Praca oryginalna *Original paper*

Determination of the effect of a monensin capsule (continuous-release capsules) on metabolic parameters in transition dairy cows[1)]

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Received 09.04.2020 *Accepted 01.06.2020*

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Summary

Monensin is an ionophore antibiotic that changes the population of rumen bacteria. The aim of this study was to determine the effects of a monensin controlled-release capsule administered 3 weeks before calving on blood metabolites (serum beta-hydroxybutiric acid (BHBA), cholesterol (CHOL), urea, creatinine (CREA), gamma glutamyl transferase (GGT), aspartate aminotransferase (AST), total protein (TP), phosphorus (P), magnesium (Mg^{+}), calcium (Ca^{++}), glucose (GLU) and plasma non-esterified fatty acids (NEFA) concentration) and milk yield before and after calving. A total of 50 Holstein-Friesian cows were selected from the same flock. Blood samples were taken 3 weeks before the expected calving date and during weeks 1, 2, 4, 6, and 8 after calving. The cows were divided into two groups: a study group (Group M, n = 40) and a control group (Group C, n = 10). Group M received orally a cylindrical device (Kexxtone, ELANCO Animal Health, Guelph, ON, Canada), and group C received no treatment. BHBA and NEFA were lower ($P < 0.05$) in group M compared with group C in weeks 6 and 8 after calving. GLU was higher ($P < 0.05$) in group M compared with group C in week 4 after calving. Urea was higher ($P < 0.05$) in group M compared with group C in week 1 after calving. There was no statistically significant difference ($P < 0.05$) between the two groups in milk yields. Although milk yield was similar in both groups, the changes in the concentrations of BHBA, NEFA, GLU and urea show that a monensin CRC could be used as a glycogenic precursor.

Keywords: monensin, transition period, metabolites, milk yield

The transition period in dairy cows is a critical period that starts with parturition and continues with the onset of lactation, both of which can lead to metabolic changes. A negative energy balance (NEB) might occur during this period in between 3 weeks pre-calving and 3 weeks post-calving (4, 12). The transition period is also a period in which many infectious and metabolic diseases may occur (18). In recent years, monensin has been used to help reduce the effects of NEB by promoting ruminal production of glucogenic precursors (7).

One of the potential ways to reduce NEB is to supplement rations with ionophore compounds. Monensin is a carboxylic polyether ionophore antibiotic that modifies the rumen bacterial population with a resultant increase in the rumen concentration of volatile fatty acid and the glucose precursor propionate, rather than acetate and butyrate. Propionate is a major precursor for glucose in the ruminant. Increased propionate in the rumen increases the availability of glucose required for milk production and reduces the risk of ketogenesis, which is one of the alternative ways of producing energy (7). Various studies have been conducted to evaluate the effects of the monensin continuous-release capsule (CRC) on blood metabolite alterations and metabolic diseases, and all of these studies show favorable results (1, 3, 8, 11, 14, 31). Studies have reported a reduction in serum beta-hydroxybutiric acid (BHBA) concentrations (1, 9, 11, 31), a reduction in serum non-esterified fatty acids (NEFA) (31), an increase in serum glucose concentrations (11), and a reduction in the incidence

[1)] The study was approved by the Local Ethics Committee for Animal Experiments at Uludag University (HADYEK), Bursa, Turkey (decision no 2014-16/04) and supported by the Uludag University Scientific Research Projects Unit (grant no KUAP(V)-2015/56).

of subclinical ketosis (9). However, He et al. (15) did not observe any effects of monensin on the yield and composition of milk. Also, a monensin CRC has been shown to decrease the incidence of displaced abomasum (DA) and many other diseases when administered to dairy cows 3 weeks before calving (6).

The aim of this study was to determine the effects of the administration of a monensin CRC 3 weeks before calving on blood metabolites and milk yield before and after calving.

