Antibiotic Treatment of Diarrhea in Preweaned Calves

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PRELIMINARY REMARKS

A consensus statement of the American College of Veterinary Internal Medicine recently provided recommendations for the prudent use of antimicrobials in veterinary medicine.[1] Briefly, the statement recommends that veterinarians should use and prescribe antimicrobial drugs conservatively to minimize the potential adverse effects on animal or human health. Furthermore, veterinarians should develop formal infection control plans, identify common case scenarios (e.g., diarrhea, respiratory disease) in which antimicrobial drugs are often employed, develop antimicrobial use protocols for their practice, and categorize all antibiotics in primary, secondary, and tertiary use categories, besides appropriate diagnostic and sensitivity measures. Monitoring and surveillance for trends in the prevalence of resistant bacteria within a practice, a farm, a region, or a nation permits continual evaluation of antimicrobial drug use on various levels.

CLINICAL IMPORTANCE

Antimicrobial agents have been used for treating calves with diarrhea for more than 50 years. Diarrhea in preweaned calves is by far the leading cause of mortality in dairy heifer calves with no change in mortality rates between 1995 and 2001 in the United States.[2] Despite the widespread availability of vaccines against enterotoxigenic *Escherichia coli,* rotavirus, and coronavirus, as well as continued emphasis on optimizing colostral transfer of passive immunity, the oral and parenteral administration of antimicrobial agents continues to play an important role in the treatment of calf diarrhea.[3-7] Evidence-based recommendations for the administration of antimicrobial agents in diarrheic calves were recently developed based on a systematic review of randomized controlled studies published in peer-reviewed journals.[8,9] This chapter is based on those recommendations and the results of recent studies on the use of antimicrobials in calves with diarrhea during the first few weeks in life (preweaning period). For a complete historic background and reference list of antimicrobial use in the treatment of calf diarrhea, the reader is referred to these reviews.[8,9]

ETIOLOGY OF CALF DIARRHEA

Neonatal calf diarrhea is usually due to infection by at least one enteropathogen (enterotoxigenic *E. coli,* rotavirus, coronavirus, cryptosporidia, *Salmonella* spp.). In many herds several agents are usually present and can be detected in neonatal calves with and without diarrhea. If calf diarrhea occurs in an outbreak situation with high morbidity, *Salmonella* bacteria may be involved. Regardless of the etiology, calves with diarrhea often have increased coliform bacterial numbers in the small intestine and this colonization is associated with altered small intestinal function, morphologic damage, and increased susceptibility to bacteremia.[9] The importance of bacterial overgrowth in calf diarrhea recently gained attention when the role of D-lactic acid in the development of acidemia in calves with diarrhea was identified. Production of D-lactic acid results from bacterial fermentation in the gastrointestinal tract and is a common finding in neonatal calves with and without diarrhea.[10-12] D-lactic acid is a major component of acidemia in diarrheic calves[13-15] and is accompanied by systemic signs of weakness and ataxia.[16]

BACTERMIA IN CALVES WITH DIARRHEA

Calves with diarrhea are more likely to have failure of transfer or partial failure of transfer of passive immunity, and these calves are more likely to have bacteremia. Bacteremia, predominantly with *E. coli,* is present in approximately 20% to 30% of calves with diarrhea or systemic illness.[17-19] The frequency of bacteremia is considered sufficiently high that treatment of calves with diarrhea that are severely ill (as manifest by reduced suckle reflex, >6% dehydration, weakness, inability to stand, or clinical depression) should include routine treatment against bacteremia, with emphasis on treating potential *E. coli* bacteremia. A clinical sepsis score to predict bacteremia is not recommended to guide antibiotic treatment decisions until further validation of the score in different calf-rearing scenarios.[20] Bacteremia should be suspected to be present in all calves with clinical signs of *Salmonella* diarrhea, although the prevalence of bacteremia in affected calves has not been determined.[21]

ANTIMICROBIAL SUSCEPTIBILITY TESTING

Bacterial enteropathogens (enterotoxigenic *E. coli* and *Salmonella* spp.) are most commonly isolated from fecal samples or from specimens obtained during necropsy of a dead calf. Submission of appropriate specimens for bacterial culture, identification of pathogens, and susceptibility

testing by standardized methods has been widely recommended to allow an evidence-based approach for drug selection and justify antibiotic use.[1] Laboratory methods and standardized breakpoints need to be established for several bacteria-drug combinations.[1]

Several fecal isolates—*E. coli, Clostridium perfringens* type A, and *Campylobacter* spp.—are normal intestinal flora. Therefore diagnostic laboratories should clearly indicate normal bacterial growth in fecal culture samples, if the cultured bacteria cannot be distinguished from normal flora by identification of species, specific virulence factors or correlated markers, or clear demonstration of overgrowth.[1] When enterotoxigenic *E. coli* or *Salmonella* is isolated, susceptibility testing may provide a useful guide for treatment decisions and antimicrobial drug selection.

