For the subsequent 72 hours, mean concentrations between 139 and 132 mM were found (Table 3).

Serum chloride concentration increased in calves receiving hypertonic saline (study I) within 60 minutes after injection significantly up to 102 ± 11 mM. Thereafter, values within the reference range were found. In study II (NaHCO₃), no significant changes of serum chloride concentration were observed after hypertonic rehydration (Tables 3 and 4).

Before hypertonic rehydration, hyperkalemia was found in calves of both studies (> 7 mM). A distinct bradycardia because of hyperkalemia, however, was not detected (Table 2). A gradual decrease to a level of about 5 mM was observed within 18 hours in both studies; during the subsequent 54 hours, the serum concentrations remained in this range without significant differences between the calves of both studies (Table 3).

**Intake of MR and ORS**

Intake of MR did not differ between the calves in both studies and tended to increase (P = .09) from day 1 to day 3 after hypertonic rehydration (day 1: 2.8 ± 1.7 L; day 2: 3.6 ± 1.5 L; day 3: 3.8 ± 1.4 L [means ± SD]). Also, intake of ORS did not differ between the calves in both studies and tended to decrease (P = .09) from day 1 to day 3 after initial treatment (day 1: 6.2 ± 4.6 L; day 2: 5.3 ± 4.2 L; day 3: 4.5 ± 3.2 L). Thus, the amount of total fluid intake remained constant and averaged 8–10 L/d.

**Fecal DM**

In study I (NaCl), the mean percentage of fecal DM remained within the investigation period without significant differences between 5 and 8%. In study II (NaHCO₃), a significant difference from calves of study I (NaCl) was evident on the 3rd day after initial treatment when fecal DM ranged between mean values of 10 and 13% (Table 2).
Discussion

The objective was to evaluate the clinical efficacy of different hypertonic IV rehydration solutions in inapparent diarrheic calves. To prevent adulteration of positive effects of hypertonic rehydration by an insufficiency of other organs, patients with additional secondary infections were disregarded. Further health problems can be explained partly by a long history of neonatal diarrhea, but also by a high proportion of hypogammaglobulinemia because of insufficient colostral supply among diarrheic calves. This is confirmed by low serum concentrations of TP after successful rehydration in both studies (Table 3); the catabolic state and low serum concentrations of TP after successful rehydration in both studies (Table 3); the catabolic state and intestinal protein losses during diarrhea may have had a further impact.

Many authors recommend hypertonic saline (7.2%) with 6% dextran for rehydration. In the present study, a different concentration of saline had to be used (5.85%); this solution is licensed and commercially available in Germany, representing prerequisites for application in food animals. Nevertheless, because of studies I and II (Table 3). Thus, the concentration of sodium in the hypertonic solution had only a short, transient effect, whereas the final success of the rehydration treatment was determined predominantly by a sufficient intake of ORS.

Unfortunately, the severe metabolic acidosis of recumbent diarrheic calves (BE: −15 to −30 mM) may be slightly aggravated by application of saline—whether administered as a continuous infusion or as a hypertonic injection. Saline creates a strong ion acidosis because the effective SID of calf plasma is 42 mEq/L, whereas the effective SID of saline is 0 mEq/L. The administration of 4 mL saline (7.2%)/kg BW within 4 minutes decreased the plasma pH in swine with hemorrhagic shock and mixed acidosis by 0.08 pH units. This decrease has been considered to be clinically inconsequential, predominantly because an improvement of the blood pH is achieved by the intake of buffers from ORS. In calves with a pre-existing severe acidemia, however, a further decrease of plasma pH because of hypertonic saline application may be detrimental. In that respect, the short-term restoration of the sucking reflex is of crucial importance because intake of ORS represents a prerequisite for successful rehydration treatment. A negative correlation has been suggested between the degree of the acidosis and the vigorousness of the sucking reflex. Also, in our studies, a sustained improvement of oral fluid intake was achieved predominantly in those calves where the acidemia could be corrected quickly. In most calves where hypertonic rehydration failed, the general condition deteriorated, concomitant with a reduction of oral fluid intake and in the face of a prolonged acidemia. The concentrations of D-lactate were most likely massively increased in the diarrheic calves studied compared with healthy calves as indicated by profoundly increased AG (Table 3). Such increased concentrations of D-lactate contribute significantly to weakness and disturbed consciousness, but they do not seem to influence the sucking reflex.

