Effect of orally administered electrolyte solution formulation on abomasal luminal pH and emptying rate in dairy calves

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Objective—To determine the effects of 3 commercially available, orally administered electrolyte solutions (OAEs) on abomasal luminal pH and emptying rate in dairy calves, compared with the effect of orally administered milk replacer.

Design—Randomized crossover study.

Animals—6 male dairy calves (age, 12 to 31 days).

Procedures—Calves were surgically instrumented with an abomasal cannula and were administered 4 treatments in randomized order: all-milk protein milk replacer, high-glucose high-bicarbonate OAE, high-glucose high-bicarbonate OAE containing glycine, and low-glucose OAE containing acetate and propionate. Abomasal luminal pH was measured with a miniature glass pH electrode prior to treatment administration and every second afterward for 24 hours.

Results—Feeding of orally administered milk replacer resulted in a rapid increase in mean abomasal luminal pH from 1.3 to 5.8, followed by a gradual decrease to preprandial values by 8 hours afterward (mean 24-hour pH, 3.2). High-glucose high-bicarbonate OAEs caused a large and sustained increase from 1.3 to 7.5 (mean 24-hour pH, 4.1 for the solution without glycine and 3.5 for the solution with glycine). In contrast, feeding of the acetate-containing OAE was followed by only a mild and transient increase (mean 24-hour pH, 2.1); luminal pH returned to preprandial values by 3 hours after ingestion.

Conclusions and Clinical Relevance—Ingestion of a bicarbonate-containing OAE resulted in sustained abomasal alkalinization in dairy calves. Because persistently high abomasal luminal pH may facilitate growth of enteropathogenic bacteria, administration of OAEs containing a high bicarbonate concentration (> 70mM) is not recommended for calves with diarrhea. (*J Am Vet Med Assoc* 2012;241:1075–1082)

Neonatal diarrhea is the leading cause of calf death in most countries and a major source of economic loss to the cattle industry. Despite progress in understanding the pathophysiology of neonatal diarrhea, recent data indicate that > 60% of dairy heifer calf deaths in the United States result from diarrhea.[1] According to the World Health Organization, the development of orally administered rehydration treatments was one of the most important advances in human medicine of the 20th century.[2] Orally administered electrolyte solutions provide a practical, effective, and inexpensive method for treating strong ion (metabolic) acidosis and dehydration in calves that have a suckle reflex.[3–5] However, the ideal formulation of OAEs for use in calves with diarrhea is still somewhat unclear.[6] Several factors need to be considered when choosing an electrolyte product for use in calves, and the usual recommendation is that OAEs contain an alkalinizing agent to correct the acidemia usually present in calves with diarrhea.[4,6,7] Examples of alkalinizing agents commonly used in OAEs include bicarbonate, acetate, propionate, and citrate.

Abbreviations

BW	Body weight
ETEC	Enterotoxigenic *Escherichia coli*
OAE	Electrolyte solution for oral administration

Gastric acidity is a barrier to colonization and infection of the gastrointestinal tract by bacteria and is a primary defense mechanism against ingested pathogens.[8,9] Bacteria such as *Escherichia coli* and *Salmonella enterica* are killed at a gastric pH between 2.5 and 3.0 but multiply at a pH > 5.0.[10,11] Therefore, maintenance of a low abomasal pH in calves is important to avoid colonization of the intestinal tract with pathogenic enteric bacteria. The authors' research group previously demonstrated that calves fed an isotonic (relative to blood plasma) solution of sodium bicarbonate (150mM) had a significant increase in abomasal pH, compared with calves fed an isotonic solution of sodium acetate.[12] From these data, we hypothesized that ingestion of commercially available OAEs containing a high concentration of bicarbonate (> 70mM) could increase abomasal pH, resulting in prolonged abomasal

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alkalinization that could be detrimental to gastrointestinal health.

