

## Effect of Monensin on some of the metabolic hormones and ketone bodies in transition dairy cows

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### SUMMARY

A study involving 40 Holstein cows from one dairy farms near Shiraz, Iran, was conducted to measure the effect of monensin 3 wk precalving on metabolic hormones and ketone bodies in dairy cows immediately postcalving. At 3 wk before expected calving, 20 cows each were allocated to a control (no monensin) and a treatment group 20 cows receiving 300 mg/cow per day of monensin in the a.m. concentrate feeding. Cows were blood sampled once per week postcalving, at the same time of day and the same day at 1, 2 and 3 of the week after calving. Serum was evaluated for IGF-1, Insulin,  $\beta$ -hydroxybutyrate (BHBA) and glucose. Monensin treated cows had no significantly on BHBA and significantly increased concentrations of serum IGF-1, Insulin and glucose in the week postcalving. Monensin treatment administered precalving significantly improved indicators of energy balance in both the immediate precalving and postcalving periods. The findings indicate better energy metabolism in monensin-treated cows as they approach calving. Improvement of energy balance before calving is important for the prevention of energy associated metabolic diseases, such as retained placenta, clinical ketosis, and displaced abomasum, which might occur immediately postcalving.

Keywords: dairy cows. Metabolic hormones, Monensin

### INTRODUCTION

Monensin is a carboxylic polyether ionophore produced by a naturally occurring strain of *Streptomycescinnamensis* (Haney and Hoehn, 1967) and is provided to cattle orally as a sodium salt. Ionophores act to alter the rumen microflora through ion transfer across cell membranes, there by creating energy loss in bacterial cells, resulting in bacterial death. Monensin selectively inhibits gram-positive bacteria rather than gram-negative bacteria because of differences in bacterial cell-wall structure. The result of this shift in rumen bacterial populations has several impacts on ruminant metabolism. These include increased efficiency of energy metabolism, improved nitrogen metabolism, and effects on digestion, including reductions in both bloat and lactic acidosis

(Schelling, 1984). Monensin is an ionophore antibiotic that alters VFA production in the rumen in favor of propionate (Richardson et al., 1976). And reducing the molar percentages of butyric and acetic. In the ruminant, propionic acid is a precursor of glucose. An increase in glucose availability in turn decreases the need for fat mobilization to support milk production. Several studies have shown monensin to reduce circulating concentrations of ketones, particularly BHBA, NEFA by increasing available gluconeogenic precursors (Abe et al., 1994; Duffield et al., 2003). Yang and Russell (1993) found that monensin feeding reduced *in vitro* and *in vivo* ruminal NH<sub>3</sub> formation from protein hydrolysates by suppressing certain bacteria with high deamination activity. Thus, monensin supplementation may improve N efficiency by increasing gut absorption of  $\alpha$ -amino N. Management and nutrition during the transition period influence milk production, the incidence of peripartum metabolic disorders, and reproductive performance. Therefore, management of cows during this critical stage is crucial for the productivity of dairy cattle (Overton and Waldron, 2004).

#### MATERIAL AND METHODS

The study was conducted on a commercial Holstein dairy farm milking 3000 cows with a milk rolling herd average of 10,700 kg. The farm is located in north Shiraz.

Forty individually fed Holstein cows were used to determine the effect of monensin.

At 3 wk before expected calving, 20 cows each were allocated to a control (no monensin) and a treatment group 20 cows receiving 300 mg/ cow per day of monensin in the a.m. concentrate feeding. All cows utilized two dry cow feeding groups (far-off and close-up). The cows using a TMR diet fed cows twice per day with the first feeding occurring after the morning milking. monensin used top-dress. Treatment was administered on the day of enrollment 3 wk before expected calving date.

From 40 cows 10 cows select randomizes, 5 cows from control group and 5 cows from treatment group were used for multiple blood sampling.

Blood samples were obtained from the coccygeal vein and collected into a 10-ml evacuated tube without anticoagulant. Blood samples were collected at 1 to 3 wk post expected calving date. Samples were allowed to clot and centrifuged, and serum was separated and frozen. Frozen serum was submitted to the Animal Health Laboratory, within 3 wk of collection for the measurement of serum BHBA, IGF-1, Insulin, glucose, using a serum auto analyzer.

Serum BHBA concentration was determined by an enzymatic-colorimetric method (Williamson and Mellanby, 1974) using a commercial kit (Pointe Scientific, Inc., Lincoln Park, MI). Glucose concentration was determined using a kit based on the Trinder reaction (Sigma Chemical Co., St. Louis, MO) (Bergmeyer and Bernt, 1974) used to determine the serum concentration of

insulin IRMA KIT and Standard ELISA methods were used to determine the serum concentration of IGF-1.

