Differentiating causes of neonatal calf enteritis to enhance management and prevention

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Abstract

There are numerous different agents that cause infectious enteritis in neonatal calves. Although each of these agents have some unique features, the pathophysiological effects on calves can be grouped into 2 categories that are useful in establishing appropriate treatment protocols and management guidelines. One group includes the viral pathogens rotavirus and coronavirus plus the protozoal agent *Cryptosporidium*. These are non-invasive, cause diarrhea with associated fluid and electrolyte loss that responds well to fluid therapy and are not affected by antibiotic treatment. The other group includes bacterial pathogens that cause different pathophysiologic changes including significant inflammatory response and invasion beyond the intestinal lining. The differences between these groups should guide treatment methods and help establish realistic prognostic expectations and preventive practices. Most affected calves are treated by the workers on a cattle operation. Educating these workers about clinical signs of disease that distinguish between causes of neonatal enteritis could help guide more successful treatment and more judicious antibiotic use.

Key words: neonatal enteritis, calf scours

Introduction

Neonatal enteritis is the most common cause of illness and death in calves between 2 and 30 days of age. Calves that die within the perinatal period of first 24 to 48 hours after birth are most commonly affected by physiologic derangements associated with in-utero problems or dystocia, as well as severe adverse weather conditions. Thereafter, infectious disease is the most common newborn calf challenge, and infectious enteritis is the premier threat during the neonatal period that goes through 30 days of age.[4,11]

Many cattle producers and veterinarians tend to view infectious enteritis as a single common group of problems, and then use a common treatment and prevention protocol for most cases. Alternatively, enteritis outbreaks are often categorized by specific etiologic agents, such as rotavirus, cryptosporidiosis, salmonellosis, etc. These groupings are understandable because these problems are well described in textbooks, which similarly either lump them all together as 'neonatal enteritis' or describe them as individual, pathogen-specific problems.[4]

The purpose of this presentation is to provide a characterization of calf enteritis problems based on 2 different groups of pathophysiologic conditions. This has utility because it can improve the focus of diagnostic methods, treatment protocols, and preventive practices. No categorization system is perfect, because there are always 'exceptions to the rule' and there is certainly variation among affected individuals, while this scheme provides just 2 broad categories. But in a field setting with practical and economic constraints, it can be very useful to have thumb rules that help guide decisions. I have consistently found that categorizing calf enteritis problems as described here is helpful in educating producers and guiding more judicious decisions about treatments.

There is a relatively easy distinction between localized, superficial infections that are not invasive, versus more aggressive, tissue-damaging infections with toxins and capability to invade and create septicemia. These can be generally differentiated based on clinical signs, historical epidemiologic features, response to treatment, and gross necropsy. Although extensive laboratory testing is not usually necessary, use of laboratory testing is also advisable both for educational purposes and to confirm that important aspects of a herd outbreak are not being overlooked.

'Calf Scours' - Viral/Protozoal Enteritis

The most common pathogens that cause neonatal calf enteritis (both beef and dairy) are rotavirus, coronavirus and *Cryptosporidium parvum*. Although there are differences between these pathogens regarding how severely they damage intestinal epithelium and how they replicate, they share some common features that effectively create the same disease entity. Because they damage intestinal epithelium, they affect digestion and absorption of intestinal fluid (i.e. malabsorption and maldigestion) as their primary pathological effects, which in turn determine clinical disease signs. The primary problem with these infections is diarrhea/scours causing fluid and electrolyte loss. These losses lead to dehydration, acidosis, depression, and weakness. When these pathophysiologic features progress severely enough and are not mitigated by fluid and electrolyte supplementation, the losses lead to calf death.[2,4]

These pathogens are not invasive. They tend to cause minimal inflammatory response either at the gut level or systemically. The pathophysiological effects and the clinical signs are closely tied together in the majority of cases;

that is, the more significant the fluid and electrolyte loss, the more severe the clinical signs, with potential to lead to hypovolemic shock, severe systemic acidosis, and ultimately death.[2,9] At necropsy it is easy to detect that there is minimal inflammatory damage to the intestinal tract or other tissues.

The common pathophysiology of disease caused by these infectious agents leads to some relatively simple guidelines for observation and management. First, affected calves typically have similar coincidence of clinical signs. The severity of diarrhea is matched by severity of fluid and electrolyte loss, and thus severity of dehydration, depression, weakness, and acidosis. It is uncommon to have, for example, severe depression but mild dehydration or to see acute death without preceding morbidity.[2,4,9] Second, the peak incidence is between 7 and 10 to 14 days of age. Some outliers may occur, but if an owner tracks age of onset it is most common to have almost all calves become sick within this narrow window. Third, if an appropriate oral electrolyte replacement supplement is used promptly and with sufficient volume, almost all calves can survive the infection and clear the pathogen.[9,10] Fourth, antibiotics have no efficacy against these pathogens, and anti-inflammatory agents have very limited beneficial effect.