The rate of abomasal emptying influences the rate at which ingesta are delivered to the small intestine. For an OAE, because the small intestine is the major site of fluid absorption, the rate of abomasal emptying influences the rate of rehydration of a sick calf. Orally administered electrolyte solutions that have a high osmolarity and glucose concentration decrease the abomasal emptying rate in calves and therefore the rate of solution delivery to the small intestine.[5,13,14] For these reasons, we hypothesized that a hypertonic OAE would be more slowly emptied from the abomasum than an isotonic OAE. The primary objective of the study reported here was to compare the abomasal luminal pH-time relationship of calves fed an all-milk protein milk replacer twice a day with that of calves fed commercially available OAEs that contained bicarbonate or acetate as the main alkalinizing agent and that varied in osmolality.

Materials and Methods

Animals—Six male colostrum-fed healthy dairy calves (5 Holstein-Friesian and 1 Ayrshire), weighing between 34 and 45 kg (74.8 and 99 lb), were obtained within 3 days after birth from a local source. Calves were anesthetized and surgically instrumented with an abomasal body cannula[a] at 3 days of age as described.[15] Following surgery, calves were housed unrestrained in individual moveable calf stalls in a climate-controlled environment, fed milk replacer (12% of BW/d) divided into 2 feedings at 12-hour intervals, and allowed free access to water. Cetfiofur[b] (0.5 mg/kg [0.23 mg/lb], IM) was administered daily for 2 days after surgery, and flunixin meglumine[c] (0.5 mg/kg, IM) was administered twice after surgery at a 12-hour interval for postoperative analgesia. The University of Illinois Laboratory Animal Care and Use Committee approved the study protocol.

Experimental design—All calves were given at least 8 days to recover from surgery. A flexible miniature glass pH electrode[d] was calibrated and placed in the abomasal lumen via the cannula as described.[16,17] The pH electrode was connected to a pH meter[e] and the analog output digitized[f] at 1 Hz. Digitized data were stored and analyzed offline with commercially available software[f] on a personal computer. The pH electrode was calibrated against reference buffer solutions (pH of 2.0 and 7.0 at 20°C) immediately before insertion and after removal.

Beginning on day 12 after birth (mean BW, 43 kg [94.6 lb]; range, 38 to 48 kg [83.6 to 105.6 lb]), abomasal luminal pH was measured once and then again 15 minutes later (baseline values). Immediately afterward, each calf received each of 4 treatments (12% of BW/d, q 12 h for 2 doses) in random order, with a minimum 24-hour washout period between treatments: all-milk protein milk replacer,[g] hypertonic bicarbonate-containing OAE,[h] hypertonic bicarbonate-containing OAE that also contained glycine,[i] and an isotonic acetate- and propionate-containing low-glucose OAE.[j] At each feeding, luminal pH was monitored continuously for at least 24 hours. The pH electrode was removed after each abomasal pH recording period and recalibrated to determine drift during the study period.

During the washout period, calves were fed milk replacer[g] (12% of BW/d), divided into 2 feedings at 12-hour intervals. This daily amount was slightly larger than as directed by the milk replacer manufacturer (10% BW/d). However, because calves were not offered calf starter (grain), the additional milk was needed to maintain BW. Calves were allowed to suckle all liquid treatments from a bottle with a nipple.

Substances fed—The contents of the milk replacer were as follows: crude protein, ≥ 22%; crude fat, ≥ 20%; crude fiber, ≤ 0.15%; calcium, ≥ 0.50%; and phosphorus, ≥ 1.00%. The product was partially agglomerated, and the protein source was dried whey, dried whey product, dried milk protein, and dried skim milk in unstated proportions (≥ 1% weight dried skim milk). All milk replacer was mixed in accordance with label directions (224 g of powder mixed with 1.9 L of water), with water at temperatures ranging between 38°C and 43°C. Neither hay nor calf starter ration was fed during the study period. Electrolyte solutions were mixed in accordance with label directions **(Appendix)**. Since completion of the study, the hypertonic bicarbonate-containing OAE that did not contain glycine[h] is no longer commercially available in the United States.

Data analysis—Abomasal pH was smoothed with a 60-point moving mean, and the lowest smoothed pH for each minute was used as the pH for that minute. The smoothing procedure minimized recording artifacts that occurred when the pH probe transiently contacted the abomasal mucosa due to changes in the calf's position or contraction of the abomasum. The mean preprandial pH (from –15 to 0 minutes), maximum postprandial pH, minimum postprandial pH, and mean postprandial pH were determined.