## RESULTS

In total, 20 cows received a monensin (topdress) and 20 cows served as negative controls. Including both treatment groups, there were 19 animals in third lactation, 14 cows in fourth lactation, and 7 cows were in fifth lactation. The mean lactation number (3.70) and mean BCS at the time of enrollment (3.29) did not differ between treatment groups. A mean of 21 d existed between the time of treatment administration and calving.

the post calving sample occurred at an average of 7,14 and 21 d after calving five animals in each treatment group were removed from their herd of origin the post calving blood sample.

The results of analysis on the blood sample obtained in the 7, 14 and 21 d immediately post calving identified significant treatment effects on serum IGF-1, Insulin and glucose. IGF-1 was higher in all days ( $P < 0.01$ ), Insulin was higher ( $P < 0.05$ ) only in 7 day after calving glucose was higher ( $P < 0.01$ ) in 7 day after calving and ( $P < 0.05$ ) decreases in 14 day postpartum and there was no mean effect at 21 day post calving. No significant treatment effects were noted for BHBA.

The BHBA concentrations were no significantly for cows that had been treated with monensin in wk 1, 2, and 3 post calving. Season of calving, sample and season of sample significantly influenced BHBA concentrations. The highest BHBA concentrations occurred for cows that calved in spring and summer, but BHBA concentrations were highest for cows that calved in fall and winter. Peak BHBA concentrations were reached by wk 3 post calving. Body condition class, parity, and change in BCS were also associated with BHBA concentrations. Increasing loss of body condition was associated with higher BHBA concentrations, and the highest BHBA concentrations were found for fat cows.

During wk 1, the glucose concentration increased for cows on treatment. However, only the cows treated with monensin had glucose concentrations that exceeded 56.8 mg/dL after cows returned to ad libitum consumption during the first week of the experiment Changes in the mean serum glucose concentration by week postpartum are shown in Table 1. The decline in glucose concentration was more severe in cows treated with monensin a low of 41 mg/dL during wk 2 and 49.8 mg/dL during wk 3 of lactation; for cows treated with monensin (Table 1).

Insulin was significantly increased in cows that received the monensin treatment during wk 1 post calving (Table 1). This difference reflected an increase in serum Insulin concentrations of 17.24 to 25.18  $\mu\text{Iu/mL}$ . Variables in the model for Insulin concentrations were the same as in the model for BHBA concentrations. Factors related to higher BHBA concentrations were generally

linked with lower Insulin concentrations, except for initial body condition class. Fat cows had the highest concentrations of BHBA and Insulin.

Table 1. Mean values for the influence Monensin on BHBA, glucose, Insulin and IGF-1.

BHBA	IGF-1	Insulin	Glucose	Samples	Post calving weeks
0.756 <sup>a</sup>	45.12 <sup>a</sup>	25.18 <sup>a</sup>	56.8 <sup>a</sup>	Treated cows	Wk 1
0.466 <sup>a</sup>	20.8 <sup>b</sup>	17.24 <sup>b</sup>	44.4 <sup>b</sup>	Control cows	
0.44	4	1.8	1.76	SE	
0.816 <sup>a</sup>	64.5 <sup>a</sup>	19.04 <sup>a</sup>	41 <sup>b</sup>	Treated cows	Wk 1
0.784 <sup>a</sup>	18.78 <sup>b</sup>	17.62 <sup>a</sup>	55.6 <sup>a</sup>	Control cows	
0.14	6.5	1.7	3.64	SE	
0.762 <sup>a</sup>	48.22 <sup>a</sup>	15.96 <sup>a</sup>	49.8 <sup>a</sup>	Treated cows	Wk 1
0.782 <sup>a</sup>	15.78 <sup>b</sup>	19.92 <sup>a</sup>	50.8 <sup>a</sup>	Control cows	
0.04	6	2	2	SE	

a,b Treatment means within lactation stage with different letters differ ( $P < 0.05$ ).

IGF-1 was increased significantly in the group receiving the monensin (top dress) during wk 1, 2 and 3 post calving (Table 1). Mean concentrations of IGF-1 were 45.12, 64.5, 48.22 ng/mL for wk 1, 2 and 3 postpartum, respectively.