The most important determinant of antimicrobial efficacy in calf diarrhea is obtaining an effective antimicrobial concentration against bacteria at the sites of infection (small intestine and blood).[9] The results of fecal antimicrobial susceptibility testing in calf diarrhea probably have clinical relevance only when applied to fecal isolates of enterotoxigenic strains of *E. coli* or pathogenic *Salmonella* spp., and possibly blood culture isolates from calves with bacteremia. Current susceptibility testing methods have not been validated for predicting treatment outcome in calves with diarrhea.[9]

The ability of fecal bacterial culture and antimicrobial susceptibility testing using the Kirby Bauer technique to guide treatment in calf diarrhea is questionable when applied to fecal *E. coli* isolates that have not been identified as enterotoxigenic pathogenic strains. No reports have demonstrated a correlation between in vitro antimicrobial susceptibility of fecal *E. coli* and *Salmonella* spp. isolates and clinical response to antimicrobial treatment. Susceptibility results obtained from dead calves should be interpreted carefully because isolates obtained from dead calves are likely to be obtained from treatment failures, and calves that died from diarrhea are likely to have bacterial overgrowth in the intestines and many organs not representing the in vivo situation. Another concern with fecal susceptibility testing is that the Kirby Bauer break points (minimum inhibitory concentration [MIC]) are not based on typical antimicrobial concentrations in the small intestine and blood of calves. The practitioner should therefore evaluate the antimicrobial efficacy based on clinical response to antibiotic treatment.[9]

The Kirby Bauer technique for antimicrobial susceptibility test has theoretically more clinical relevance for predicting the clinical response to antimicrobial treatment when applied to blood isolates than fecal isolates. This is because the Kirby Bauer break points (minimum inhibitory concentration [MIC]) are based on achievable antimicrobial concentrations in human plasma and MIC$_{90}$ (MIC for 90% of the isolates) values for human *E. coli* isolates, which provide a reasonable approximation to achievable MIC values in calf plasma and MIC$_{90}$ values for bovine *E. coli* isolates.[9]

SUCCESS OF ANTIMICROBIAL THERAPY

Important considerations for treating calf diarrhea are (1) administering an antibiotic as directed on the label whenever possible, (2) using an antimicrobial agent with an appropriate spectrum of activity, (3) selecting an antimicrobial agent that attains and maintains an effective therapeutic concentration at the site of infection, (4) treating for an appropriate duration, and (5) avoiding adverse local or systemic effects and violative residues.[9] Important critical measures of success of antimicrobial therapy in calf diarrhea are (in decreasing order of importance) (1) mortality rate, (2) growth rate in survivors, (3) severity of diarrhea in survivors, and (4) duration of diarrhea in survivors.

Success of antimicrobial therapy varies with the route of administration and whether the antimicrobial is dissolved in milk, oral electrolyte solutions, or water. Oral antimicrobials administered as a bolus, a tablet, or in a gelatin capsule may be swallowed into the rumen and exhibit a different serum concentration-time profile to antimicrobials dissolved in milk replacers that are suckled by the calf or administered as an oral drench at the back of the pharynx. Antimicrobials that bypass the rumen are not thought to alter rumen microflora, potentially permitting bacterial recolonization of the small intestine from the rumen. The normal intestinal flora is always exposed to varying amounts of antimicrobial drugs regardless of the type of administration.[1] Historic studies reported that some orally administered antibiotics (e.g., potassium and procaine penicillin, neomycin sulfate, ampicillin trihydrate, tetracycline hydrochloride) may increase the incidence of diarrhea, produce malabsorption, and reduce growth rate.[9]

