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Calf Note #231 – Recent research on cryptosporidiosis, part 4

Introduction

Because cryptosporidiosis is such an economically important disease to young dairy calves, many therapeutic approaches have been evaluated in the scientific literature. Some of these approaches are traditional therapeutic approaches – i.e., identifying specific molecules that reduce or eliminate growth of the organism, or are directly toxic to the organism in some way. Control of cryptosporidiosis with these approaches have produced one drug – halofuginone – that is approved for treatment of cryptosporidiosis.

Besides halofuginone, there are a number of compounds / products / approaches that are purported to eliminate *C. parvum*, reduce shedding of organisms, or at least reduce clinical effects of the disease in your calves. Mechanisms for these approaches are often unclear, but at least some data suggests improvement in clinical signs or changes in body weight when these approaches are taken. Note that these are not approved as treatments and any decision on using one or more of these approaches should be made in consultation with your veterinarian. I make no recommendations on use of any of these compounds or approaches; they are presented only on an informational basis.

Antibiotics and Coccidiostats

A large body of research is available regarding the use of antibiotics and coccidiostats in control or treatment of cryptosporidiosis. Generally, these treatment approaches must be made in consultation with your veterinarian. Many reviews are available in the literature regarding antibiotic approaches to cryptosporidiosis (Brainard et al., 2020; de Graff et al. 2020), so I will refer the interested reader to these resources.

To date, only halofuginone (Halocure) is licensed to treat cryptosporidiosis. Here is an excerpt from an article written by Thomson et al. (2017) regarding the use of halofuginone in the treatment of cryptosporidium: *"The only licensed treatment for cryptosporidiosis in calves is halofuginone lactate, the mechanism of action of this drug is unknown but it is thought to affect the merozoite and sporozoite stage of the parasite. This drug is approved for use in both prevention and treatment of cryptosporidiosis in calves but cannot be used in animals have shown signs of diarrhoea for > 24 h. As a prophylactic measure the drug should be given within 48 h of birth and as a therapeutic agent, within 24 h of the onset of symptoms. Halofuginone lactate must be given for 7 consecutive days, which can be difficult to manage, particularly for beef calves that are kept with their dams. Treatment with halofuginone lactate does not completely prevent or cure disease but can reduce oocyst shedding and the duration of diarrhoea. There are no licensed treatments for cryptosporidiosis in sheep, goats, or pigs.* This is a nice review of how *C. parvum* causes the diarrhea in young calves, so if you're interested in some great background, this is the article for you. It should be noted that paromomycin is licensed in some countries as a treatment for *C. parvum* in some animal species.

Natural feed additives

Non-antibiotic approaches to control or treatment of cryptosporidiosis have been evaluated in the literature, and I'd like to focus on the potential for these approaches in this Calf Note. There are a number of different technologies that have been attempted, listed in general categories below.

Pine bark extracts are purported to contain compounds such as condensed tannins that may have antiparasitic properties as proposed by Blomstrand et al. (2021). These researchers tested bark extracts from Scots pine

trees in a cell culture model. Adding methanol or acetone extracts of bark extract to cell culture at 24 to 25 µg tannins/ml inhibited development of *C. parvum* in cell culture. Kim et al. (2001) also suggested that pine bark administered orally at 30 mg/kg daily reduced shedding of oocysts in immunocompromised mice. However, it doesn't appear that this product has been tested in calves.

An interesting adaptation on feeding pine bark is feeding activated charcoal containing wood vinegar. Watarai and Koiwa (2008) experimentally infected calves (n = 6) with 10^5 cfu of *C. parvum* at 7 d of age and monitored fecal excretion of oocysts for 4 days, then calves were sacrificed to determine adherence of oocysts to intestinal surfaces. Calves fed 10 g of the product at 8 hr intervals for the 4-day trial shed significantly fewer oocysts than control calves. Further, the vinegar product eliminated adherence of oocysts to intestinal surfaces.

Yeast fermentation products are produced by growing *Saccharomyces cerevisiae* in controlled fermentation conditions to produce a broad array of fermentation by-products that have multiple effects on animals when included in the diet. Yeast culture can increase intake and improve feed efficiency in young calves and adult cows. Recent research by Vélez et al. (2019) in Germany evaluated effectiveness of yeast products (1 g/d of SmartCare in milk and 5 g/d of NutriTek in starter for 63 d), halofuginone (0.1 mg/kg body weight daily for 7 d). Control calves were fed neither additive. Most calves shed *C. parvum* and had diarrhea at least once during the study. Halofuginone reduced shedding as compared to the two other groups. Both halofuginone and yeast products reduced the intensity of infection compared to the untreated group. Neither the proportion of diarrheic calves nor the intensity and duration of diarrhea differed among the 3 treatment groups significantly.

