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Efficacy of monensin sodium for the reduction of fecal shedding of *Mycobacterium avium* subsp. *paratuberculosis* in infected dairy cattle

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Abstract

Reducing the quantity of *Mycobacterium avium* subsp. *paratuberculosis* (MAP) being shed by cows with Johne's disease should decrease the risk of spread of this disease to young stock. Previous work has suggested that monensin sodium decreases the pathologic lesions associated with Johne's disease, but the impact on shedding of viable MAP remains unknown. After serologic screening of 32 dairy herds in southwestern Ontario, 228 cows from 13 of these herds were enrolled into a randomized clinical trial. Fecal culture and PCR were used to identify 114 cows as potential fecal shedders, while another 114 cows were enrolled as ELISA negative, herd and parity matched controls. All cows were randomized to receive either a monensin controlled release capsule (CRC) or a placebo capsule. Serial fecal and blood samples were collected for fecal culture and serum ELISA testing over a 98-day period. On day 98 of the study, treatments were switched for all cows continuing in the trial. These remaining cows were followed for another 98 days with a similar sampling protocol. Mixed effect models were used to measure the impact of treatment on the number of colony

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forming units identified on fecal cultures over time. During the first 98 days of the study, cows treated with a monensin CRC were found to shed 3.4 cfu per tube less than placebo treated cows ($P = 0.05$). The serum ELISA S/P ratio was reduced by 1.39 units in cows given monensin ($P = 0.06$). However, treatment with monensin did not reduce the odds of testing positive on serology. Only the cows shedding MAP on day 0 were found to have a reduced odds of testing positive on fecal culture when treated with monensin (OR = 0.27; $P = 0.03$). Monensin sodium administered to infected animals at 335 mg/day marginally reduced fecal shedding of MAP in mature dairy cattle, but the biological significance of this reduction is unknown.

Keywords: Paratuberculosis; Johne's disease; Monensin; Cattle-microbiological diseases

1. Introduction

Johne's disease, or bovine paratuberculosis, has long plagued the cattle industry worldwide (Chiodini et al., 1984). Progressive weight loss and chronic diarrhea are the cardinal signs for advanced stages of the disease. There are currently no drugs approved for the prevention or treatment of Johne's disease. Several drugs have been used to treat individual animals, but none have been shown to be efficacious or economical for treatment of commercial dairy cattle (St-Jean and Jernigan, 1991). Many infected dairy cows are culled prematurely due to low milk production and unthriftiness. When the cost of culling is combined with lost milk revenue, the economic impact of Johne's disease becomes quite significant at both the herd and industry level (Ott et al., 1999). More recently, there has also been increasing human health concerns in regards to a potential link between Johne's and Crohn's disease (Selby, 2000).

Many countries have moved towards developing voluntary control programs to help producers manage Johne's disease. The recommended approach to managing this disease is prevention and control (Rossiter and Burhans, 1996). Minimizing the amount of *Mycobacterium avium* subsp. *paratuberculosis* (MAP) being shed by infected cattle may help to reduce the environmental contamination and risk of spread to susceptible calves (Goodger et al., 1996; Wells and Wager, 2000). Culling fecal shedding cows may help reduce the environmental burden of MAP, but identifying these cattle can be difficult with the current diagnostic tests available.

It has been hypothesized that monensin sodium may be beneficial in limiting fecal shedding and thus the spread of Johne's disease (Brumbaugh et al., 2000). Recent studies have indicated that MAP infected cattle and mice responded favourably to monensin sodium treatment, as demonstrated by an improvement in histological lesions in the gastrointestinal system following therapy (Brumbaugh et al., 1992, 2000). Monensin sodium is a polyether ionophore that modifies the bacterial cell membrane permeability (Prescott et al., 2000). Its large spectrum of activity includes several Gram-positive bacteria, some *Campylobacter* spp., *Serpulina* spp., *Mycobacterium* spp. as well as coccidia and toxoplasma (Prescott et al., 2000; Liu, 1982). Its minimum inhibitory concentration (MIC) for MAP was recently reported to be 0.3 μm/ml (Brumbaugh et al., 2004). To date, the use of monensin has not been evaluated clinically for its impact on fecal