EVIDENCED-BASED RECOMMENDATIONS FOR ANTIMICROBIAL ADMINISTRATION IN CALF DIARRHEA

Oxytetracycline and sulfachlorpyridazine administered parenterally and amoxicillin, chlortetracycline, neomycin, oxytetracycline, streptomycin, sulfachlorpyridazine, sulfamethazine, and tetracycline administered orally have been labeled by the U.S. Food and Drug Administration (FDA) for the **treatment and aid in the control** of bacterial enteritis (scours, colibacillosis) caused by *E. coli* bacteria susceptible to the antimicrobial.[9] Four of the eight antibiotics (oral administration of chlortetracycline, oxytetracycline, tetracycline, and neomycin) approved for treatment of calf diarrhea are labeled by the FDA for the **control or aid in the control** of bacterial enteritis (scours, colibacillosis) caused by *E. coli* and *Salmonella* spp. bacteria susceptible to the antimicrobial.[8]

Studies supporting the efficacy of parenteral oxytetracycline and sulfachlorpyridazine, and of oral amoxicillin, chlortetracycline, neomycin, oxytetracycline, streptomycin, sulfachlorpyridazine, sulfamethazine, and tetracycline in treating calves with naturally acquired diarrhea do not appear to have been published in peer-reviewed journals.[9] Oral amoxicillin was effective in the treatment of experimentally induced diarrhea[22,23] but was not efficacious in the treatment of naturally acquired diarrhea in beef calves.[24] In view of the apparent lack of published studies documenting clinical efficacy of antimicrobials with a label claim for the treatment of naturally occurring calf diarrhea, and because the health of the animal is threatened and suffering or death may result from failure

to treat systemically ill calves, extra-label antimicrobial use (excluding prohibited antimicrobials) is justified for the treatment of calf diarrhea.[9]

Antimicrobials for the treatment of calf diarrhea should have local (small intestine) and systemic efficacy because the predominant sites of infection in calf diarrhea are the small intestine and blood.[9] The antimicrobial must reach therapeutic concentrations at the site of infection for a long enough period and, ideally, have only a narrow gram-negative spectrum of activity in order to minimize effects on normal intestinal flora.

The results of several studies indicate that oral and parenteral administration of broad-spectrum β-lactam and fluoroquinolone antimicrobials is efficacious in treating naturally acquired and experimentally induced diarrhea. It must be highlighted that administration of fluoroquinolone antimicrobials in a extralabel manner is illegal in the United States.* Parenteral administration of trimethoprim/sulfadiazine and ceftiofur (high extra-label dose) has proven efficacy in treating experimentally induced infections with *Salmonella enterica* serotype Dublin and serotype Typhimurium, respectively.[21,25] Orally administered apramycin has proven efficacy in treating naturally acquired diarrhea but is poorly absorbed after oral administration (oral bioavailability <15%) and has relatively high MIC values against *Salmonella* spp. and *E. coli* (MIC_{90} >3 μg/ml) in the calf.[26] Based on these issues, treatment recommendations focus on the use of broad-spectrum β-lactam antimicrobials such as amoxicillin, ampicillin, ceftiofur, and potentiated sulfonamides (trimethoprim/sulfadiazine).

Administration of Oral Antimicrobials to Treat *E. Coli* Overgrowth of the Small Intestine

In neonatal calves with diarrhea and mild systemic illness (defined as depressed suckling but normal rectal temperature, hydration status, and heart rate), the veterinarian should continue to monitor the calf's health or orally administer amoxicillin trihydrate (10 mg/kg, q12h) or amoxicillin trihydrate-clavulanate potassium (12.5 mg combined drug/kg, q12h) for at least 3 days; the latter constitutes extralabel drug use. Oral amoxicillin trihydrate (10 mg/kg, q12h for 4 days) was efficacious in decreasing mortality rate and duration of diarrhea in two studies where diarrhea was experimentally induced with enterotoxigenic *E. coli* bacteria.[22,23] The absorption rate of amoxicillin trihydrate from the calf small intestine is 30% when administered in milk.[27] High amoxicillin concentrations are present in the bile and intestinal contents, with lower antimicrobial concentrations in serum.[21] Feeding of amoxicillin with milk does not change the bioavailability of amoxicillin, although amoxicillin is absorbed faster when dissolved in an oral electrolyte solution

than in milk replacer.[28] Amoxicillin absorption is slowed during endotoxemia, presumably because of a decrease in abomasal emptying rate.[29] Amoxicillin trihydrate is preferred to ampicillin trihydrate for oral administration in calves because it is labeled for the treatment of calf diarrhea in the United States and is absorbed to a much greater extent.[27,28,30] However, a field study comparing equal amounts (400 mg, q12h) of oral amoxicillin and ampicillin for the treatment of diarrhea reported similar proportions of calves with a good to excellent clinical response.[31] The addition of clavulanate potassium to amoxicillin trihydrate is recommended because clavulanate potassium is a potent irreversible inhibitor of β-lactamase, increasing the antimicrobial spectrum of activity.