Abomasal luminal pH return time was calculated as the interval from solution ingestion to the point at which the postprandial luminal pH returned to a pH of 1.0 greater than the mean preprandial pH. This cut-point provides the best method for describing the abomasal emptying rate in suckling calves.[k]

Statistical analysis—Data are expressed as least squares mean ± SD. Values of $P < 0.05$ were considered significant for all analyses. Outcome variables of interest were least squares mean preprandial pH, mean 24-hour pH, maximum pH, minimum pH, pH return time, and percentage of time luminal pH exceeded various pH thresholds. A 2-way repeated-measures ANOVA with variance partitioned into treatment, time, and treatment-time interaction and with repeated measures for time and treatment was performed. On the basis of published recommendations,[18] mean pH was calculated rather than median pH because of the homogeneity of the treatment response. Least squares mean 24-hour pH and pH threshold curves were developed from pH values obtained from 1 minute to 24 hours in 1-minute intervals; this provided 1,440 data points for each 24-hour recording period. The temporal change in abomasal luminal pH over 24 hours was graphically depicted. The pH threshold curve was

developed by calculating the percentage of the 24-hour study period that pH was > 0 to > 6 in increments of 0.5. Commercial software[l] was used for statistical analyses.

Results

Animals—The abomasal cannulae were well tolerated by all calves, with no apparent loss of appetite and no change in rectal temperature throughout the study period. The abomasal luminal pH measurements were valid for all trials except 1 involving 1 calf fed the glycine-free hypertonic bicarbonate-containing OAE. Therefore, data were obtained for 6 calves fed milk replacer, 5 calves fed the glycine-free hypertonic bicarbonate-containing OAE, 6 calves fed the glycine-containing hypertonic bicarbonate-containing OAE, and 6 calves fed the isotonic acetate-containing OAE. The mean time required for calves to ingest the allotted volume of milk replacer or OAE was 5 minutes (range, 2 to 10 minutes). Fecal consistency and output were not noticeably altered during the study period.

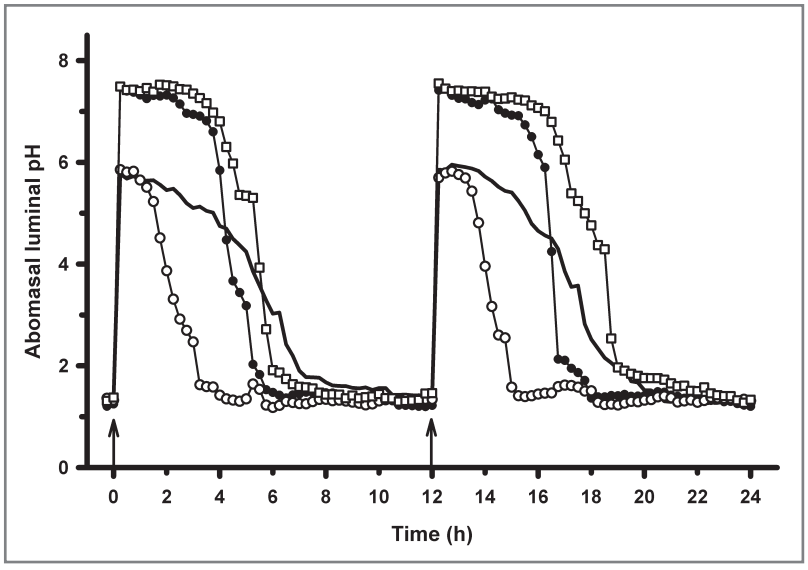

Figure 1—Mean abomasal luminal pH in dairy calves (n = 6) fed an all-milk protein milk replacer (solid line), a high-glucose high-bicarbonate OAE (black circles), a high-glucose high-bicarbonate OAE that also contained glycine (squares), and an isotonic acetate- and propionate-containing low-glucose OAE (white circles) in random order at 0 and 12 hours (arrows).