Plant extracts and essential oils are widely available alone or in combinations that have been evaluated as therapy for calves infected with *C. parvum*; however, published research is conflicting regarding efficacy of products. For example, Volpato et al. (2019) fed 30 newborn calves without or with 10 g of a blend of carvacrol, cinnamaldehyde, eucalyptus aroma and paprika oleoresin (Activo Calf®) once daily for 30 days. The authors monitored feces for presence of *C. parvum*, but there was no difference between control and treated calves, though total fecal bacterial counts were reduced in treated calves. Also, allicin (a sulfur containing component of garlic) was ineffective in reducing the duration of diarrhea due to *C. parvum* (Olson et al., 1998).

Because cryptosporidiosis is an important disease in children, some researchers have evaluated effects of oils in human models. For example, Gaur et al. (2018) evaluated the potential for essential oils from oregano and carvacrol to inhibit growth of *C. parvum* on monolayers of human intestinal cells. Treatment with both products reduced viability of *C. parvum*, suggesting that these compounds might have a positive impact under more practical conditions. Though this research was done in children, the potential to have similar effects in calves is very real.

Woolsey et al. (2019) evaluated the effects of leaf and root extracts from chicory containing sesquiterpene lactones (*Cichorium intybus* cv. Spadona) was investigated using human colon cells infected with *C. parvum*. Oocysts were inoculated onto a monolayer of colon cells and incubated with various levels of extracts. Extracts inhibited growth of *C. parvum*, though not in a dose-dependent manner, suggesting that the content of lactones was not the only factor inhibiting growth. Conversely, Katsoulos et al. (2017) conducted a field trial with 91 newborn calves fed control or essential oil at 12.5 mg/kg body weight daily for the first 10 days of life. Feeding the oil improved fecal score and incidence and severity of diarrhea; there was a significant reduction of oocyst shedding from day 3 to day 10 of the experiment in the treated group whereas it remained constant in the control group.

Finally, Stefańska et a. (2021) reported that a combination of 250 mg/calf of a multi-strain Lactobacillus probiotic plus 50 mg/calf rosmarinic acid daily added to colostrum and milk replacer reduced fecal scores,

reduced excretion of oocysts on d 28 and reduced percent of calves positive for C. parvum on days 28 and 56.

A review of the effects of essential oils on cryptosporidium species was published in 2017 (Hikal and Said-Al Ahl, 2017) and the reader is directed to this reference for more information.

Bovine serum was evaluated as an approach to reduce the negative effects of infection by *C. parvum* on intestinal damage. Serum is produced from bovine blood collected at abattoirs and carefully processed to remove red cells and fibrin components. The resulting spray-dried products contains >85% protein and about 20% IgG which may have activity against C. parvum. Hunt et al. (2002) reported that calves experimentally infected with C. parvum at 8 days of age and fed 57 g/d of bovine serum concentrate until day 18 had lower diarrhea volume and lower intestinal permeability compared to untreated controls. Calves fed serum shed 33% fewer oocysts and overall improved intestinal health.

Hyperimmune bovine colostrum is prepared by vaccinating dry cows against *C. parvum* and collecting colostrum immediately post-calving. This colostrum contains large amounts of anti-cryptosporidium antibodies which are highly effective against *C. parvum*. Two studies have shown that this approach is highly effective against infection with cryptosporidium. Fayer et al. (1989) infected 12 neonatal calves and fed 6 of them with hyperimmune colostrum. Treated calves had diarrhea for an average of 2 days whereas control calves had diarrhea for an average of 5 days. Calves shed oocysts for 6 vs. 9 days, respectively. Perryman et al. (1999) also reported that feeding hyperimmune colostrum during the first 24 hours to neonatal calves challenged with *C. parvum* shed significantly fewer oocysts (99.8% reduction in fecal excretion) and had no diarrhea compared to calves fed colostrum from control cows, suggesting that colostral antibodies may be valuable in control of *C. parvum*. Other data suggest that colostrum may not eliminate infection with *C. parvum*, but adequate colostrum – and potentially, hyperimmunized colostrum – may dramatically reduce the severity of diarrhea caused by cryptosporidium.

Summary

There are a number of potential "natural" approaches to control or treatment of cryptosporidiosis. I've tried to summarize some of the more recent articles available in the scientific literature for your use. More information will be available as novel approaches are developed. It's really important that non-antibiotic approaches are developed. Natural approaches such as yeast fermentation products, essential oils and feeding antibodies from hyperimmunized cows seem to be viable approaches. Of course, good management, hygiene are MOST important to controlling infection of calves. Good luck!

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