Oral administration of potentiated sulfonamides is not recommended for treating calf diarrhea because of the lack of efficacy studies. Oral administration of gentamicin is not recommended because antimicrobials administered to calves with diarrhea should have both local and systemic effects, and orally administered gentamicin is poorly absorbed. No other orally administered antimicrobial currently available in the United States is likely to be effective in treating neonatal calves with diarrhea.[9]

Fluoroquinolones clearly have proven efficacy in treating calf diarrhea, and a label indication exists in Europe for oral and parenteral enrofloxacin, oral marbofloxacin, and parenteral danofloxacin for the treatment of calf diarrhea. In those countries where their administration is permitted to treat calf diarrhea, oral fluoroquinolones are recommended because of their high oral bioavailability. However, it must be emphasized that extralabel use of the fluoroquinolone class of antimicrobials in food-producing animals in the United States is illegal and obviously not recommended.

Experts currently believe that salmonellosis is more of a systemic infection than local (intestinal) infection. Accordingly, parenteral administration is preferred when treating calves with salmonellosis.

It is possible that the widespread use of antibiotics in milk replacer in the United States may lead to a decreased incidence of D-lactic acidosis in calves with diarrhea, when compared with calves in Germany and Canada. Both Germany and Canada have a milk quota system that promotes feeding whole milk instead of milk replacer to calves. Because D-lactic acidosis in calves results from bacterial fermentation of milk in the gastrointestinal tract,[10] feeding milk-replacer that contains antibiotics could decrease the generation of D-lactic acid in calf intestine, assuming that the antibiotic promotes growth of non–D-lactate–producing bacteria.

Administration of Parenteral Antimicrobials to Treat *E. Coli* Bacteremia and Salmonellosis

In calves with diarrhea and moderate to severe systemic illness, the predictive accuracy of clinical and laboratory tests for detecting bacteremia are too low assuming reasonable estimates for the prevalence of bacteremia (20%-30%) in the field.[18-20] Bacteremia constitutes a significant cause of mortality and threat to the life of the calf. Therefore the authors recommend that clinicians routinely assume 20% to 30% of ill calves with diarrhea

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*Extralabel administration of fluoroquinolones in food-producing animals in the United States is prohibited by law because of concerns regarding assisting the emergence of bacteria with multiple antimicrobial resistance, particularly pathogenic enteric bacteria in humans.

are bacteremic. Parenteral antimicrobial treatment is required for these calves.

Administration of ceftiofur (2.2 mg/kg [1 mg/lb], SC/IM, q12h) for at least 3 days is the most logical parenteral treatment for *E. coli* bacteremia.[9] Treatment of experimental salmonellosis with high extralabel dose of ceftiofur (5 mg/kg, IM, q24h) for 5 days was recommended to maintain antimicrobial concentrations above the MIC_{90} (1 µg/ml) for the *Salmonella enterica* serovar Typhimurium challenge strain.[21] Because other *Salmonella* serotypes present on a farm may have much higher MIC_{90} values, determination of MIC values is recommended before the start of treatment.[21] Ceftiofur constitutes an extralabel drug use for the treatment of *E. coli* bacteremia and salmonellosis, and ceftiofur should not be administered to calves to be processed as veal.

The second recommended treatment for *E. coli* bacteremia is parenteral amoxicillin trihydrate or ampicillin trihydrate (10 mg/kg, IM, q12h) for at least 3 days.[9] Both drugs are theoretically inferior to ceftiofur because parenterally administered ampicillin and amoxicillin reach lower plasma concentrations and require a higher MIC than ceftiofur, and they are not β-lactamase resistant. Even though the rate and extent of absorption is reduced with subcutaneous (SC) injection, relative to IM injection of amoxicillin and ampicillin,[32] SC administration is preferred in order to minimize potentially more painful IM injections, especially when repeated doses are administered. The most crucial issue in sick calves with diarrhea is maintaining or restoring a good suckle reflex for successful and adequate intake of milk and oral electrolyte solutions. Calves suffering from pain from whatever reason probably have a weak or absent suckle response as compared with calves without pain.

