
IONOPHORES IN DAIRY RATIONS

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Introduction

Ionophores have been used extensively in the beef industry in Canada since 1977. Until recently, there has been no label indication for use of ionophores in lactating dairy cattle. Ionophores are feed additives that alter rumen microbial populations through ion transfer across cell membranes. In Canada, the label warning prohibiting the use of Rumensin® premix in lactating dairy cattle was removed in June 1996. Following this, a controlled release capsule containing monensin was approved for use in dairy cattle as an aid to prevent subclinical ketosis in December 1997. In 2004, both Canada and the United States received approvals for the use of monensin in lactating cow diets for improving milk production efficiency. Although other ionophores such as lasalocid and salinomycin are available for use in other cattle, only monensin is currently approved for dairy cows in North America. This paper discusses the production and health benefits of feeding or administering monensin to dairy cattle.

Effects of Ionophores on Ruminant Digestion and Metabolism

Monensin is a carboxylic polyether ionophore produced by a naturally occurring strain of *Streptomyces cinnamonensis* (Haney and Hoehn, 1967) and is provided to cattle orally, as a sodium salt. The basic function of ionophores is to create a flux of ion transport across cell membranes. Monensin binds to bacterial cell membranes and first causes an efflux of potassium from the cell and an influx of hydrogen into the cell (Russell, 1996). The increased hydrogen is exported out of the cell either by active transport involving adenosine triphosphate or passively via sodium entry into cells in exchange for hydrogen. In order to maintain inner cell equilibrium, the bacterial cell expends energy and this results in death or reduced growth of the bacterium (Bergen and Bates, 1984). Since gram-negative bacteria have complex outer cell membranes, they are usually more resistant to the action of ionophores than are gram-positive bacteria. Ionophores,

therefore, selectively inhibit gram-positive bacteria rather than gram-negative bacteria because of differences in bacterial cell wall structure.

Monensin exerts its many effects by shifting the microbial populations in the rumen (Bergen and Bates, 1984). Bergen and Bates (1984) identified 3 major areas of animal metabolism influenced by monensin. These include increased efficiency of energy metabolism, improved nitrogen metabolism, and general digestive effects, including reductions in both bloat and lactic acidosis. Monensin changes the ratio of volatile fatty acids in the rumen, increasing propionic acid and reducing the molar percentages of butyric and acetic acids. Increased rumen propionic acid improves gluconeogenesis.

Improved Energy Metabolism

The gluconeogenic potential of monensin has attracted researchers to investigate its possible role as an antiketogenic agent in dairy cattle. The antiketogenic properties of monensin were first investigated in a Canadian trial involving 2 levels of monensin and 3 groups of 12 Holstein cows (Sauer et al, 1989). Monensin included at 30 grams per ton of total ration (high group), decreased the incidence of subclinical ketosis and significantly reduced blood beta-hydroxybutyrate (BHBA) levels in the first 3 wk postpartum (Sauer et al, 1989). The incidence of subclinical ketosis defined as total blood ketones > 9 mg/100 ml (900 µmol/L) was decreased, and blood BHBA levels were reduced by 40% for the high monensin group. The lower monensin dose did not significantly impact blood BHBA or subclinical ketosis in this study.

Several studies involving intraruminal controlled release capsules (CRC) have been used to evaluate the metabolic, health and production effects of monensin in dairy cattle. This spring-loaded capsule contains 32 g of monensin in a hexaglycerol distearate matrix core. In Canadian studies, it has been demonstrated that a CRC containing monensin

delivers a constant daily dose of approximately 335 mg for about 95 d in dairy cows. Cows in Australia treated with a monensin CRC during the first week postcalving had significantly lower plasma BHBA levels and tended to have higher glucose concentrations than did controls receiving no monensin (Abe et al, 1994). Monensin-treated cows had significantly higher levels of serum urea; however, no significant effects of monensin on glucose or BHBA were shown in a New Zealand trial (Hayes et al, 1996). In this study, monensin CRCs were administered one month prior to artificial insemination. This time of administration would likely have been beyond the first 30 d after calving, which is the primary risk period for subclinical ketosis. Therefore, cows in this study were probably not in a negative energy balance during monensin treatment.