Material and methods

Study design. The study was carried out in a commercial dairy farm located in Bursa, Turkey. A total of 50 Holstein-Friesian dairy cows with body condition scores (BCS) between 3.25 and 3.5 were selected from the same flock. The cows were divided into two groups: a study group (Group M, n = 40) and a control group (Group C, n = 10). At day 21 ± 3 prior to expected calving, group M took orally a cylindrical bolus (Kexxtone, ELANCO Animal Health, Guelph, ON, Canada), which remained in the rumen and constantly released 32.4 g of monensin (equivalent to 35.2 g of monensin sodium). Group C did not receive any treatment. Milk yields from the first 100 and 305 days were recorded for both groups. All cows in each group were housed together in separate barns, and each group was fed the same total mix ration (TMR) under the same conditions. Lactating cows were housed in a dry-lot system and fed a total mixed ration three times a day to meet or exceed the nutritional requirements of NRC (2001) (Tab. 1 and 2). All experimental cows kept in the same lot were fed the same diets and were subjected to the same environmental and management conditions.

Clinical examinations of groups. Clinical examination of the cows was performed and recorded daily from 3 weeks before parturition to 8 weeks after parturition. The cows with any disease in the pre- or postpartum period were recorded. To determine whether cows were ill after calving, daily rectal temperatures and post-calving records of abnormal milk were collected. Rectal body temperatures were taken by the milker twice daily. Ketosis was diagnosed by BHBA measurement. Cows with serum BHBA concentrations > 1.2 mg/dl were considered to have subclinical ketosis (SK), and those with serum BHBA concentrations > 1.5 mg/dl were considered to have clinical ketosis (CK) (30). Left and right displacements of abomasum (LDA and RDA) were determined by clinical and radiological evaluations. *Mastitis* was diagnosed by visual evaluation of abnormal milk from each quarter, based on the color and consistency of milk, as well as by somatic cell count analysis. Signs of *mastitis* were recorded twice daily. A retained placenta was diagnosed when fetal membranes were not expelled within 24 hours of calving; endometritis/metritis was determined by rectal and ultrasonographic examinations (29).

Blood sample collection and lab analysis. Blood samples were taken from the coccygeal vein into tubes without anticoagulant (Vacutainer1, Becton Dickinson, Rutherford, NJ) and with anticoagulant 3 weeks before the expected calving date and during weeks 1, 2, 4, 6 and 8 after calving for determination of serum BHBA, cholesterol (CHOL), urea, creatinine (CREA), gamma glutamyl transferase (GGT), aspartate aminotransferase (AST), total protein (TP), phosphorus (P), magnesium (Mg^{+}), calcium (Ca^{++}), glucose (GLU) and plasma NEFA concentration. The samples were centrifuged at 1500 × *g* for 20 minutes and stored at –20°C until analyzed. Serum levels of P, Mg^{+}, Ca^{++}, AST, GGT, TP were determined with a Vet-Scan, Large Animal

Tab. 1. Ingredients of the experimental diets for cows in prepartum and early lactation periods

Ingredient (kg/d) AF	Early lactation	Prepartum
Hay	0.0	3.0
Alfalfa	4.0	0.0
Alfalfa silage	1.0	0.0
Corn silage	17.0	7.5
Wheat silage	2.0	3.0
Barley	3.5	3.0
Sunflower meal	0.5	0.5
Soybean meal	2.0	0.75
DDGS[a]	1.25	0.5
Canola	1.5	0.75
Wheat bran	0.75	2.0
Soybean hulls	0.0	0.0
Beet pulp	0.0	0.0
Steam flake corn	5.0	3.0
Molasses	0.25	0.0
Water	4.75	4.0
NPN[b]	0.08	0.0
Yeast	0.02	0.02
Toxin binder	0.02	0.02
Sodium bicarbonate	0.2	0.0
Magnesium oxide	0.06	0.07
Potassium carbonate	0.04	0.0
Marble dust	0.25	0.5
Salt	0.05	0.0

Explanations: a – corn dried distillers grains; b – non-protein nitrogen

Tab. 2. Composition of the experimental diets for cows in prepartum and early lactation periods

