Johne’s Disease: the Effect of Feeding Monensin to Reduce the Bioburden of Mycobacterium avium subspecies paratuberculosis in Neonatal Calves

R.H. Whitlock, DVM PhD1; R.W. Sweeney, VMD1; T. Frycock, AD1; S. McAdams, BS1;
I.A. Gardner, BVSc, PhD2; D.G. McClary, DVM, MS3
1 Department of Clinical Studies, New Bolton Center, School of Veterinary Medicine, University of Pennsylvania, 382 West Street Road, Kennett Square, PA 19348
2 Department of Medicine & Epidemiology, College of Veterinary Medicine, University of California, Davis, CA 95616
3 Elanco Animal Health, A Division of Eli Lilly & Company, Indianapolis, IN 46285

Introduction

Johne’s disease (paratuberculosis) is a chronic, granulomatous infection of the intestinal tract of ruminants caused by Mycobacterium avium subspecies paratuberculosis (MAP). There is no approved treatment, no known way to eliminate the infection once established, nor is there an effective vaccine for the disease. Johne’s disease (JD) has emerged as an important disease of cattle due to the economic impact and the potential link to human Crohn’s disease. The recently introduced herd Risk Assessment (RA) and Herd Management Plan (HMP) developed by the National Johne’s Working Group (NJWG) have been incorporated into the national program standards by USDA, APHIS. Increased state and federal funding for Johne’s disease has increased the focus on ways to control the condition. Methods to control the spread and to reduce within herd transmission of Johne’s disease (JD) are being adopted by both dairy and beef herds in many states through implementation of the national Johne’s disease program. Implementation of best management practices (BMP) following a herd risk assessment (RA) designed to reduce the risk of transmission of JD remains the focal point of the national effort to reduce the prevalence of JD in cattle herds today. Although a vaccine for JD is available in many states, its use is closely regulated by individual state veterinarians and usage by the profession remains less than 2,000 herds nationally. Test and culling of culture-positive cattle seems a low priority if the infected animals are profitable. Reduction of the herd bioburden of MAP seems a lower priority for many producers. Brumbaugh et al1 demonstrated a reduction in the number of colony forming units (cfu) of MAP from the livers of experimentally MAP-infected mice treated with monensin compared to non-treated controls. More recently he showed monensin reduced the severity of histological lesions in cattle with clinical signs of Johne’s disease, including weight loss and diarrhea.2 Initial infection with MAP is generally considered to occur in the neonatal calves. Our laboratory at the University of Pennsylvania, New Bolton Center has successfully induced experimental MAP infection in neonatal calves via oral gavage of MAP on two consecutive days.3 The current experiment was designed to assess the efficacy of monensin4 to reduce pass-through fecal shedding and to reduce tissue bacterial load (bioburden) of MAP in calves.

Materials and Methods

Twelve neonatal Holstein heifer calves (one to three days of age) were purchased from a local dairy. The herd had no evidence of clinical Johne’s disease and was considered a low-risk herd with excellent biosecurity measures for newborn calves. Calves were randomly assigned to receive a carrier containing 35 mg monensin (n=6) or placebo (n=6) added to the milk replacer at each twice-a-day feeding upon arrival at the research facility. The trial was conducted as a randomized double blind trial. Both groups of calves were administered two oral doses of viable Mycobacterium avium subspecies paratuberculosis (MAP) on two consecutive days between days seven and nine of the trial or days eight to 11 of age. The viable MAP was mixed in two ounces of milk replacer and administered via oral gavage from a two-ounce dose syringe. The MAP dose (cfu/calf) was designed to result in a modest or moderate level of infection in the tissues when harvested at necropsy approximately 60 days later. Fecal samples were collected from each calf twice daily at feeding time beginning on the evening of the second MAP dose. Calves were housed in individual pens and had free access to water. Calf starter grain was offered beginning at 10 days of age. Serum samples were taken when calves entered the research facility, 30 days later and just prior to necropsy. These samples were later tested by ELISA for antibodies to MAP. Calves were weighed weekly and grain intake was measured daily after three weeks of age. Calves were euthanized between days 65 and 67 days after starting the trial. Fifty individual tissues (2
gm each) were harvested from each calf for culture on Herrold’s egg yolk media (HEYM). The collected tissues included multiple sections of intestine, abdominal organs, and mesenteric and peripheral lymph nodes. The feces and tissues were processed at the same time period using HEYM.5

Results

There were no significant differences in feed consumption or weight gain between the two groups. Calves fed monensin had fewer culture-positive (55%) fecal samples, fewer total HEYM positive tubes (63%) and less MAP cfu (72%) detected in the manure compared to controls. Furthermore, monensin fed calves had fewer culture-positive tissues (66%), fewer total culture positive HEYM tissue tubes (68%) and lower MAP cfu (87%) in the tissues compared to controls. All MAP isolates from both groups were from tissues within the abdominal cavity. No isolations of MAP were made from liver, hepatic lymph node or kidney tissues of either group of calves.

Significance

Results of this study suggest that monensin effectively reduced tissue colonization with MAP following oral challenge, and also reduced fecal pass-through shedding of the organism. The MAP detected in fecal samples was clearly the result of pass-through3 and not active shedding from infected mucosal epithelial cells. Monensin may act directly on MAP by inhibiting growth of the mycobacterial cell as preliminary evidence in our laboratory has shown, or it may enhance phagocytic killing of mycobacteria, or both. Presumably, reduced tissue colonization in the short-term model would translate to lower mycobacterial burden and likelihood of shedding MAP in manure and clinical disease in adulthood. In a prior study,2 monensin was shown to either halt the progression of lesions or reverse the lesions in cattle with clinical signs of Johne’s disease.2 Sections of tissues including liver, ileum and adjacent mesenteric lymph node and a rectal mucosal biopsy were compared histologically to similar tissues obtained at necropsy after feeding 450 mg monensin for 120 days. Taken together, the results of these two studies suggest that monensin may play a useful role both in the prevention of MAP infection in young cattle, and in the treatment of established infection in adults. The amount of monensin (70 mg) administered per day to calves in this study is higher than the amount that would normally be consumed by a neonatal calf in a calf starter. This study was a proof-of-concept study to determine the efficacy of monensin in controlling infection with MAP in the neonatal calf. Additional work to determine efficacy for controlling infection with MAP with normal inclusion rates in a calf starter are indicated. Monensin added to cattle rations at all phases of their life, coupled with stringent implementation of biosecurity management practices at the farm level, offers new hope to help reduce the unyielding spread of this disease among the nation’s cattle herds. The costs are modest compared to many other management tools designed to reduce MAP bioburden within cattle herds. No other management technique evaluated to date has been shown to reduce MAP shed in manure of cattle and to reduce the tissue uptake of MAP to this extent. Nearly all investigators agree that Johne’s vaccine will greatly reduce the frequency of exposed cattle from developing clinical disease, but the quantitative decrease in MAP uptake by the tissues and reduction in fecal shedding has not been well documented. In these experimental calves, monensin greatly reduced (>60%) both the pass-through fecal shedding and systemic tissue uptake.

Footnote

3 Rumensin® (monensin), Elanco Animal Health, a Division of Eli Lilly & Company, Indianapolis, IN 46285

References