Green (1997) reported that administration of a monensin CRC 3 wk prior to expected calving, significantly reduced the concentrations of BHBA and increased those of glucose. Monensin treatment in this study was also reported to reduce both the onset and severity of subclinical ketosis when cows were restricted to 90% of ad libitum feed intake commencing at 2 wk postcalving. Duffield et al (1998b) reported that monensin CRC administration at 3 wk prior to calving reduced the incidence, prevalence, and duration of subclinical ketosis in a 1010-cow multi herd field study. Monensin treatment also significantly reduced the concentrations of serum BHBA and aspartate aminotransferase and increased the concentrations of serum glucose and urea (Duffield et al, 1998a).

Stephenson et al (1997) conducted a small study involving 24 cows from 2 farms where monensin CRCs were administered 50 d precalving. A significant decrease in non esterified fatty acids, BHBA and glucose were noted in the precalving period. No significant effects on these energy indicators were observed post calving. However, a significant elevation in ceruloplasmin concentration was noted in monensin-treated cows, post calving. The authors suggested that this increase in copper absorption may assist the cow in fighting oxidative challenges. Cows from this study were also evaluated for their neutrophil function. Monensin significantly improved the chemotactic function of neutrophils (Stephenson et al, 1996), indicating that monensin

may improve immune function indirectly via an improvement in energy status.

Impact on Nitrogen Metabolism

Several studies in dairy cattle have demonstrated increased serum urea in cows treated with monensin (Hayes et al, 1996; Duffield et al, 1998a; Green 1997). This appears paradoxical since monensin decreases rumen ammonia levels. However, monensin increases the quantity of undegraded protein to the small intestine via ruminal inhibition of proteolysis.

This may result in an increased absorption of amino acids and subsequently higher serum urea via deamination of nonessential amino acids in the liver. Recent research in transition cows has shown that monensin improves nitrogen digestion. Cows given a monensin CRC had a 12% increase in the apparent N digestibility when measured during the first week postcalving. All cows were in a negative nitrogen balance but this deficit was reduced from -77.8 g/d in the control cows to -44.9 g/d in the monensin CRC treated-cows (Plaizier et al, 2000).

Impact of Monensin on Cow Health

A CRC containing monensin has been found efficacious for the prevention of pasture bloat in dairy cattle in several studies conducted in Australia and New Zealand (Lynch et al, 1990; Lowe et al, 1991). However, bloat is generally not a common problem in North American dairy cattle.

Monensin has also been reported to reduce the incidence of subclinical ketosis. Sauer (Sauer et al, 1989) reported a reduction in subclinical ketosis from 6 out of 12 in the untreated group to 4 and 1 out of 12 in the low (208 mg/cow/d) and high (399 mg/cow/d) monensin groups respectively. This was a relatively small trial conducted in one research herd. The high dose of monensin did significantly reduce the incidence of subclinical ketosis; however, at the low dose the incidence of subclinical ketosis was not significantly different from that of control. Duffield et al (1998b) reported that monensin delivered in a controlled release capsule (335 mg) reduced the incidence of subclinical ketosis by 50%, at threshold values for defining subclinical ketosis of 1200, 1400, and 2000 $\mu\text{mol/L}$ BHBA in 1010 cows from 25 commercial dairy farms. Monensin also significantly reduced the duration of subclinical ketosis.

The use of Rumensin CRCs precalving have been shown to significantly reduce the risk of abomasal displacement and multiple illness (more than one disease in early lactation) (Duffield et al, 1999, 2002). In the first study, there was a tendency for monensin-treated cows to be at reduced risk of clinical ketosis and culling. These health effects were presumably associated with the observed reduced incidence of subclinical ketosis. Pooled analysis of the 1010 cow study in 1995 in Ontario and a 1999 study involving 1156 cows in Ontario, Quebec, and the Maritimes has shown that the Rumensin® CRC significantly reduces both the incidence of abomasal displacement and clinical ketosis by approximately 40% (Duffield et al, 2002). The work of Beckett et al (1998) demonstrated no significant health effects of the Rumensin® CRC when it was administered 40 d prior to expected calving. However, disease incidence was substantially lower in this study than would be expected for typical North American dairies. Interestingly, the incidence of retained placenta in monensin-treated cows was numerically lower in this study. This tendency has also been observed in both Canadian studies.