These are ubiquitous pathogens, found in virtually all cattle operations. All of these agents require a very low infectious dose to cause infection, but multiply in the intestine at remarkably high rates and contaminate the environment through fecal shedding.[4] Therefore, if management is not targeted to specifically reduce calf exposure then a propagated epidemic can ensue. In beef herds this typically manifests such that during the first couple weeks of the calving season no cases are seen, and then the incidence rate escalates though the later part of the calving season as exposure from older shedding calves produces increasing infection rates in younger calves. Preventing this propagated epidemic is the key feature of successful prevention efforts.[8]

There are certainly some variations between individually affected calves, and these are emphasized in textbooks.[4] Some calves may have significant depression and acidosis, but only limited observable diarrhea. The clinical severity of disease can be quite variable, as with most infectious problems, such that some calves can recover regardless of how they are treated, while other calves require aggressive fluid therapy to survive. Some calves can have documented shedding of pathogens and almost no clinical disease. Disease associated with coronavirus infection tends to be more severe. Age ranges of onset of disease have been described to occur between the first week of life and up to 3 weeks or even 30 days. However, as bovine veterinarians we have the advantage of working with herds more than unique individuals, and so the commonality between affected calves is relatively easy to see if multiple individuals are affected, i.e. the majority of calves show clinical signs closely linked to the degree of diarrhea, and with peak age of onset between 7 and 14 days.

It's important to include enterotoxigenic *E. coli* (ETEC), or K99 *E. coli*, in this discussion. It is neither viral, nor protozoal, but the effects of K99 *E. coli* put it in the same category of "calf scours". The K99 pilus attaches the bacteria to the enterocytes, where the bacteria can then affect the cells via its heat-stable enterotoxin. The toxin produces aberrant secretion by the cells, leading to severe diarrhea and fluid and electrolyte loss as its pathophysiologic effect.[2] Again, there is minimal inflammatory change and no invasion beyond the mucosa. Forty years ago, this was a primary killer of baby calves because it was a common disease and the fluid and electrolyte losses were so extreme that it was very difficult to save affected calves. However, one of the unique features of this pathogen is that it is only capable of affecting calves in the first 3 to 5 days of life. Because the K99 antigen can be effectively blocked with specific antibodies, it is a relatively easy problem to prevent with colostrum or monoclonal antibody products making it relatively uncommon in recent years. Assuring that cows have protective antibodies against this pathogen in their colostrum is one of the most compelling reasons for use of the maternal colostrum vaccines.

Bacterial Enteritis/Inflammatory Enteritis and Septicemia

The bacterial enteric pathogens of baby calves represent a very different threat compared to classic 'calf scours' resulting from viral and protozoal enteritis. The most common of these are *Salmonella* spp and enteropathogenic *E. coli*.[1,4,6] One might also include clostridial enteritis in this group. Although it's worth emphasizing that most strains of *E. coli* are normal gut inhabitants, the pathogenic 'attaching and effacing' strains, or Shiga toxin strains, are highly pathogenic. These agents typically create a very different disease scenario.[1,4,6] By nature, they have toxic and invasive capabilities, depending on the particular strain of bacteria. Both salmonella and *E. coli* are gram-negative and therefore have endotoxin. They can produce extreme inflammatory responses. The clostridial agents are well known producers of exotoxins and can damage both the intestinal tissues and other organ tissues.

The disease scenario that unfolds with these agents may or may not manifest as diarrhea. The intestinal tract will be affected, and feces will be abnormal, but most commonly this will not be high-volume, fluid feces resulting in electrolyte and fluid loss as the primary cause of disease signs. Rather, affected calves may have blood and protein in the feces, or may develop ileus and abdominal filling with minimal feces. Importantly, the intestinal damage commonly leads to invasion of deeper tissues either by the primary pathogen or by other bacteria, thus leading to septicemia. Affected calves may die acutely without preceding signs of diarrhea. Calves commonly show multi-systemic signs such as pneumonia, meningitis, renal disease, and septic arthritis.[1,4,6]

Physical examination of affected calves will reflect this very different pathophysiology. Rather than seeing a fairly close relationship between diarrhea, fluid loss, dehydration and depression, most calves with bacterial enteritis will demonstrate significant inflammatory response. This can appear as depression and weakness with minimal dehydration, significant signs of pneumonia, swollen joints, abnormal feces without significant fluid loss, acute death, injected scleral vessels, and congested mucous membranes.[1,6] Affected calves are not suffering from hypovolemic shock, but rather from septic shock or toxemic shock. This has very important implications for treatment and prognosis.