Nutrients	Early lactation	Prepartum
NEL[c], Mcal/kg DM	1.75	1.45
Crude protein, % DM	17.02	14.58
Ether extract, % DM	5.85	3.78
NDF[d], % DM	31.77	41.73
ADF[e], % DM	18.84	22.46
NFC[f], % DM	39.70	33.02
Ca, % DM	1.05	1.45
P, % DM	0.45	0.50

Explanations: c – net energy for lactation; d – neutral detergent fiber; e – acid detergent fiber; f – non-fiber carbohydrates

Profile® device (Abaxis Inc., Union City, CA 94587) in the central laboratory of the animal hospital of the veterinary faculty at Uludag University. GLU, CHOL, CREA, and urea values were analyzed by an enzymatic colorimetric test (Roche Cobas Integra 400 Plus) in the same laboratory. Serum BHBA levels were measured using a ketone test kit and a corresponding reading device (Ketosite® BHBA test card, Ketosite® instruments, Stanbio Laboratory, Texas, USA). Plasma NEFA levels were determined spectrophotometrically with a commercial NEFA kit (NEFA-HR (2) Wako Chemicals GmbH, Germany).

Statistical analysis. The Shapiro-Wilk test was used to determine whether data from the study were normally distributed. When data were normally distributed, the Student T-test was used, whereas for non-normally distributed data, the Mann-Whitney U test was used. All statistical analyses were performed using the SigmaStat program (SigmaStat 3.1, Systat Software GmbH, Germany) for Windows; $P < 0.05$ was the significance cut-off.

Results and discussion

A total of 12 cows included in this study were in their first lactation (n: 6 in each group), 16 were in their second lactation (n: 8 in each group), and 22 were in their third lactation (n:11 in each group). The mean BCS at the time of enrollment (3.43) did not differ between the groups. Cows in both groups tended ($P = 0.09$) to have normal CBT (38.91 ± 0.04°C in group M, 39.01 ± 0.02°C in group C). Out of the 40 cows in group M, 21 had postpartum diseases (LDA/RDA n = 2, CK n =1, SK n = 1, metritis n = 10, retained placenta n = 2, mucopurulent vaginal discharge n =13, other diseases n = 2), and 19 cows were healthy. Out of the 10 cows in group C, 8 had postpartum diseases (LDA/RDA n = 2, CK n = 2, SK n = 2, metritis n = 4, retained placenta n = 2, mucopurulent vaginal discharge n = 5, other diseases n = 2), and 2 cows were healthy. In both groups, some animals showed more than one disease.

The average milk yield of the animals was approximately 12 414.5 kg/305 days (12 444 kg in group M and 12 298 kg in group C). The 100-day milk yields were 4667.15 kg in group M and 4591 kg in group C. There was no statistically significant difference between the two groups ($P < 0.05$).

The results of biochemical analysis indicate significant effects of the treatment on serum BHBA, glucose,

Table 3. Mean (± SEM) blood biochemical results of week 3 pre-calving and weeks 1, 2, 4, 6, 8 post-calving

