ABSTRACT
The effects of monensin on plasma concentrations and changes in plasma concentrations of energy metabolites and minerals over time were investigated using 24 multiparous Holstein cows. Cows were paired according to farm, predicted date of calving, and body condition score and were randomly allocated to two groups. Treated cows were given a ruminal bolus containing 32 g of monensin at 50 ± 7 d before predicted calving. Treated cows had lower plasma concentrations of glucose, free fatty acid (FFA), and β-hydroxybutyrate (BHBA) than did control cows before calving, indicating that monensin influenced energy metabolism. However, no significant differences in plasma concentrations of glucose, FFA, and BHBA were found between groups after calving. Plasma BHBA concentrations increased more before calving in control cows, and plasma FFA and urea concentrations increased significantly before calving in all cows. No significant differences in body weight, plasma concentrations of urea, or whole blood concentrations of glutathione peroxidase were detected between groups before or after calving. Plasma ceruloplasmin activity did not differ between groups before calving, but was significantly higher in treated cows after calving. Plasma concentrations of Ca did not significantly differ between groups before or after calving. Monensin altered both energy and mineral metabolism and has the potential to improve the health and production of dairy cows.

Key words: monensin, metabolism, periparturient cows

INTRODUCTION
During early lactation, the mammary gland of dairy cows has a requirement for nutrients that is usually greater than that provided by feed intake. The consequent nutrient deficiency is met by partitioning nutrients from tissue stores and by mobilizing labile tissue reserves of lipid, protein, glycogen, and minerals. Uptake of glucose by the mammary gland during early lactation results in decreased plasma concentrations of glucose, which are strongly correlated with increased plasma concentrations of FFA and BHBA (18). Excessive mobilization of body tissue is associated with metabolic disorders such as ketonemia and fatty liver (6). Administration of monensin may increase plasma concentrations of glucose (1, 10) by increasing ruminal propionate production (21) and possibly by mechanisms that are independent of ruminal function (2). Increased glucose flux should decrease tissue mobilization and have beneficial impacts on the health and reproductive performance of cows.

The requirement of mammary gland for minerals increases with the onset of lactation, and the sudden increase in demand for Ca is reflected in a marked decrease in plasma concentrations of Ca (14) and, in some cases, clinical hypocalcemia. Increased Ca demand is met by increased Ca absorption from the rumen and intestines and increased resorption from Ca stores in bone. Unfortunately, increased Ca flux from these sources is not evident until 24 to 48 h after calving (8, 9). Monensin increases the uptake of Ca from the intestines (26), influences the absorption of bivalent cations, and, therefore, may modify the risk or severity of parturient paresis. Similarly, absorption of Se (5) and Cu (34) is increased by monensin treatment. Deficiencies in Se have been associated with increased incidence of retained placenta (32) and uterine infection (12), and Se and Cu have important roles in antioxidant defense mechanisms. Increased availability of these minerals might modify the periparturient risk of disease for herds that are deficient in Se and Cu.

Abe et al. (1) commenced monensin treatment of lactating cows in the period immediately after calving (1), and Sauer et al. (22) commenced monensin treatment before calving. Those studies (1, 22) found
higher plasma concentrations of glucose and lower plasma concentrations of ketones and FFA after calving. The goal of this study was to evaluate the effects of monensin administered in a controlled-release capsule on metabolic and mineral responses of cows during the periparturient period. Because feed intake can be depressed shortly after monensin treatment (23), we administered the capsules early in the dry period when nutritional requirements are lower. Our hypothesis was that monensin administration would increase plasma concentrations of glucose, ceruloplasmin (Cp), glutathione peroxidase (GSHPx), and Ca and decrease plasma concentrations of FFA, urea, and BHBA. This study examined the impact of monensin capsules that were administered during the dry period at 50 d before expected calving on metabolism of dairy cows and evaluated the periods when treatment effects of monensin were likely to be the greatest.