Age of disease onset is also highly variable. In herds with bacterial inflammatory enteritis it is common to have calves showing severe disease at 3 to 7 days of age, in addition to calves between 7 and 14 days and commonly calves well beyond 2 weeks of age. It is uncommon for a herd outbreak of the disease to be restricted to calves specifically in the 7 to 14 day-of-age window.[1,6]

Gross necropsy very commonly demonstrates significant intestinal inflammatory lesions plus other organ system damage. Antemortem, a simple CBC can show compelling evidence of rampant inflammation with the presence of degenerative neutropenia or severe neutrophilia. Fecal culture for salmonella can be helpful antemortem, or postmortem culture of other organ tissues such as lung or liver can demonstrate bacteremia. Unfortunately fecal culture for *E. coli* has limited utility because most diagnostic labs do not differentiate A&E or Shiga toxin strains, and *E. coli* overgrowth in the intestine is common with most cases of enteritis or ileus.[2,4] Recognizing signs of inflammatory change in the bowel or extra-intestinal tissues is compelling evidence of bacterial disease rather than viral or protozoal infection of intestinal lining cells.

Implications of this Categorization for Treatment and Prognosis

This distinction between 2 types of neonatal calf enteritis is very useful for establishing prognosis, guiding therapy, and developing preventive measures. The prognosis for calves with simple viral and protozoal calf scours is really very good, assuming fluid and electrolyte therapy is properly administered.[4,9,10] Some recent reviews of research over the last 20 years provide excellent guidance for treating this problem.[8,10] Fluid therapy is the key to success. Oral fluid and electrolyte replacement solutions (ORS) are relatively inexpensive, easy to use, and highly effective. Of the many electrolyte products available on the market, only a very few are really designed properly for treatment of scouring calves, but those that appropriately replace fluids and electrolytes and combat acidosis are remarkably effective. To correct these scours problems, the oral fluids need to have the right composition of electrolytes, glucose or glycine to promote electrolyte and fluid absorption, and an appropriate concentration of an alkalinizing agent. The fluids need to be administered early in the course of disease to avoid severe dehydration, and provided in sufficient volume and frequency to keep the calf hydrated and replete with appropriate electrolytes.[9,10] These principles have been well established, and it is easy to help a producer select the right product and administer it properly. Alternatively, severely affected calves can be administered IV replacement fluids, and if done properly most of these calves can be saved as well. The most important education for producers is to help them recognize sick calves, degree of dehydration, and appropriate fluid treatment measures.

By contrast, the fluid, electrolyte, and acid-base disturbances that result from bacterial enteritis are not routine. Since the primary problem is not fluid and electrolyte loss, the severity of disease signs is not linked to body fluid pathophysiology. The thumb rules that guide fluid therapy for scouring calves do not apply in these cases. Many affected calves have no significant body fluid loss. IV fluid support may be beneficial, but if there is vascular damage then colloid fluids (such as plasma administration) may be more beneficial in supporting cardiovascular problems than crystalloid solutions.[1,6]

Other treatment measures used for scouring calves have limited or questionable efficacy, including gut protectants, gelling agents, anti-inflammatory medications, and probiotics.[4] For the most part these treatments are not harmful, but their efficacy is not even close to the impact of appropriate fluid and electrolyte therapy.[9,10] Unfortunately, many producers still employ some of the oral antibiotic products that were approved for use decades ago and are still marketed. Oral antibiotics obviously have no impact on the viral disease agents, and they can be harmful in some instances. Several of the antibiotics used in 'scours boluses' have been shown to induce diarrhea in healthy calves and can affect absorptive function of the gut.[5,7] They most certainly negatively impact the gut microbiome. The pharmacokinetics and pharmacodynamics of these oral antibiotics are for the most part not well established, and in the face of abnormal gut function these important parameters of antibiotic selection would not be valid anyway. Therefore, I consider oral antibiotic treatment of scouring calves to be an abuse of these drugs. Some calves with viral/protozoal enteritis may be predisposed to other infections, but if that is suspected, then parenteral antibiotic administration would be the rational approach. For many producers, however, oral scours boluses are the first treatment deployed, delaying the use of oral fluid therapy until later in the course of disease, which is counterproductive.