	–3rd week	+1st week	+2nd week	+4th week	+6th week	+8th week	Ref. Value (Smith, 2009)
BHBA-M	0.44 ± 0.03^{a,A}	0.53 ± 0.04^{b}	0.72 ± 0.04^{a}	0.68 ± 0.05	0.69 ± 0.05^{A}	0.73 ± 0.07^{A,a,b}	0-1.2 mg/dl
BHBA-C	0.60 ± 0.05^{aA}	0.60 ± 0.07^{b}	0.75 ± 0.1^{c}	0.77 ± 0.03	0.80 ± 0.05^{a,b,A}	0.94 ± 0.05^{a,b,c,A}	
NEFA-M	0.32 ± 0.04^{A,a}	0.35 ± 0.05^{a}	0.38 ± 0.05^{a,c}	0.26 ± 0.03^{c,a}	0.22 ± 0.01^{A,a}	0.25 ± 0.05^{A,a}	0.03-0.4 mmol/L
NEFA-C	0.21 ± 0.01^{a,A}	0.30 ± 0.03^{b}	0.40 ± 0.06^{a,b}	0.33 ± 0.02^{a,b}	0.32 ± 0.02^{a,b,A}	0.38 ± 0.02^{a,b,A}	
GLU-M	51.0 ± 1^{a,A}	46.4 ± 1.2^{b}	44.6 ± 1.7	46.3 ± 1.8^{A}	47.7 ± 2.05	49.9 ± 3.7	42-68 mg/dl
GLU-C	45.8 ± 3.2^{a,A}	45.6 ± 2.5^{b}	40.4 ± 1^{a,b,c}	42.1 ± 0.9^{a,b,d,A}	47.6 ± 1.2^{c,d}	45.0 ± 1.4^{a,b}	
CHOL-M	122.7 ± 2.4^{a}	118.2 ± 3.2^{b,A}	130.6 ± 4.6^{c,A}	145.3 ± 5.1^{a,b,c}	148.7 ± 5.1^{a,b,c}	151.3 ± 4.8^{a,b,c}	65-220 mg/dl
CHOL-C	131.4 ± 4.6^{a}	140.3 ± 6.8^{b,A}	155.8 ± 8.6^{a,b,A}	156.0 ± 7.4^{a,b}	158.3 ± 7.8^{a,b}	159.7 ± 8.1^{a,b}	
AST-M	87.5 ± 3.01^{a}	84.7 ± 2.44	81.5 ± 3.14	82.5 ± 1.61^{a}	83.7 ± 1.99	83.1 ± 2.05^{a}	51-127 IU/L
AST-C	73.7 ± 2.17^{a}	80.5 ± 2.54	76.7 ± 2.08	76.5 ± 1.81^{a}	78.5 ± 1.68	77.6 ± 2.43^{a}	
GGT-M	22.4 ± 1.55^{a}	23.3 ± 1.42^{b}	25.4 ± 1.41	32.3 ± 4.27^{a}	31.4 ± 3.86^{a}	33.6 ± 3.19^{a,b}	6.1-25 IU/L
GGT-C	23.1 ± 1.21	25.9 ± 2.97	29.2 ± 3.89	27.4 ± 3.08	26.7 ± 2.39	28.2 ± 2.82	
TP-M	7.10 ± 0.02	7.00 ± 0.02	7.00 ± 0.02	7.10 ± 0.02	7.10 ± 0.02	7.10 ± 0.02	5.8-8.4g/dl
TP-C	7.10 ± 0.04	6.90 ± 0.07	7.10 ± 0.07	7.00 ± 0.04	7.00 ± 0.03	7.10 ± 0.03	
CREA-M	0.77 ± 0.02^{a}	0.90 ± 0.02^{A}	0.89 ± 0.02^{A}	0.85 ± 0.02^{a}	0.85 ± 0.01^{a}	0.87 ± 0.01^{a}	0.6-1.3 mg/dl
CREA-C	0.94 ± 0.03	0.78 ± 0.03^{A}	0.78 ± 0.03^{A}	0.81 ± 0.03	0.78 ± 0.03	0.84 ± 0.02	
UREA-M	32.10 ± 0.76^{a}	35.9 ± 0.68^{b,A}	34.8 ± 0.58^{a,b}	35.1 ± 0.68^{a,b}	34.4 ± 0.58^{a,b}	35.5 ± 0.66^{a}	20-30 mg/dl
UREA-C	34.50 ± 1.42	30.6 ± 1.38^{A}	33.3 ± 1.71	34.4 ± 1.35	33.5 ± 1.17	37.2 ± 1.04	
Ca-M	9.13 ± 0.07	9.24 ± 0.13	9.35 ± 0.11	9.26 ± 0.09	9.43 ± 0.06	9.42 ± 0.07	8.3-12 mg/dl
Ca-C	9.32 ± 0.55	9.46 ± 0.20	9.33 ± 0.19	9.34 ± 0.20	9.4 ± 0.20	9.46 ± 0.17	
P-M	7.46 ± 0.12^{a}	5.82 ± 0.16^{a}	5.57 ± 0.13^{a}	5.62 ± 0.15^{a}	5.11 ± 0.12^{a}	5.57 ± 0.21^{a}	4.5-6.5 mg/dl
P-C	7.23 ± 0.38^{a}	5.46 ± 0.18^{a}	5.05 ± 0.32^{a}	4.93 ± 0.21^{a}	4.69 ± 0.21^{a}	5.05 ± 0.35^{a}	
Mg-M	2.30 ± 0.04	2.18 ± 0.03	2.20 ± 0.03	2.27 ± 0.04	2.17 ± 0.02	2.15 ± 0.02	1.8-2.3 mg/dl
Mg-C	2.26 ± 0.08	2.23 ± 0.09	2.34 ± 0.05	2.37 ± 0.08	2.28 ± 0.04	2.28 ± 0.06	