**MATERIALS AND METHODS**

Twenty-four multiparous Holstein-Friesian cows from two farms were used in the study, which was conducted over a 12-wk period during autumn in New South Wales, Australia. Cows entered the trial at 50 ± 7 d before predicted calving. Upon entering the trial, cows were paired according to body condition score, calving date, and farm before being allocated randomly into treatment groups. The operators handling the cows were unaware of treatment allocation. The control group was given a sham treatment (the gun used for capsule administration was placed in the mouth of the cow and was discharged), and the treatment group was given one capsule of controlled-release monensin (Rumensin Antibloat Capsule; Elanco Animal Health, West Ryde, New South Wales, Australia) orally. The capsules contained 32 g of monensin, which was released at 300 mg/d over approximately 100 d.

All cows were fed on pasture. For nonlactating cows, the pasture consisted primarily of couch (*Cynodon dactylon*) and kikuyu (*Pennisetum clandestinum*). After calving, all cows were fed pasture containing primarily kikuyu and ryegrass (*Lolium spp.*). In addition, cows from one farm were fed pelleted concentrate at approximately 4 kg/d, and cows from the second farm were fed pellets at approximately 10 kg/d and 1 kg of hay beginning 2 wk before calving and when milking. The pelleted concentrates used on both farms were identical in formulation and included approximately 30% sorghum, 50% wheat bran and pollard, 8% meat meal, 8% cottonseed meal, 1% tallow, and 1% sodium bicarbonate to provide 18% CP.

Feed samples were collected every 14 d and analyzed by near infrared reflectance spectroscopy using equations developed for local pastures and concentrates (28). Analyses of pasture and pellets are presented in Figures 1 and 2 and Table 1, respectively.

All cows were weighed and scored for body condition every 14 d. The accuracy of the scales was verified by placing a known weight on the scales before and after weighing. The standard error was < ±5 kg. Body condition was scored using 0.25 increments (1 = thin to 5 = obese) (7).

Blood (25 ml) was taken weekly from the coccygeal vessels using vacutainers (Becton-Dickinson Vacutainer Systems, Rutherford, NJ). The last blood samples were taken 3 wk after calving. The blood was transported on ice before centrifugation, decanting, and storage at −20°C for later analyses. Enzymatic colorimetric methods were used to determine glucose (24), BHBA (36), FFA (NEFA-C; Wako Pure Chemicals Industries, Ltd., Osaka, Japan), plasma urea (11), GSHPx (32), and Cp activities (13). Plasma Ca was determined by atomic absorption spectroscopy (Varian Spectra AA-20; Varian Techtron, Pty. Ltd., Melbourne, Victoria, Australia).

### TABLE 1. Analysis of concentrate hay and pellets.1

<table>
<thead>
<tr>
<th></th>
<th>Energy (MJ of ME2 of DM/kg)</th>
<th>CP (± SD)</th>
<th>Crude fiber (% of DM)</th>
<th>Fat (± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>SD</td>
<td>X</td>
<td>SD</td>
</tr>
<tr>
<td>Hay</td>
<td>7.64</td>
<td>0.31</td>
<td>10.53</td>
<td>4.74</td>
</tr>
<tr>
<td>Pellets</td>
<td>12.254</td>
<td>0.51</td>
<td>9.85</td>
<td>1.37</td>
</tr>
</tbody>
</table>

1Means for seven pellet and two hay analyses.

2Metabolizable energy.

3Not available.

4Estimated from crude fiber, CP, and fat.
Body weight and plasma concentrations of glucose, FFA, BHBA, plasma urea, Cp, GSHPx, and Ca were assessed by repeated measures of variance with covariables (BMDP 2V; BMDP Statistical Software Inc., Los Angeles, CA). The covariables were farm, interval from treatment to calving, and pretreatment values of the variables. Because the direction of some responses varied before and after calving and because 1 cow died of milk fever at calving, data before and after calving were analyzed separately, except for BW data. Because of the variation in time to calving, some values between 50 and 35 d before calving were missed; consequently, only data collected from blood analysis between 35 d before calving and 14 d after calving were analyzed. Plasma Ca determinations were made on samples collected before treatment and between 14 d before and 14 d after calving. Body weight data were collected every 14 d and were evaluated for the period between 28 d before and 14 d after calving. Missing values were extrapolated or interpolated to allow analysis, and one extrapolated value each was needed for data for the FFA, BHBA, Cp, and GSHPx. Plasma urea and glucose required one extrapolated and one interpolated value, and BW required one extrapolated and four interpolated values. The effects of treatment, time, and treatment by time effects (differences between treatment groups in change of variables over time) were tested. The null hypotheses examined were that the effect of treatment on outcome variables was not significant, that the pattern of change in variables between treatment groups over time was not different. The effects of farm, interval from treatment to calving, and pretreatment differences between group values were adjusted for using covariables.