The administration of HBS represents a therapeutic option to correct the metabolic acidosis faster than by hypertonic saline. Even calves with a BE of −10 to explained predominantly by an advantage of bicarbonate solution in the treatment of diarrheic calves with a severe metabolic acidosis. No differences existed in the status of the calves before hypertonic rehydration between successfully treated calves and treatment failures, except for a more severe acidemia in the latter. Calves that failed to respond were on average older than the successfully treated calves, which indirectly confirms the findings that diarrheic calves older than 1 week of age exhibit a more severe acidemia than younger calves (Table 1). As an explanation, infections with rotavirus, coronavirus, or C. parvum induce an osmotic diarrhea, accompanied by microbial fermentation of substrates in the large intestine, leading to excessive production of predominantly D-lactate.

Calves treated with HBS (study II) received a double load of sodium compared with calves in study I (NaCl). Sodium is regarded as the major determinant of rehydration success; however, no obvious differences were found with respect to the velocity of rehydration between calves of studies I and II (Table 3). Thus, the concentration of sodium in the hypertonic solution had only a short, transient effect, whereas the final success of the rehydration treatment was determined predominantly by a sufficient intake of ORS.

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The buffering capacity of bicarbonate requires an effective removal of CO₂ by the respiratory system. The tachypnea being more pronounced in calves receiving hypertonic bicarbonate than saline is most likely because of the hypercapnia (Table 4). In study II (NaHCO₃), several calves with only slight metabolic acidosis were treated, which did not require buffer capacity at all. Nevertheless, also these patients had had no problem in coping with the application of hypertonic bicarbonate by enhancing ventilation. Even newborn calves with mixed respiratory acidosis because of dystocia (mean blood pH 7.06) were successfully treated by infusion of 300 mL sodium bicarbonate solution (5%) over 15 minutes, combined with doxapram IV and intranasal oxygen insufflation; no negative effects compared with calves treated with carbicarb were found. Also, rapid IV administration of HBS (8.4%; 5 mL/kg over 5 minutes) was found to be effective and safe for treating strong ion acidosis in normovolemic calves with experimentally induced respiratory and strong ion acidosis. In these 2 studies, however, lower amounts of bicarbonate were infused than in study II presented here. Many calves, especially with a longer history of diarrhea, also suffer from respiratory infections. It remains unknown whether removal of excessive CO₂ after application of HBS by hyperventilation is possible in such patients. Reports of practitioners about sudden fatalities in calves after hypertonic bicarbonate infusion may be an indication that such incidents could be related to respiratory insufficiencies. At present, it is recommended to avoid the application of hypertonic bicarbonate in calves suffering from severe respiratory disease, whereas hypertonic saline can also be applied in such patients.

Especially in patients with an impaired ability to remove carbon dioxide, a PIA after rapid injection of large quantities of bicarbonate has been discussed as a matter of concern. Accordingly, bicarbonate ions react with H⁺ ions to form CO₂, which readily enters cells and overwhelms the blood-brain barrier because of its high solubility. Thus, the intracellular PCO₂ increases, which induces a local respiratory acidosis. The clinical consequences are unclear; it has been postulated that an acidification of the cerebrospinal fluid (CSF) may exaggerate a depression and increase the respiratory rate. A PIA has been demonstrated in in vitro studies after increasing the extracellular PCO₂ by approximately 70 mmHg. However, in vivo the PCO₂ rarely increases more than 15 mmHg. It has been suggested that the increase of PCO₂ after bicarbonate application can be aggravated by the concomitant release of protons from extracellular nonbicarbonate buffers in severely acidotic patients. Berchtold et al induced experimentally a mixed respiratory and metabolic acidosis in calves and found, after subsequent injection of bicarbonate solution (8.4%, 5 mL/kg BW over 5 minutes), no pH change in the CSF irrespective of a transient increase of arterial PCO₂ from 81 to 93 mmHg. A turnover rate of CO₂ into the CSF of 0.01 minute⁻¹ was calculated. In our patients, a statistical trend (P = .08) was found for the relation between plasma pH before injection of hypertonic bicarbonate and the increase of venous PCO₂ after injection (Table 4). However, PCO₂ increased only by an average 17 mmHg directly after the initial treatment. Thus, PIA seems not to be a reason for profound problems after hypertonic bicarbonate application in calves with a healthy respiratory tract.