By contrast, for treatment of bacterial, inflammatory enteritis, antibiotic therapy has a rationale. The problems with oral antibiotics are the same–lack of adequate knowledge about absorption, distribution and efficacy.[4,5,7] Furthermore, the problem with these invasive pathogens is distribution within tissues, which again suggests that parenteral antibiotics should be preferable.[1,6] Although there is a theoretical

rationale for antibiotic use, the prognosis for affected calves, particularly calves with septicemia, is guarded to poor with any treatment method. Some anecdotal evidence suggests that off-label oral use of penicillin for clostridial enteritis, or TMP-sulfa for salmonellosis may be helpful, but I have not seen any published trials that confirm the efficacy of these treatments.

With these considerations, education of producers about how to distinguish between simple scours and aggressive bacterial enteritis can guide both treatment decisions and expectations for success. Importantly, with increased focus on judicious antibiotic use, guiding producers on appropriate use and expectations of antibiotic efficacy is important. Guidelines on the appropriate selection and use of ORS can be very beneficial for achieving successful treatment of scouring calves in an economical fashion. My guidelines for producers are that if they suspect simple scours and they use the right ORS in the right time and quantity, they should expect very favorable results. If, on the other hand, they do not see good results, or if they see signs of multi-systemic disease, then they should call the veterinarian, perform necropsies, and pursue an accurate diagnosis.

Implications of this Categorization Scheme for Prevention

Appropriate colostrum acquisition and passive immunity are keystones of neonatal health.[3] Infectious disease problems and disease outbreaks are a function of level of resistance vs level of infectious disease challenge. We see outbreaks of disease when resistance is low, or challenge is high, or both. For neonatal calves, infectious disease resistance is enhanced by good adaptation to extra-uterine life, good maternal care, dryness and warmth, good nutrition, and good colostrum consumption. Of these, colostrum is considered to be the most important.[3] Exposure risks for infectious disease primarily relate to the environment including crowding, exposure to shedding animals, and hygiene.[8]

For bacterial enteritis, all of these features are important, but colostral transfer of immunoglobulin is particularly important for preventing severe disease. Since these bacterial problems involve toxins and bacterial invasion, circulating IgG can be quite effective in limiting disease severity and occurrence of bacteremia or toxemia, such as clostridial exotoxin movement.[1,4,6] Many outbreaks of salmonellosis are attributable to the introduction of a new strain of salmonella to which cows have not developed protective antibody, or to circumstances that produce poor colostrum production by the dam or consumption by the calf.

Conversely, for calf scours manifested by viral/protozoal enteritis, colostrum acquisition and Ig transfer have a much more limited effect. Because the disease agents remain in the gut lumen and are associated with the lining epithelium, circulating IgG has limited efficacy for prevention. IgM and IgA within the gut would presumably be more effective, but they are only present in the gut for a limited number of days. Prevention of ETEC via colostrum antibodies is highly effective because the pathogen has such a limited time to affect calves and can be neutralized by colostral Ig.[2] But for pathogens that can replicate and affect cells beyond about 7 days of age, the protective antibodies are no longer in high concentration. After colostrum, the lacteal Ig of cattle is vastly reduced.[3] This is likely a part of the reason that rotavirus, coronavirus, and cryptosporidium infections strongly tend to peak at 7 to 14 days. This is not to say that vaccination against the viral agents is unimportant, but to emphasize that other means of controlling these infections are proportionally more important. Relying on vaccination to prevent simple scours is not a highly successful approach. Instead, increasing resistance with management that emphasizes decreased dystocia, improved nutrition, and protection from environmental pressures becomes more critical. Decreasing infection pressure through hygiene, decreased crowding, limited exposure to shedding herdmates and a dry environment are critically important for preventing outbreaks. These are the reasons the Sandhills calving method and similar strategies for decreasing calf exposure to contagious older calves are so successful.[8] Minimizing fecal-oral spread and decreasing the risks of a propagated epidemic by minimizing contact between older shedding calves and younger susceptible calves is highly effective in prevention.

Conclusions

Neonatal enteritis is the leading cause of calf illness and death from 2 to 30 days of age. There are numerous pathogens that can cause neonatal enteritis in calves, and it is common for cattle producers and veterinarians to view neonatal enteritis as a single disease complex and treat cases with a uniform approach. Such an approach tends to overuse antibiotics, while underutilizing fluid therapy in cases where a bacterial enteritis is assumed. There is utility in recognizing a distinction between enteritis associated primarily with fluid and electrolyte loss, vs enteritis caused by destructive and invasive bacterial pathogens. In many herd outbreaks this distinction can be made by careful observation of clinical signs, typical age of disease onset, response to fluid therapy, and necropsy findings from calves that die. These observations can guide treatment decisions for more judicious use of antibiotics, more appropriate use of oral fluid therapy and direct laboratory submissions to help confirm specific pathogens. Identifying the difference between these different types of enteritis can also be helpful in directing efforts for prevention of the disease by emphasizing the importance of environmental control of pathogen spread.

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