Power calculations on the results analyzed by repeated measures were made using SOLO Statistical System Power Analysis (BMDP Statistical Software Inc.). Significance was tested at $P \leq 0.1$ because of the relatively small number of cows used in the study. Thus, the statistical power in this study was relatively low. Plasma BHBA had the largest difference between means, and the coefficient of variation was low; the power to evaluate the difference in means was greatest for this variable. The power to evaluate the difference of 24% in means for plasma BHBA differences between treatments, treatment by time effects (differences between groups in the pattern of change in BHBA over time), and change in BHBA over time was 0.30, 0.59, and 0.85, respectively.

RESULTS AND DISCUSSION

Although Sauer et al. (22) commenced monensin treatment before calving, we could find no previously published data on the effects of monensin in dry cows. The mean interval from treatment to calving was 50.3 ± 6.9 d. For all cows, plasma concentrations of glucose (Figure 3) remained stable ($P = 0.73$), and plasma concentrations of FFA (Figure 4) increased ($P =...
0.001), as calving approached. Plasma concentrations of BHBA (Figure 5) tended to increase ($P = 0.11$) for both groups, but concentrations increased more ($P = 0.05$) for control cows as calving approached. These findings of increased plasma concentrations of FFA and BHBA and relatively stable glucose concentrations immediately prior to calving for cows fed diets based on pasture were very similar to those results found by Vazquez-Anon et al. (35) for cows that were fed rations based on hay and silage in herds under housed conditions. In our study, plasma glucose concentrations were lower ($P = 0.10$) in treated cows than in control cows before calving. Previous studies (1, 10), however, have identified significant increases in blood concentrations of glucose in cows treated with monensin after calving (1, 10), which initially appear to be inconsistent with the glucogenic action of monensin. 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 fetus (4). Increased birth weight of calves born to cows treated with monensin before calving has been reported (N. B. Williamson, 1996, unpublished data). 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 (19) and with the lower sensitivity of adipocytes harvested after calving to insulin (3). 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 plasma concentrations of FFA ($P = 0.06$) and BHBA ($P = 0.08$) before calving, a result that is consistent with changes in those metabolites after calving that have been reported in other studies (1, 22, 30). The lower concentrations of plasma BHBA and FFA might have resulted from several actions of monensin, including a decrease in the ruminal acetate to propionate ratio (21), which
subsequently increased hepatic oxidation of glucose in the TCA cycle; a decrease in ruminal production of butyrate (25), which reduced dietary entry of BHBA precursors; a glucogenic effect that was independent of ruminal function modification (2); reduced demand for FFA mobilization as a result of increased glucose availability; or decreased ruminal degradation of dietary protein (20), which increased amino acid availability for gluconeogenesis. However, no differences in plasma urea concentrations (Figure 6) were detected between treatment groups before ($P = 0.85$) or after ($P = 0.18$) calving, possibly indicating that any increase in the available protein was negligible or that the measurement of plasma concentrations of urea was not sufficiently sensitive to detect differences in protein metabolism between the groups. Plasma concentrations of urea ($P = 0.001$), increased before calving in association with greater protein availability in rations and body tissue mobilization in a manner similar to the increase in FFA concentrations. Body weights decreased over time ($P = 0.001$) for all cows (Figure 7), but no differences in BW were found between treatment groups ($P = 0.47$).

After calving, glucose concentrations did not differ between treatment groups ($P = 0.73$), a finding that was consistent with the results of Sauer et al. (22) but not with those of Abe et al. (1), who found higher glucose concentrations in cows treated with monensin. Sauer et al. (22), however, noted that plasma concentrations of glucose were higher in cows treated with monensin, and the power to determine differences between groups in that study was low. Monensin might have increased glucose availability, but high demands for glucose by the mammary gland of the lactating cow kept plasma concentrations relatively constant.