A third recommended treatment for the treatment of *E. coli* bacteremia is parenteral potentiated sulfonamides (20 mg/kg sulfadiazine with 5 mg/kg trimethoprim; IV or IM depending on the formulation characteristics, q24h for 5 days). Efficacy of potentiated sulfonamides has only been proven when treatment commenced before clinical signs of diarrhea were present.[25] Therefore it is unknown whether potentiated sulfonamides are efficacious when administered to calves with diarrhea and depression, although potentiated sulfonamides are likely efficacious in the treatment of salmonellosis.

Oral administration of potentiated sulfonamides is not recommended for the treatment of bacteremia because of poor oral bioavailability. Oxytetracycline and chlortetracycline may have some efficacy for treating *E. coli* bacterial overgrowth of the small intestine but are not recommended for the treatment of bacteremia.[9] Oral bioavailability of tetracycline antimicrobials is significantly decreased because they are bound to calcium. Oxytetracycline must be administered at 20 mg/kg, q12h, PO to achieve minimal serum concentrations to treat *E. coli* bacteremia (MIC_{50} = 4 µg/ml).[33]

Parenteral administration of gentamicin and other aminoglycosides (amikacin, kanamycin) cannot be currently recommended as part of the treatment for calf diarrhea in the United States because of prolonged slaughter withdrawal times (15-18 months); potential for nephrotoxicity in dehydrated animals; and availability of ceftiofur,

amoxicillin, and ampicillin. However, in two studies from Europe parenteral administration of gentamicin was equally effective as danofloxacin or fourth-generation cephalosporin cefquinome for the treatment of diarrhea or calves with clinical signs of septicemia.[19,34] Both studies were conducted in the field and did not include a negative control group.

In Europe a label indication exists for parenteral fluoroquinolones for the treatment of *E. coli* diarrhea and salmonellosis in calves. In those countries where administration is permitted to treat calves with *E. coli* diarrhea and salmonellosis, parenteral fluoroquinolones are only recommended when specific evidence from culture and susceptibility results suggest that these drugs are necessary and efficacious. For these reasons, it is preferable that parenteral fluoroquinolone administration be reserved for critically ill calves such as those also requiring intravenous fluid administration. However, it must be emphasized that extralabel use of the fluoroquinolone class of antimicrobials in food-producing animals is illegal in the United States.

In calves with diarrhea but no evidence of systemic illness (i.e., normal appetite for milk or milk replacer, no fever), we recommend that the clinician monitor the health of the calf and not administer parenteral antimicrobials. A recent study from Sweden concluded that most calves with uncomplicated diarrhea (i.e., the absence of concurrent infections such as pneumonia or omphalophlebitis) do not benefit from antibiotic treatment.[4]

Long-Term Administration of Oral Antibiotics for Prevention and Therapy of Calf Diarrhea

Antimicrobials in milk replacer are intended to prevent or treat bacterial scours and decrease the incidence of other common calf diseases during the neonatal period. Dairy heifer calves were fed with milk replacer containing antibiotics on 56% of herds in 2001 in the United States.[6] Local surveys reported between 45% (Michigan, Minnesota, New York, Wisconsin)[7] and 70% (Pennsylvania)[5] of dairy herds are using medicated milk replacer. Oxytetracycline in combination with neomycin followed by oxytetracycline alone are the most common medications.[6] Several studies reported inconsistent results of the effects of antibiotics containing milk replacer on the incidence of diarrhea (scours). The incidence of diarrhea was not influenced when antibiotics in milk replacer were compared with oligosaccharides or bovine plasma as nonantibiotic alternative treatments.[35-37] A more extensive recent study found that the onset and overall morbidity of important diseases in calves during their first weeks of life (diarrhea, respiratory disease, navel infection) were significantly lower in calves receiving antibiotics neomycin sulphate (22 mg/kg/day) and tetracycline HCl (22 mg/kg/day) in milk replacer than in control calves without in-feed antibiotics.[38] This study did not exclusively consider diarrhea as the primary outcome, but the findings are valuable because they reflect the pattern of diseases in newborn calves in a specialized calf-rearing facility with high disease incidence in a stressful environment.