#### DISCUSSIONS

The administration of a monensin Topdress to dairy cows at 3 wk postpartum significantly increase serum IGF-1 concentrations and affected other measures of energy balance in early lactation compared with that of control cows. There have not been many reports of the effects of an ionophore on serum concentrations of IGF-I. In sheep, monensin has been reported to increase circulating concentrations of IGF-I at the periovulatory stage (Peclaris et al., 1999). In male goats, (Strauch et al., 2001) found no additional benefit of monensin supplementation over that of energy supplementation for circulating concentrations of IGF-I; however, there was increased expression of IGF-I messenger RNA in the liver due to monensin supplementation. The results of studied did not indicate an effect of lasalocid supplementation on circulating concentrations of IGF-I.

Administration of monensin CRC during the periparturient period significantly lowered the serum concentrations of BHBA in the first 2 wk postcalving. This finding is in agreement with previous studies. Duffield et al. (1998a) reported that the administration of monensin CRC reduced serum concentrations of BHBA by 150 to 200  $\mu$ mol/L in the first 3 wk postpartum. A smaller study (Duffield et al., 2003) reported, whereby serum BHBA concentrations were significantly lower within the first week precalving and tended to be lower within the first week postcalving. Similarly, Green et al. (1999)

The serum BHBA concentrations for animals receiving the monensin premix were also significantly reduced. The BHBA concentration was reduced by 25% in the first week postpartum and by 26% in the second week postpartum. This is consistent with previously published work. Heuer et al. (2001) reported treatment with monensin premix significantly lowered serum BHBA concentrations when monensin was added to the diet at 2 wk prior to expected calving date. Heuer et al. (2001) combined 3 dosages of monensin topdress (150, 300, 450 mg/cow per d) into 1 treatment effect and did not indicate a percent reduction in BHBA concentration. However, the study did indicate the reduction was significant and involved a large number of animals. An earlier study examined various feeding rates of monensin (Sauer et al., 1989). Results indicated animals fed monensin premix (30 mg/kg) had significantly decreased BHBA concentrations (45%). Additionally, the incidence of subclinical ketosis was reduced 42%. The low monensin group (15 mg/kg) showed a numeric reduction in BHBA concentrations, but the difference was not significant when compared with the control cows (Sauer et al., 1989).

In the present study, there was no significant treatment effect of supplementing dairy cattle with monensin on serum BHBA concentrations.

In this trial, the significant increase of serum glucose concentrations in cattle that received monensin. increased serum glucose concentrations in the first and decreased in the second weeks postpartum. Glucose concentrations were not significantly affected by monensin in the third week. However, numerical trends support previous studies. There may have been a lack of power to illustrate significant effects in the current project. Stephenson et al. (1997) reported that monensin CRC treated-cows had significantly lower glucose values in the immediate precalving period. Other researchers have reported significantly higher glucose concentrations in monensin treated cows postcalving (Duffield et al., 1998a; Abe et al., 1994). There were numerical tendencies for both of these effects in this study. However, a smaller study (Duffield et al., 2003) reported no significant effect on monensin CRC administration on postpartum glucose concentrations. Similarly, Hayes et al., (1996) reported no significant effect of monensin CRC administration on serum glucose concentrations in pasture-fed dairy cows. Pasture-fed dairy cattle tend to have lower milk production; therefore, it is possible that these animals did not experience the degree of negative energy balance associated with higher milk production.

Experimental group did not significantly affect serum insulin concentrations in 2 and 3 week after calving. However, concentrations were higher prepartum than in the postpartum period. Due to the inherent drop in DMI immediately prepartum, and the high energy demand in early lactation, a negative effect on serum insulin concentration has been shown (Hayirli et al., 2002; Holtenius et al., 2003). This is consistent with results from the current study. The heat stress associated with the warmer summer temperatures can cause reduced DMI, regardless of DIM. This drop in energy intake has

repercussions similar to the characteristic peripartum drop, including body fat mobilization resulting in NEFA and BHBA production. The decline in DMI subsequently affects circulating serum insulin concentration. A seasonal effect was shown in the current study. Animals calving in the summer had the lowest serum insulin concentration compared with all other calving seasons. These results are similar to previous work, which showed serum BHBA concentrations increased during the spring and summer months (Duffield et al., 1998a).

Monensin alters energy metabolism (Stephenson et al., 1997) and has the potential to improve the health of dairy cows. In some previous studies a measured increase in glucose by monensin might have also resulted in a corresponding increase in serum insulin, had it been measured. However, in the current study, animals treated with monensin, as a feed additive or from a monensin topdress, had serum insulin concentrations in 2 and 3 week after calving that were not different from the control group. The simplest explanation of this finding is that there was also no effect of monensin on serum glucose in 3 week after calving in this study.

A decrease in free fatty acids that circulate in the blood is an indirect action of monensin and results from an increase in the glucose concentration and subsequently insulin concentration (Abe et al., 1994).