Most studies investigating changes in energy metabolites in the periparturient period have evaluated plasma concentrations of metabolites after calving. In the present study, the pattern of change in plasma concentrations of glucose, FFA, and BHBA after calving was typical of that previously found in studies by Abe et al. (1) and Lean et al. (18) in which plasma concentrations of glucose declined and plasma concentrations of BHBA and FFA increased. No differences were detected in mean plasma concentrations of FFA ($P = 0.45$) and BHBA ($P = 0.32$) or changes in plasma concentrations of FFA ($P = 0.74$) and BHBA ($P = 0.65$) between groups after calving, although plasma concentrations of FFA and BHBA were lower in the treated cows. Other studies (1, 22) have reported decreased plasma concentrations of FFA and BHBA in cows treated with monensin. In this study, plasma concentrations of FFA and BHBA before and after calving suggest that FFA mobilization and BHBA production were reduced, but the statistical power of the study was insufficient to detect changes in the concentrations of these metabolites after calving.

The GSHPx activity (Figure 8) tended to increase ($P = 0.11$) prior to calving. Whole blood concentra-
tions of GSHPx did not differ between treatment
groups before \((P = 0.98)\) or after \((P = 0.98)\) calving, 
nor did the pattern of change differ before or after 
calving \((P = 0.83\) and \(P = 0.13\), respectively). On both 
farms used in the study, GSHPx activity was low 
\((29)\), which indicated Se deficiency \((33)\), despite con-
siderable interlaboratory variation in GSHPx assay 
methods \((17)\). The GSHPx present in blood is 
predominantly present in erythrocytes, which remain 
in circulation for approximately 100 d. Whole blood 
concentrations of GSHPx, therefore, reflect Se intake 
over the previous 100 d and may not reflect immedi-
ate changes in the availability of Se. Although Costa 
et al. \((5)\) found that Se uptake was increased by 
monensin administration in steers, Vay Ryssen \((34)\) 
found no significant difference in blood concentrations 
of GSHPx between cows treated with monensin and 
control cows. Horvath et al. \((15)\), however, found 
significant increased in blood concentrations of 
GSHPx in pigs within 28 d of the commencement of 
monensin administration, indicating the potential for 
monensin supplementation to modify Se metabolism 
and GSHPx activity over a relatively short period.

Plasma Cp activity (Figure 9) did not differ be-
tween treatment groups before calving \((P = 0.87)\) but 
was higher in treated cows after calving \((P = 0.04)\). 
Changes over time in plasma Cp activity were not 
different between groups before \((P = 0.85)\) or after \((P 
= 0.34)\) calving. The increase in Cp that occurred in 
treated cows after calving might reflect an improved 
capacity of treated cows to mobilize Cp, an acute 
phase protein that is important in controlling oxida-
tive challenge from free radicals. Ceruloplasmin is an 
accurate measure of Cu status when Cu supply is 
deficient because Cp-binding sites are unsaturated at 
a low Cu intake. Cows in this trial might have been 
deficient in Cu because soils in the area are deficient 
in Cu \((16)\) and the farms did not provide supplemen-
tal Cu. Van Ryssen \((34)\) demonstrated that monensin 
increased Cu activity in the liver of sheep by using
liver biopsies, a more sensitive measure of Cu status than Cp. Our results support the findings of Van Rysse (34), indicating a potential for monensin to improve Cu absorption.

Mean plasma concentrations of Ca (Figure 10) did not differ between treatment groups before \( (P = 0.99) \) or after \( (P = 0.62) \) calving. Plasma Ca decreased \( (P = 0.001) \) as cows neared parturition, which was consistent with results of other studies (14), and there was a difference \( (P < 0.001) \) between groups in the pattern of change in plasma concentrations of Ca; control cows maintained more constant concentrations of Ca; control cows in concentrations of glucose, BHBA, and FFA and in Cp and Ca metabolism during the period of adaptation to lactation. The study also identified times when plasma metabolites were likely to differ between treatment groups. The decreased plasma concentrations of glucose prior to calving in treated cows probably reflect greater glucose availability and loss to the fetus. The reduction in plasma concentrations of FFA and BHBA should act to reduce the risk of metabolic disorders related to lipid mobilization after calving. Increased Cp activity indicated enhanced Cu absorption and a greater potential for control of oxidative challenge. Further studies should be conducted to explore the potential for monensin to modify both the metabolic adaptive responses of dairy cows to lactation and to examine the effects of monensin on health, reproduction, and production on a population basis.

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REFERENCES