Milk Production and Milk Components

Trials from both Australia and New Zealand have evaluated the effects of monensin on milk production in pasture-fed cattle. A seven to eight percent increase in milk yield over a 14-wk period was observed, in a single herd study of 90 cows on pasture given a monensin CRC at 46 d postcalving (Lynch et al, 1990). An increase in protein, but not fat yield was also found. In agreement with these findings, Lowe et al (1991) demonstrated increased milk production of 1.1 kg/d (6.2%) associated with monensin treatment in 368 cows from four herds that were randomly allocated to a monensin CRC treatment between 0 and 100 d postpartum. In a New Zealand trial involving all the cows from 3 pasture-fed herds, monensin-treated cows produced 0.41 L more milk per day over a 4-month period, and 1.38 L more milk per day than did untreated control cows at the 2nd month after treatment (Thomas et al, 1993). Treated cows also produced slightly less protein (0.006 kg/d) and less fat (0.015 kg/d). Treated cows were administered a monensin CRC, which would have been depleted after the 3rd month, but the effects on production lasted into the 4th month post-treatment. Two other trials involving a monensin CRC treatment reported conflicting results. In one, sixteen cows fed ryegrass pasture and 3 kg of dairy

supplement were randomized to receive a monensin CRC or no treatment within 48 h of calving (Abe et al, 1994). No difference in milk yield was found, but milk fat percent was significantly lower in the monensin-treated cows. In the other, involving 1061 lactating cows from 6 different herds, milk fat and milk protein production were not significantly influenced by monensin treatment (Lean et al, 1994). Milk production was significantly increased in only one of the herds. Cows in this trial were randomly assigned to control or monensin CRC treatment within 7 d of calving. Five herds were pasture-fed with supplementary concentrates, and the 6th herd was a large dairy that fed a total mixed ration. The herd with the positive milk production response was a pasture-fed herd. The finding of one herd with a production effect suggests that there may be herd characteristics (possibly nutritional interactions) that either reduce or enhance the production impact of ionophores. The cows in most of these trials were pasture-fed and the effects discovered may not apply to North American systems. In addition, the treatment evaluated was in all cases a monensin CRC, and it was consistently administered in the first 100 d after parturition.

There have been few studies that evaluated the effect of the monensin CRC administered precalving on milk production. In a large Canadian field study, Duffield et al (1999) found a significant monensin by body condition score (BCS) interaction on milk production. A total of 503 cows were given a monensin CRC and 507 were treated with a placebo capsule at 3 wk prior to expected calving. Cows classified as thin (BCS ≤ 3.0) at 3 wk prior to calving had no significant production response to monensin CRC treatment for the first 90 days of lactation. Cows classified in good body condition (BCS 3.25 to 3.75) prior to calving had significantly higher milk yield (+0.85 kg) at peak lactation, while cows that were considered in fat body condition (BCS ≥ 4.0) showed a significant production increase of 1.2 kg per day for the first 90 d of lactation. The BCS-monensin interaction may be the result of alleviation of the detrimental impact of subclinical ketosis on milk production, which is more likely in moderate and overconditioned cows. There were no significant effects of monensin treatment on either milk fat or milk protein percent. However, treatment would have ceased in this trial around 75 days in milk, thus there could be impacts of monensin on milk components beyond this stage of lactation. Beckett et al (1998)

measured milk yield in 915 cows given either a monensin CRC 40 d prior to and 50 d post expected calving date or nothing and found an increase in the lactation milk yield of 0.75 kg/d in the monensin-treated cows. This effect was different among the 12 herds in the study. No significant effects of monensin on milk fat or milk protein percentage were reported.