Abomasal luminal pH—Electrode drift during the 24-hour recording period was minimal for buffers with a pH of 2.0 (mean change, 0.03; range, –0.10 to 0.08) and 7.0 (mean change, 0.05; range, –0.02 to 0.10). Therefore, the actual (measured) pH values were used for statistical analysis.

Mean preprandial pH was < 1.50 for all 4 treatments (**Figure 1**). When milk replacer was fed every 12 hours, abomasal luminal pH increased from a baseline value of 1.34 to 5.86 within 3 minutes, remained constant for approximately 2 hours, and then decreased to the preprandial value by 7 to 8 hours after feeding. Abomasal luminal pH was constant from 8 to 12 hours and increased again after the second feeding of milk replacer at 12 hours. Least squares mean postprandial luminal pH when feeding milk replacer twice a day was 3.28 (**Table 1**).

With both bicarbonate-containing high-glucose OAEs, abomasal pH increased to > 7.50 and remained elevated for several hours (Figure 1). Least squares mean 24-hour pH for the glycine-free hypertonic OAE was 3.53 and for the glycine-containing hypertonic OAE was 4.18; the value for the solution containing glycine was higher, compared with that for milk replacer. After feeding the isotonic acetate- and propionate-containing solution, abomasal luminal pH increased similarly to milk replacer and decreased to preprandial values within approximately 3 hours. The least squares mean postprandial luminal pH for the isotonic solution was 2.15, which was lower than that achieved with feeding milk replacer.

The percentage of time during the 24-hour recording period that abomasal pH exceeded a pH threshold of 5.5 was longer for both hypertonic OAEs, compared with the percentage for milk replacer (**Figure 2**). The isotonic OAE yielded a significantly lower pH threshold than did milk replacer for all pH cutpoints from 1.5 to 5.5.

Abomasal luminal pH return time—The pH return time was longest for milk replacer and the glycine-con-

Table 1—Least squares mean ± SD abomasal pH at various points in dairy calves (n = 6) fed milk replacer or 1 of 3 OAEs twice a day, at 12-hour intervals.

		OAE		
Variable	**Milk replacer**	**A**	**B**	**C**
Preprandial pH	1.34 ± 0.14[a]	1.25 ± 0.11[a]	1.36 ± 0.22[a]	1.36 ± 0.27[a]
Mean postprandial pH	3.28 ± 0.29[a]	3.50 ± 0.20[a]	4.18 ± 0.37[b]	2.15 ± 0.22[c]
Maximum postprandial pH	6.09 ± 0.05[a]	7.74 ± 0.24[b]	7.73 ± 0.24[b]	6.14 ± 0.23[a]
Minimum postprandial pH	1.02 ± 0.15[a]	1.06 ± 0.19[a]	1.10 ± 0.19[a]	1.05 ± 0.14[a]
pH return time (min)	383 ± 59[a]	283 ± 35[b]	366 ± 74[a]	131 ± 24[c]
Percentage of 24-hour recording period that pH exceeded 5.5	20.1 ± 7.6[a]	35.2 ± 2.4[b]	43.8 ± 6.1[b]	9.6 ± 6.4[c]

The pH return time is the interval from solution ingestion to achievement of a luminal pH of 1 unit greater than the mean preprandial pH.

[a–c]Within a row, values with different superscript letters are significantly ($P < 0.05$) different.

A = High-glucose high-bicarbonate OAE. B = High-glucose high-bicarbonate OAE that also contained glycine. C = Isotonic acetate- and propionate-containing OAE with low glucose concentration.