Concerns were expressed with respect to IV treatment of diarrheic calves with bicarbonate solutions because the concomitant hypercapnia and removal of metabolic acidosis may worsen the oxygen extraction in peripheral tissues of such patients. Based on the results presented here, these concerns seem to be inappropriate despite an extensive transient metabolic alkalosis immediately after injection of HBS (Table 4), which can be explained by incomplete distribution of bicarbonate in the extracellular space. The general condition of most calves that received bicarbonate solution improved rapidly—presumably, the improved blood flow because of increased plasma volume overwhelms the negative impact of a left shift of the oxygen equilibrium curve.

Because oral fluid intake is of crucial importance for the success of hypertonic rehydration, an intensive fostering of the calf after initial treatment represents a prerequisite. The recovery of critically ill patients is undoubtedly facilitated by providing many small meals. The variation of milk as well as ORS intake during each meal after hypertonic rehydration is high. Thus, calves in studies I and II were fed 8 times per day. Moreover, a high feeding frequency reduces the risk of long periods with a low pH in the abomasum, favoring the development of abomasal ulcerations.
immediately after completing the injection of HBS by 20 mM, triggering an increase of plasma osmolarity of roughly 20–25 mOsmol/L; an increase in this range has also been reported. The immediate dilution of extracellular compartment by an influx of intracellular and transcellular fluid excludes the risk of a clinically significant hypernatremia. However, hypertonic rehydration is inappropriate in calves that already suffer from hypernatremia before the initial treatment.

In conclusion, hypertonic rehydration represented a safe and reliable method to improve the hydration status of inappetent diarrheic calves. Hypertonic saline seems to be most appropriate for calves within the 1st week of life as most of these patients suffer from a slight to moderate metabolic acidosis (BE > -10 mM). HBS allows successful treatment of diarrheic calves even with severe metabolic acidosis (BE -10 to -20 mM) frequently found in calves older than 1 week. Diarrheic patients also suffering from respiratory disease should not be treated with HBS. A high oral fluid intake is a precondition for successful hypertonic treatment requiring an adequate fosterage.

Footnotes

1. Digestive Kit: Rota, Corona, E. coli F 5; Cryptosporidium, Bio-X Diagnostics Sprl., Innovation for veterinary diagnostics, Jemelle, Belgium
2. Veterinärinstitut Hannover, Hannover, Germany
3. Vygonüle T, 1.8, 45 mm; Vygon GmbH & Co KG, Aachen, Germany
4. Kochsalzlösung 1 M, 5.85%, 100 mL; sodium chloride (ingredient): 1 mmol/mL; aqua dest (excipient); Serumwerke Bernburg AG, Bernburg, Germany
5. Natriumhydrogenocarbonat 8.4% Infusionslösung B. Braun, 250 mL; sodium bicarbonate (ingredient): 1 mmol/mL; aqua dest (excipient); B. Braun Melsungen AG, Melsungen, Germany
6. Calf Drencher flexible, 2 L; Jorgen Kruse, Marslev, Denmark
7. Proctilin, benzylpenicillin (ingredient): 300,000 IU/mL (excipient); Alvetra GmbH, Neumünster, Germany
8. Normi Typ F 10; Nordmilch Zeven, Industriestrasse, Zeven, Germany
9. Hematology Analyzer Modell MEK-6108G, Nihon Kohden Europe GmbH, Rosbach v. d. H., Germany
10. Rapidlab, Bayer Vital GmbH, Fernwald, Germany
11. Cobas Mira, Hoffmann-La Roche Ltd, Basel, Switzerland
12. Sigma Diagnostics Laktat, Nr. 826-UV, Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany
13. Jandel Scientific Corp, Los Angeles, CA

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