Glucose concentrations were higher for treated cows in 1 week after calving. We anticipated that this increase would also be observed for insulin, because Bines (2) showed that more production of propionate in the rumen after absorption increased the production of insulin by the pancreas. The increase in insulin had a decreasing effect on the production of somatotropin and diverted nutrients to body tissues rather than to milk production. A shift from milk production to growth was not really observed; although in later lactation, the additional energy tended to be used for BW gain rather than for milk production. In this study, we saw no consistent treatment effects on insulin in 2 and 3 week postpartum.

However, increased glucogenic flux might have stimulated the release of insulin and resulted in lower plasma concentrations of glucose in treated cows, perhaps from an increased partitioning of glucose to the rapidly growing foetus (Genstat., 1993). A decrease in glucose concentrations is also consistent with reduced rates of lipogenesis for bovine adipocytes harvested after calving compared with those harvested before calving (Pike et al., 1980) and with the lower sensitivity of adipocytes harvested after calving to insulin (Farries et al., 1993). However, partitioning of glucose to adipose tissue would be a minor effect of the limited role of glucose in ruminant adipose synthesis. Treated cows had lower.

#### REFERENCES

- Abe, N., I. J. Lean, A. Rabiee, J. Porter, and C. Graham. 1994. Effects of sodium monensin on reproductive performance of dairy cattle. II. Effects on

- metabolites in plasma, resumption of ovarian cyclicity and oestrus in lactating cows. *Aust. Vet. J.* 71:277–282.
- Association of Official Analytical Chemists. 1984. *Official Methods of Analysis*. Vol. I. 14th ed. AOAC, Arlington, VA.
- Duffield, T. F., S. LeBlanc, R. Bagg, K. Leslie, J. Ten Hag, and P. Dick. 2003. Effect of a monensin controlled release capsule on metabolic parameters in transition dairy cows. *J. Dairy Sci.* 86:1171–1176.
- Duffield, T. F., K. E. Leslie, D. Sandals, K. Lissemore, B. W. McBride, J. H. Lumsden, P. Dick, and R. Bagg. 1998. Effect of prepartum administration of monensin in a controlled-release capsule on postpartum energy indicators in lactating dairy cows. *J. Dairy Sci.* 81:2354–2361.
- Farries, E., and D. Smidt. 1993. Untersuchungen zur antiketogenen Wirksamkeit von monensin bei milchkuhen. *Züchtungskunde* 65:394–402.
- Genstat V. 1993. *Release 3 Reference Manual*. Oxford Sci. Publ., Oxford, United Kingdom.
- Green, B. L., B. W. McBride, D. Sandals, K. E. Leslie, R. Bagg, and P. Dick. 1999. The impact of a monensin controlled-release capsule on subclinical ketosis in the transition dairy cow. *J. Dairy Sci.* 82:333–342.
- Haney, M., and M. Hoehn. 1967. Monensin, a new biologically active compound I: Discovery and isolation. *Antimicrob. Agents Chemother.* 349:349
- Hayes, D. P., D. U. Pfeiffer, and N. B. Williamson. 1996. Effect of intraruminal monensin capsules on reproductive performance and milk production of dairy cows fed pasture. *J. Dairy Sci.* 79:1000–1008.
- Heuer, C., Y. H. Schukken, L. J. Jonker, J. I. D. Wilkinson, and J. P. T. M. Noordhuizen. 2001. Effect of monensin on blood ketone bodies, incidence and recurrence of disease and fertility in dairy cows. *J. Dairy Sci.* 84:1085–1097.
- Overton, T. R., and M. R. Waldron. 2004. Nutritional management of transition dairy cows: Strategies to optimize metabolic health. *J. Dairy Sci.* 87(E Suppl.):E105–E119.
- Pike, B. V., and C. J. Roberts. 1980. The metabolic activity of bovine adipocytes before and after parturition. *Res. Vet. Sci.* 29: 108.
- Richardson, L., A. Raun, E. Potter, C. Cooley, and R. Rathmacher. 1976. Effect of monensin on rumen fermentation in vitro and in vivo. *J. Anim. Sci.* 43:657–664.
- Sauer, F. D., J. K. G. Kramer, and W. J. Cantwell. 1989. Antiketogenic effects of monensin in early lactation. *J. Dairy Sci.* 72:436–442.
- Schelling, G. 1984. Monensin mode of action in the rumen. *J. Anim. Sci.* 58:1518–1527.
- Stephenson, K. A., I. J. Lean, M. L. Hyde, M. A. Curtis, J. K. Garvin, and L. B. Lowe. 1997. Effects of monensin on the metabolism of periparturient dairy cows. *J. Dairy Sci.* 80:830–837.