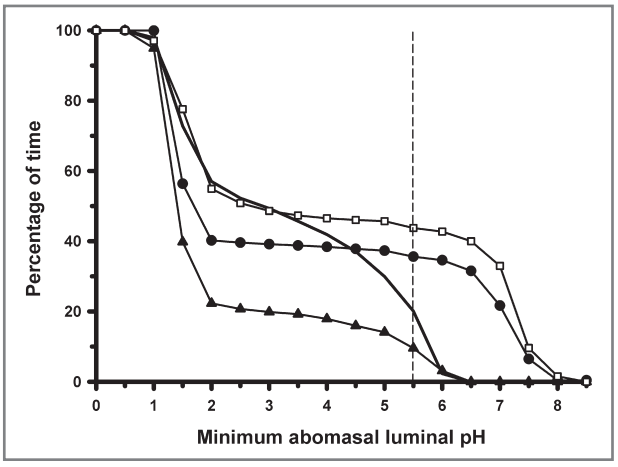

Figure 2—Mean percentage of time during the 24-hour recording period that abomasal luminal pH exceeded various pH thresholds for the dairy calves in Figure 1. The dashed vertical line at a pH of 5.5 represents the luminal pH at which growth of *Escherichia coli* and *Salmonella enterica* is promoted. *See* Figure 1 for remainder of key.

taining hypertonic OAE (Table 1). It was intermediate for the glycine-free hypertonic OAE and was shortest for the isotonic acetate- and propionate-containing OAE.

Discussion

The major finding of the present study was that 2 hypertonic bicarbonate-based OAEs caused significant and prolonged abomasal alkalinization and decreased the abomasal emptying rate in calves. In contrast, an isotonic OAE containing acetate and propionate did not cause any increase in abomasal pH and increased the abomasal emptying rate in calves, compared with orally administered milk replacer. Abomasal acidity provides a natural barrier to ingested bacteria, and maintaining a low abomasal pH decreases the number of viable pathogenic bacteria that reach the small intestine.[8,9] Therefore, the increase in abomasal pH that occurred with feeding OAEs containing a high bicarbonate concentration may facilitate growth of bacterial diarrheal pathogens and thus could increase the severity, duration, and mortality rate associated with diarrhea in calves. Consequently, we believe that feeding OAEs containing acetate or propionate would be preferred to feeding those containing a high bicarbonate concentration that excessively alkalinize abomasal luminal pH when treating calves with diarrhea.

Gastric production of hydrochloric acid is found in all vertebrates, and preservation of this energy-consuming and at times deleterious function (eg, promotion of gastric ulcers) reflects its biological importance.[9] Gastric acid denatures proteins, activates pepsinogen, enhances the intestinal absorption of dietary iron and calcium, and initiates the biochemical cascade responsible for milk clot formation within the abomasum of neonatal calves. However, the primary function of gastric acid is generally believed to be inactivation of ingested bacteria.[19] The concept of the gastric bactericidal barrier was introduced in 1925,[20] and its importance has been established in human medicine. The bactericidal effects of the stomach are mainly attributable to the acidic pH, given that other constituents of gastric fluid appear to contribute little to the barrier function.[8,9] At a pH < 4.0, the stomach has a potent bactericidal effect, killing exogenous bacteria within 15 minutes after entry. Increasing intragastric pH to > 4.0 has the potential to permit bacterial overgrowth.[8]

In humans, iatrogenic hypochlorhydria often develops because of the common use of drugs that inhibit acid secretion, such as histamine-2 receptor antagonists and proton pump inhibitors.[21,22] Although humans taking acid-suppressing drugs may have relief from heartburn or gastric reflux, numerous studies[23–27] have shown they have a significant increase in the risk of developing bacterial diarrhea, compared with in untreated humans. For example, a large retrospective study[23] found that patients taking acid-suppressing drugs had a risk of developing bacterial diarrhea of approximately 3 times as high as in untreated patients. Another study[24,27] found that taking histamine-2 receptor antagonists was associated with increased risk of travelers' diarrhea caused by various pathogens, including *Campylobacter* spp, *S enterica*, and *Vibrio cholerae*. Gastric acid suppression can also increase the development of hospital-acquired *Clostridium difficile* diarrhea.[25,26]

An important example of the influence of abomasal pH on susceptibility to disease in calves is ETEC, which is an important cause of profuse watery diarrhea in calves < 2 to 3 days of age. The pathophysiologic effect of ETEC infection is dependent on several factors. First is the exposure to and ingestion of the organism. Once ingested, ETEC must survive the acidic pH of the abomasum. Survival is facilitated in neonatal calves because the pH of their abomasum ranges from approximately 6 to 7. Once ETEC reaches the ileum, the K99 fimbrial antigen is expressed to facilitate bacterial attachment to intestinal epithelial cells and STa enterotoxin is secreted. Because the K99 antigen is only expressed at an environmental pH > 6.5[28] and production of STa enterotoxin by bovine ETEC strains is greatly promoted at pH > 7.2,[29] the distal portion of the small intestine is the initial site of colonization.[30] However, abomasal pH decreases to < 2 by 5 days of age, which is low enough to kill ETEC strains.[30]