It should be recognized that in one report the use of antibiotics in milk replacer was associated with a decreased risk of infection with *C. parvum* in preweaning dairy calves,[39] even though cryptosporidia are not directly susceptible to antibiotics. Another study reported that lack of routine feeding of medicated milk replacer (name of antibiotics not presented) increased the odds for isolation of *Salmonella* bacteria from calves.[40]

ANCILLARY TREATMENTS FOR CALF DIARRHEA

Oral and Intravenous Fluids

Administration of oral and parenteral fluids to calves with diarrhea is essential for adequate rehydration and restoration of circulating blood volume, correction of acidemia, electrolyte abnormalities, energy deficits, and mental depression to restore the suckle reflex and assist repair of the damaged intestinal surface. Oral administration of electrolyte-containing solutions may cover episodes of diarrhea with minimal or moderate dehydration and good suckle reflex. Calves that are unable to suckle, recumbent, severely depressed, or comatose need intravenous fluids for effective resuscitation. (See Chapter 104 for further discussion of fluid therapy.)

Nonsteroidal Antiinflammatory Drugs

Flunixin meglumine is probably the most widely antiinflammatory treatment of diarrheic calves. The administration of a single dose of flunixin meglumine (2.2 mg/kg [1 mg/lb] IM) as an adjunct treatment for naturally occurring diarrhea resulted in fewer morbid-days and antimicrobial treatments only when calves had fecal blood in their feces.[41] In calves with experimentally induced enterotoxigenic *E. coli* infection, flunixin meglumine (2.2 mg/kg [1 mg/lb] q8h IM) reduced fecal output perhaps by acting as an antisecretory agent.[42] Flunixin meglumine (2.2 mg/kg [1 mg/lb] q12h) is indicated in severely sick calves with presumed endotoxemia when hydration status is adequate to prevent nephrotoxicity. A rule of thumb is to administer flunixin meglumine once at a dose 2.2 mg/kg (1 mg/lb) and not to exceed three doses of flunixin meglumine for the treatment of diarrhea and respiratory disease to avoid potential damage of the intestinal mucosa of the abomasum, especially in intensive calf-rearing facilities with a history of case fatalities from perforated abomasal ulcers. An important effect of flunixin meglumine administration is the clinical impression that calves show a better suckle behavior after therapy. This impression is supported by a recent statement that "the use of flunixin meglumine is valuable in improving the well-being of the calves."[38]

Motility Modifiers and Intestinal Protectants

Administration of intestinal protectants (e.g., kaolin-pectin, activated attapulgite) or motility modifiers (e.g., hyoscine N-butylbromide, atropine) is not recommended despite their widespread use. No data on efficacy are available, and a recent study showed that nonantibiotic treatments including bismuth, kaolin-pectin, activated attapulgite, and activated charcoal for calf diarrhea resulted in prolonged duration of treatment and increased risk for morbidity and mortality compared with oral antibiotics in milk replacer (neomycin sulfate and tetracycline HCl) and parenteral administration of ceftiofur hydrochloride (2.2 mg/kg, 3-5 days).[38]

Probiotics

Administration of probiotics to diarrheic calves is done in some dairy herds. A recent study under field conditions showed that prophylactic administration of the probiotic bacteria *E. coli* strain Nissle 1917 for the first 10 or 12 days of life to calves with unknown status of passive transfer was associated with a significant decrease in the number of calves developing diarrhea.[43] In calves with spontaneous diarrhea, *Lactobacillus rhamnosus GG* administration for therapy of diarrhea was not associated with lower mortality or a decrease of scours in a clinical setting.[44] Another recent study in neonatal foals documented that administration of a different *Lactobacillus* strain for the prevention of diarrhea was associated with the development of diarrhea and further clinical abnormalities requiring veterinary intervention.[45] Based on these reports, administration of *E. coli* strain Nissle 1917 may be of value for the prevention of diarrhea in calves.

Oligosaccharides

Oligosaccharides in milk replacer are minimally absorbed in the small intestine and are thought to decrease binding of bacterial pathogens to enterocytes. Studies in calves reported that prophylactic addition of oligosaccharides to milk replacer resulted in fecal scores (scours) in calves that were similar to those observed when calves were fed milk replacer containing antibiotics.[35,36,46] It must be noted that in these studies data on morbidity and mortality were either low or remained undetermined.[46] Likely observed scours resulted primarily from nutritional origin rather than from infectious origins.[36]

Vitamins

Administration of B vitamins and fat-soluble vitamins may have beneficial effects in colostrum-deprived calves and in calves with chronic diarrhea. However, data supporting the beneficial effects of vitamins in calf diarrhea are lacking.