Several studies have investigated the production effects on various concentrations of feed-delivered monensin. Erasmus (1993) evaluated the effects of 2 treatment groups of 10 ppm and 20 ppm of monensin fed 4 wk prepartum until 12 wk postpartum in 60 multiparous cows in South Africa. Significant increases in milk production of over 3 kg/d were observed compared with untreated controls; however, no significant effects of monensin were noted for milk fat or milk protein percent. In a subsequent trial conducted in the United States that was designed to evaluate the impact of monensin fed prepartum and continuing through early lactation, no effect of treatment on milk yield or milk composition was observed (Thomas et al, 1993). This project involved 47 Holstein cows and evaluated three levels of monensin (150, 300 or 450 mg/d) starting at 2 to 4 wk prepartum and fed until 84 d postpartum. The last 2 studies evaluated the impact of monensin on milk yield in early lactation. Few studies have assessed ionophore use throughout lactation. A study conducted in the United Kingdom, evaluated the same levels of monensin (150, 300, or 450 mg/d) fed to 60 multiparous cows, commencing during the 6th wk of lactation (Phipps et al, 2000). Monensin was associated with a non significant decrease in feed intake, and a significant increase in milk yield of 2.8 kg/d and 2.5 kg/d for the 150 mg and 300 mg monensin levels, respectively. Both milk fat and milk protein yield were reduced and the effect seemed to increase with the higher levels of monensin in the feed. This suggests a possible linear dose effect for monensin on milk fat percentage. A follow-up to this study showed that monensin fed through the dry period and into the subsequent lactation continued to exert similar milk production increases and milk fat percentage decreases (Phipps et al, 2000). In the first of 2 trials, Van Der Werf et al (1998) randomly assigned 64 Dutch Friesian cows to either no treatment or monensin at doses of 150, 300, and 450 mg/cow/d. They reported no significant effects of monensin on milk production but found a significant decrease in milk fat percentage associated with monensin treatment at 450 mg/cow/d. In the 2nd trial,

involving 58 Holstein and 22 Jersey cows, the authors observed increases in milk production but no effect on milk fat percentage for cows treated with monensin at 300 mg/cow/d. The authors reported better production responses to monensin in Holstein rather than Jersey cows and in Holsteins of higher genetic merit. Interactions of ionophore treatment with breed or genetic merit have not been noted in previous studies, thus, these potential effects need further investigation.

The impact of monensin on milk fat is variable across studies and herds. It is quite possible that dietary factors may interact with, and either enhance or mitigate the effects of monensin on milk fat. One such factor is the quantity of effective fibre in the diet. In a cross sectional study, herds that had less than 6% of their total mixed ration (TMR) on the top screen of the Penn State particle separator had a greater depression in milk fat with monensin than those herds with more effective fibre in the TMR (Duffield et al, 2003). Another factor appears to be the concentration of unsaturated fatty acid in the diet. A significant interaction between concentration of soybean oil and monensin (22 ppm) on milk fat percentage was recently reported (Alzahal et al, 2005).

Milk Production Efficiency

Label claims for monensin in lactating dairy cow diets in North America are based on milk production efficiency data collected from 9 trial sites in Canada and the United States measured on 966 cows. Monensin improved milk production in early lactation with no impact on dry matter intake. In mid and late lactation there was little to no impact on milk production, however, dry matter intake was reduced. The net effect is an improvement in milk production efficiency in the 2 to 4% range.

Conclusions

The literature strongly supports that monensin administered precalving has positive effects on energy metabolism in early lactation. These effects include a reduction in circulating ketone body concentrations and an increase in serum glucose. In addition, administration of the Rumensin® controlled release capsule has been shown to reduce the incidence and duration of subclinical ketosis, and the risk of several periparturient diseases, including clinical ketosis and abomasal displacement. It appears that improved

health would be the primary benefit of monensin when used in early lactation.

Studies indicate that monensin causes an increase in milk production of about 1 kg/d. This milk production increase is primarily in early lactation and is likely a result of reduced impact of subclinical ketosis. Monensin tends to cause depression of milk fat, which may result in decreased milk fat yield. This effect appears to be dependent on dose and, possibly, other factors such as stage of lactation and diet. Additional research is required to better ascertain the effect of monensin on milk production and components throughout lactation and in different dairy rations.

The use of monensin in dairy cattle appears to have many applications and thus implementation strategies will vary with each farm and depend on the dairy producers' goals. Based on the current literature, monensin will be helpful in reducing the incidence of subclinical ketosis and other associated periparturient diseases, when treatment commences a few weeks precalving and extends toward peak lactation. Monensin will be of particular benefit to moderately and overly conditioned cows. Beyond the early lactation period, monensin offers the benefit of milk production efficiency.

Selected References (all references available from author on request)

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