Diarrhea caused by ETEC infection can be experimentally reproduced in calves < 48 hours of age by orally administering large inoculums (typically 10^9 to 10^{11}) of viable ETEC organisms.[31,32] In older calves, this experimental protocol must be modified by orally administering sodium bicarbonate (4 to 10 g in 60 to 150 mL of water) to alkalinize the abomasum and ameliorate the effect of abomasal sterilization, followed immediately by oral administration of viable ETEC organisms.[33–36] The modified protocol was able to induce diarrhea in 100 of 150 (67%) calves 5 to 10 days of age,[33] 32 of 60 (53%) calves > 1 day of age,[34] 31 of 51 (61%) calves < 7 days of age,[33] and 38 of 75 (51%) calves 7 to 14 days of age.[36] The high rate of successful diarrhea induction raises concern regarding the appropriateness of OAEs containing bicarbonate for use in calves with diarrhea. The results of our study suggested that such solutions would promote abomasal alkalinization and thus in-

crease the number of bacteria able to colonize the small intestine. Although additional studies are needed, this alkalinization could potentially facilitate the development of diarrhea caused by ETEC and other bacteria.

An increase in abomasal pH also appears to be important in facilitating salmonellosis in calves. Cattle develop an age-dependent resistance to *S enterica* infection that is associated with development of a functional rumen, a diverse small intestinal bacterial flora, and a low abomasal pH.[37,38] The optimum pH for growth of *Salmonella* organisms is from 6.5 to 7.5,[31] and salmonellae are susceptible to destruction by exposure to acidic pH[10,39,40]; salmonellae isolated from cattle are killed at a pH < 3.4 and multiply at a pH > 5.5.[10] Maintaining a low abomasal pH provides a natural barrier to prevent ingested *Salmonella* organisms from reaching the small intestine and is therefore important for increasing nonspecific resistance to intestinal colonization and decreasing the incidence of clinical disease.[8,9] This has also been demonstrated in human medicine; the incidence of salmonellosis increases in people with impaired gastric acid secretion.[41–44]

Low gastric pH may also play a role in inactivating enteropathogenic viruses. Few studies have focused on the effects of gastric acidity on susceptibility to viral infections, and enteroviruses are generally known for their stability at a low pH.[9] However, 1 study[45] found rapid inactivation of bovine rotaviruses by exposure to gastric fluid at a pH of 2 but not at a pH of 4. Some evidence also exists for gastric pH being important in the prevention of giardiasis, *Strongyloides* infection, and potentially transmissible spongiform encephalopathies or prion infections.[9]

Other findings[46] by our research group have also suggested bicarbonate-containing OAEs have the potential to cause abomasal alkalinization. In a study[46] performed with the same experimental model as used in the present study, abomasal pH was monitored in calves fed an all-milk protein milk replacer or isotonic solutions of sodium bicarbonate, sodium acetate, or sodium chloride. Mean abomasal luminal pH was 1.42 prior to milk replacer feeding and increased to between 5 and 6 after feeding. Whereas sodium acetate and sodium chloride did not cause abomasal alkalinization, abomasal luminal pH increased to almost 8 after calves ingested isotonic sodium bicarbonate solution. In another study,[47] abomasal fluid samples were collected from calves at several points within the first 4 hours after feeding milk replacer or mixtures of milk replacer and OAEs. Calves had a consistently higher abomasal pH when mixtures were fed, compared with when just milk replacer was used. The abomasal alkalinization in that study occurred regardless of the type of alkalinizing agent (buffer) in the OAE. A study[48] from our research group found only a slight increase in maximum abomasal pH (pH increase, 0.8) when calves were fed a bicarbonate-based OAE versus cows' milk at 0 at 12 hours. However, the commercially available OAE used in that study[48] had a much lower concentration of bicarbonate (25mM), compared with the products used in the present study. These findings suggest that OAE formulations with a high bicarbonate concentration (> 70mM), such as both bicarbonate-containing high-glucose OAEs used in the study reported here, will yield more severe abomasal alkalinization than will OAEs with lower bicarbonate concentrations (< 40mM) and potentially result in an increase in the number of pathogenic bacteria colonizing the small intestine.