References

1. Morley PS, Apley MD, Besser TE et al: Antimicrobial drug use in veterinary medicine, *J Vet Intern Med* 19:617, 2005.
2. U.S. Department of Agriculture: 2002. Part II: Changes in the United States Dairy Industry, 1991-2002 USDA:APHIS: VS:CEAH, National Animal Health Monitoring System, Fort Collins, Colo #N388.0603.
3. Busani L, Graziani C, Franco A et al: Survey of the knowledge, attitudes and practice of Italian beef and dairy cattle veterinarians concerning the use of antibiotics, *Vet Rec* 155:733, 2004.

4. Ortman K, Svensson C: Use of antimicrobial drugs in Swedish dairy calves and replacement heifers, *Vet Rec* 154:136, 2004.

5. Sawant AA, Sordillo LM, Jayarao BM: A survey on antibiotic usage in dairy herds in Pennsylvania, *J Dairy Sci* 88:2991, 2005.

6. USDA: 2005. Part IV: Antimicrobial Use on U.S. Dairy Operations, 2002 USDA:APHIS:VS:CEAH, National Animal Health Monitoring System, Fort Collins, Colo #430.0905.

7. Zwald AG, Ruegg PL, Kaneene JB et al: Management practices and reported antimicrobial usage on conventional and organic dairy farms, *J Dairy Sci* 87:191, 2004.

8. Constable PD: Use of antibiotics to prevent calf diarrhea and septicaemia, *Bov Pract* 37:137, 2003.

9. Constable PD: Antimicrobial use in the treatment of calf diarrhea, *J Vet Intern Med* 18:8, 2004.

10. Ewaschuk JB, Naylor JM, Palmer R: D-lactate production and excretion in diarrheic calves, *J Vet Intern Med* 18:744, 2004.

11. Navetat H, Biron P, Contrepois M et al: Les gastroentérites paralysantes: maladie ou syndrome? *Bull Acad Vet France* 70:327, 1997.

12. Schlecher F, Marcillaud S, Braun JP et al: Metabolic acidosis without dehydration and no or minimal diarrhoea in suckler calves is caused by hyper D-lactatemia, *Proc World Buiatrics Congress* 89:371, 1998.

13. Constable PD, Staempfli HR, Navetat H et al: Use of a quantitative strong ion approach to determine the mechanism for acid-base abnormalities in sick calves with or without diarrhea, *J Vet Intern Med* 19:581, 2005.

14. Ewaschuk JB, Naylor JM, Zello GA: Anion gap correlates with serum D- and DL-Lactate concentration in diarrheic neonatal calves, *J Vet Intern Med* 17:940, 2003.

15. Lorenz I: Influence of D-lactate on metabolic acidosis and on prognosis in neonatal calves with diarrhoea, *J Vet Med A Physiol Pathol Clin Med* 51:425, 2004a.

16. Lorenz I: Investigations on the influence of serum D-lactate levels on clinical signs in calves with metabolic acidosis, *Vet J* 168:323, 2004b.

17. Fecteau G, Van Metre DC, Paré J et al: Bacteriological culture of blood from critically ill neonatal calves, *Can Vet J* 38:95, 1997a.

18. Lofstedt J, Dohoo IR, Duizer G: Model to predict septicaemia in diarrheic calves, *J Vet Intern Med* 13:81, 1999.

19. Thomas E, Roy O, Skowronski V et al: Comparative field efficacy study between cefquinome and gentamicin in neonatal calves with clinical signs of septicaemia, *Revue Méd Vét* 155:489, 2004.

20. Fecteau G, Paré J, Van Metre DC et al: Use of a clinical sepsis score for predicting bacteremia in neonatal dairy calves on a calf rearing farm, *Can Vet J* 38:101, 1997b.

21. Fecteau ME, House JK, Kotarski SF et al: Efficacy of ceftiofur for treatment of experimental salmonellosis in neonatal calves, *Am J Vet Res* 64:918, 2003.

22. Bywater J: Evaluation of an oral glucose-glycine-electrolyte formulation and amoxicillin for treatment of diarrhea in calves, *Am J Vet Res* 38:1983, 1977.

23. Palmer GH, Bywater RJ, Francis ME: Amoxycillin: distribution and clinical efficacy in calves, *Vet Rec* 100:487, 1977.

24. Radostits OM, Rhodes CS, Mitchell ME et al: A clinical evaluation of antimicrobial agents and temporary starvation in the treatment of acute undifferentiated diarrhea in newborn calves, *Can Vet J* 16:219, 1975.

25. White G, Piercy DWT, Gibbs HA: Use of a calf salmonellosis model to evaluate the therapeutic properties of trimethoprim and sulphadiazine and their mutual potentiation in vivo, *Res Vet Sci* 31:27, 1981.