The rate of abomasal emptying influences the rate at which OAE is delivered to the small intestine and therefore the speed of rehydration in dehydrated calves with diarrhea.[49] The most important determinant of gastric emptying rate is the volume of the ingested fluid meal,[50,51] which was standardized in the study reported here. Other physiologically important determinants are the energy density (ie, caloric content) of a meal,[13,14,51] type of protein or fat,[52] and osmolarity of the solution.[13,14,53] Our finding that 2 commercially available high-glucose, high-osmolality OAEs slowed abomasal emptying rate in the present study was consistent with the findings of previous studies involving suckling calves with[5] or without[13,14] diarrhea and dehydration. Whether slowing of the abomasal emptying rate in dehydrated diarrheic calves receiving an OAE is clinically important remains to be determined.

The formation of a milk clot in the abomasum of milk-fed calves is another factor that could also influence abomasal emptying rate. It has been hypothesized that bicarbonate-containing OAEs interfere with the usual milk clot formation in calves[54–56]; however, this hypothesis has not been supported by any studies reported to date. In 1 study,[48] feeding an OAE containing a low concentration of bicarbonate (25mM/L) as well as acetate (12mM/L) and citrate (12mM/L), which was mixed with cows' milk, had little effect on clot formation in the abomasums of calves.

The primary determinant of milk clotting time has been shown to be abomasal pH.[57] In particular, as the pH of cows' milk increases from 6.4 to 7.2, there is an increase in the clotting time from 1.5 to 13 minutes. In vitro studies[55,56] have revealed that ingestion of bicarbonate-containing OAEs delays or inhibits milk clotting times at a pH > 6.6; however, in vitro studies are not relevant to in vivo clotting. This is because postprandial abomasal pH is markedly less than the pH of the OAE as fed. In the study[46] of the effects of an OAE containing a low concentration of bicarbonate (25mM/L) on milk clot formation, the addition of the electrolyte solution to the cows' milk increased milk and abomasal fluid pH by only 0.8. It remains to be determined whether OAEs containing a higher bicarbonate concentration (40 to 80mM/L) might delay or inhibit milk clot formation in calves.

The primary energy source in an OAE is glucose, which is usually fed at 1 to 3 g/kg (0.45 to 1.4 g/lb) in commercially available formulations, with 3.6 g/kg (1.64 g/lb) appearing to be the theoretical upper limit for glucose concentration in an OAE.[14] Doses of glucose > 3.6 g/kg may lead to glucosuria, urinary loss of energy and free water, and carryover of unabsorbed glucose into the large intestine, where glucose may be fermented to short-chain volatile fatty acids, exacerbate fecal water loss, and cause loose feces.[14] For comparison, in the glycine-free and glycine-containing hypertonic bicarbonate-containing OAEs and the isotonic acetate- and propionate-containing low-glucose OAE

used in the present study, glucose was administered at a dose of 4.3, 4.4, and 0.9 g/kg (1.95, 2, and 0.41 g/lb), respectively; however, the volume of the OAEs administered (60 mL/kg [27.3 mL/lb] or 2.7 L for a typical 45-kg dairy calf) exceeded the recommended label doses of 0.95 to 1.89 L (the 2 hypertonic solutions) and 1.5 L (the isotonic solution). At the dose recommended for a typical 45-kg calf, glucose would be administered through use of the aforementioned OAEs at a dose of 1.5 to 3.0, 1.6 to 3.1, and 0.5 g/kg (0.68 to 1.4, 0.73 to 1.41, and 0.23 g/lb), respectively. In other words, the 2 hypertonic solutions contain close to the theoretical maximum amount of glucose that can be administered to calves without potentially exacerbating free water losses. Such solutions may be best suited for use when milk replacer or whole milk is being withheld because of the high energy content relative to other OAEs.