26. Ziv G, Bor A, Soback S et al: Clinical pharmacology of apramycin in calves, *J Vet Pharmacol Ther* 8:95, 1985.

27. Ziv G, Nouws JFM, Groothuis DG et al: Oral absorption and bioavailability of ampicillin derivatives in calves, *Am J Vet Res* 38:1007, 1977.

28. Palmer GH, Bywater RJ, Stanton A: Absorption in calves of amoxycillin, ampicillin, and oxytetracycline in milk replacer, water, or an oral rehydration formulation, *Am J Vet Res* 44:68, 1983.

29. Groothuis DG, van Miert ASJPAM, Ziv G et al: Effects of experimental *Escherichia coli* endotoxemia on ampicillin: amoxicillin blood levels after oral and parenteral administration in calves, *J Vet Pharmacol Ther* 1:81, 1978.

30. Larkin PJ: The distribution of a 400 mg dose of ampicillin administered orally to calves, *Vet Rec* 90:476, 1972.

31. Keefe TJ: Clinical efficacy of amoxicillin in calves with colibacillosis, *Vet Med Small Anim Clin* 72(suppl):783, 1977.

32. Rutgers LJE, Van Miert ASJPAM, Nouws JFM et al: Effect of the injection site on the bioavailability of amoxicillin trihydrate in dairy cows, *J Vet Pharmacol Ther* 3:125, 1980.

33. Schifferli D, Galeazzi RL, Nicolet J et al: Pharmacokinetics of oxytetracycline and therapeutic implications in veal calves, *J Vet Pharmacol Ther* 5:247, 1982.

34. Sunderland SJ, Sarasola P, Rowan TG et al: Efficacy of danofloxacin 18% injectable solution in the treatment of *Escherichia coli* diarrhoea in young calves in Europe, *Res Vet Sci* 74:171, 2003.

35. Donovan DC, Franklin ST, Chase CCL et al: Growth and health of Holstein calves fed milk replacers supplemented with antibiotics or Enteroguard, *J Dairy Sci* 85:947, 2002.

36. Heinrichs AJ, Jones CM, Heinrichs BS: Effects of mannan oligosaccharide or antibiotics in neonatal diets on health and growth of dairy calves, *J Dairy Sci* 86:4064, 2003.

37. Quigley JD III, Drew MD: Effects of oral antibiotics of bovine plasma on survival, health and growth in dairy calves challenged with, *Escherichia coli, Food Agric Immunol* 12:311, 2000.

38. Berge ACB, Lindeque P, Moore DA et al: A clinical trial evaluating prophylactic and therapeutic antibiotic use on health and performance of preweaned calves, *J Dairy Sci* 88:2166, 2005.

39. Mohammed HO, Wade SE, Schaaf S: Risk factors associated with Cryptosporidium parvum infection in dairy cattle in southeastern New York State, *Vet Parasitol* 83:1, 1999.

40. Fossler CP, Wells SJ, Kaneene JB et al: Herd-level factors associated with isolation of Salmonella in a multi-state study of conventional and organic dairy farms II. Salmonella shedding in calves, *Prev Vet Med* 70:279, 2005.

41. Barnett SC, Sischo WM, Moore DA et al: Evaluation of flunixin meglumine as an adjunct treatment for diarrhea in dairy calves, *J Am Vet Med Assoc* 223:1329, 2003.

42. Roussel AJ, Sriranganathan N, Brown SA et al: Effect of flunixin meglumine on *Escherichia coli* heat-stable enterotoxin-induced diarrhea in calves, *Am J Vet Res* 49:1431, 1988.

43. Buenau R von, Jaekel L, Schubotz E et al: *Escherichia coli* strain Nissle 1917: Significant reduction of neonatal calf diarrhea, *J Dairy Sci* 88:317, 2005.

44. Ewaschuk JB, Zello GM, Naylor JM: Lactobacillus GG does not affect D-lactic acidosis in diarrheic calves, in a clinical setting, *J Vet Intern Med* 20:614, 2006.

45. Weese JS, Rousseau J: Evaluation of Lactobacillus pentosus WE7 for prevention of diarrhea in neonatal foals, *J Am Vet Med Assoc* 226:2031, 2005.

46. Quigley JD III, Drewry JJ, Murray LM et al: Body weight gain, feed efficiency, and fecal scores of dairy calves in response to galactosyl-lactose or antibiotics in milk replacers, *J Dairy Sci* 80:1751, 1997.