The optimal abomasal pH curve for a 24-hour period in a calf has not been determined. However, given that enteric pathogens are killed at a pH < 3.0 to 3.5 and multiply at a pH > 5.0 to 5.5, it would not be beneficial for a calf to maintain gastric pH > 5.5 for a substantial portion of the 24-hour period. In the present study, calves fed an all-milk protein milk replacer had an abomasal pH > 5.5 for approximately 20% of the recording period. This value was similar to those obtained in studies[16,17,58] involving dairy calves fed the same or similar milk replacer. In contrast, calves fed either of the 2 bicarbonate-containing OAEs had an abomasal pH > 5.5 for at least 35% of the recording period (Figure 2) and it is possible that pH would exceed 5.5 for a longer percentage of each day should calves be fed and housed under typical dairy conditions.

In our experience, calves with mild to moderate diarrhea are generally fed fresh milk, milk replacer, or pasteurized waste milk twice a day and then an OAE at 1 to 2 additional feedings. Such feeding would create further abomasal alkalinization and would increase the mean 24-hour pH and the percentage of the 24-hour period that abomasal pH exceeded 5.5. A study[16] demonstrated that calves maintain a higher abomasal pH when feeding frequency is increased. Considering that the number of feedings per day increases in calves with diarrhea and abomasal alkalinization occurs associated with bicarbonate-containing OAEs, the potential exists for abomasal pH to be > 5.5 for > 35% of the day, allowing a greater number than usual of enteropathogenic bacteria to reach the intestinal tract.

Bicarbonate, acetate, propionate, and citrate are all considered alkalinizing agents and are common components of commercially available OAEs. Bicarbonate-containing OAEs are effective at correcting acidemia[3] because bicarbonate reacts directly with protons to form CO_2 and H_2O. Acetate and propionate have been shown to have alkalinizing effects similar to bicarbonate.[3,59] These short-chain volatile fatty acids have several theoretical advantages over bicarbonate in that they facilitate sodium and water absorption in the small intestines of calves, whereas bicarbonate does not; acetate and propionate also produce energy when metabolized, whereas bicarbonate does not.[6] In addition, acetate and propionate inhibit the growth of salmonellae, even in concentrations as low as 20mM,[39,60] which are typical of OAEs administered to calves with diarrhea.[4,6] These properties would appear to mark OAEs containing acetate and propionate as more appropriate for administering to diarrheic calves than those containing bicarbonate. Additional studies are needed to investigate this hypothesis.

a. 20F percutaneous endoscopic gastrostomy tubes, Mila International Inc, Florence, Ky.
b. Naxcel, Pfizer Animal Health, New York, NY.
c. Banamine, Intervet/Schering-Plough Animal Health, Millsboro, Del.
d. M3 internal reference glass pH electrode, Medical Instruments Corp, Solothurn, Switzerland.
e. Cole-Parmer pH/mV benchtop meter, Cole-Parmer Instrument Co, Vernon Hills, Ill.
f. Windaq, DATAQ Instruments, Akron, Ohio.
g. Supreme Calf Milk Replacer, Agrimaster, Janesville, Wis.
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Appendix

Composition of a high-glucose high-bicarbonate OAE (A), a high-glucose high-bicarbonate OAE that also contained glycine (B), and an isotonic acetate- and propionate-containing low-glucose OAE (C) fed to dairy calves.

	OAE		
Analyte	**A**	**B**	**C**
Sodium (mM)	142	106	81
Potassium (mM)	24	26	24
Chloride (mM)	80	51	53
Calcium (mM)	0	5	0
Magnesium (mM)	3	3	5
Glycine (mM)	0	33	0
Glucose (mM)	399	405	85
Bicarbonate (mM)	86	80	0
Acetate (mM)	0	0	43
Propionate (mM)	0	0	10
Effective strong ion difference (mEq/L)	86	80	53
Calculated osmolality (mOsm/L)	732	739	307

Effective strong ion difference is the net difference (in mM) between strong (nonmetabolizable or fixed) cation charge and strong anion charge.