Explanations: a, b, c – Differences between values with different letters in the same row are statistically significant ($P < 0.05$); A – Differences between values with different letters in the same column are statistically significant ($P < 0.05$)

urea, and plasma NEFA (Tab. 3). BHBA and NEFA were lower ($P < 0.05$) in group M compared with group C in weeks 6 and 8 after calving. GLU was higher ($P < 0.05$) in group M compared with group C in week 4 after calving. Urea was higher ($P < 0.05$) in group M compared with group C in week 1 after calving. No significant differences were found in CHOL, AST, GGT, TP, Ca, Mg and P either before or after calving.

There are different reports about the effect of monensin on milk yield. Melendez et al. (22) found that long-term monensin administration can increase milk production. However, they reported that there was no change in the mature equivalent 305-day milk yield after monensin administration. There are also many studies that correlate the effects of monensin treatment on BCS and milk yield findings (7, 21, 23, 26, 31). In our study, BCS was not taken into consideration, and the increase in milk yield was not different between the two groups during the 8 weeks of this study. Some researchers reported that monensin administration increased milk yield, whereas others found that it did not affect milk production. These differences may also be due to such factors as herd size, breed, BCS, and genetic merit (25).

Supplementation of monensin results in some changes in ruminal activity, such as an increase in propionate (27, 28) and a decrease in butyrate concentrations (11), which are a potential benefit of this precursor for energy metabolism. Duffield et al. (6) found that the administration of a monensin CRC to dairy cows 3 weeks before calving reduced the incidence of SK. It is likely that these effects on clinical health are mediated by the improved energy balance in monensin-treated cows. In our study, serum BHBA concentrations in both groups increased at week 6 after calving. These concentrations were lower ($P \leq 0.001$) in cows administered a monensin CRC compared with group C at weeks 6 and 8 after calving. The significant decrease in the BHBA level after 6 weeks due to the increase in glucose metabolism shows that the BHBA level is adversely affected by glucose metabolism in terms of energy metabolism. In this study, the glucose concentration was statistically higher in group M than in group C at week 4 after calving. These results are supported by studies that have shown improvements in energy indicators, such as increased glucose and decreased BHBA concentrations, in cows treated with monensin (5, 8, 11, 20, 28), and it was shown that monensin increases glucose and other blood constituents through modification of ruminal microbial populations reflected by changes in fermentation end products (19).

In this study, plasma NEFA concentrations increased significantly ($P < 0.001$) during week 1 and reached a peaked at week 2 after calving in both groups. Plasma NEFA concentrations in group M were higher at weeks 4, 6 and 8 after calving compared with those at week 3 before calving ($P < 0.05$) (Tab. 3). The decrease in non-esterified fatty acids after 2 weeks may be due to the increase in dry matter intake (10, 17), and this low level of NEFA may also be associated with a negative energy balance that resulted from increasing metabolic requirements after calving (2, 16, 32). The observed decreases in plasma NEFA levels in this study might be related to changes in adipose tissue density in response to the administration of a monensin CRC before calving (19, 24). Grummer et al. (12) reported that the lower NEFA concentration indicates less fat mobilization in these cows. In our study, no statistically significant difference was found between the groups. The serum total cholesterol concentration was lower in group M, but the difference was not statistically significant. As in a study by Abe et al. (1), the monensin CRC did not significantly affect serum cholesterol concentrations. In addition, Duffield et al. (7), suggested that studies with a large number of cows should be performed to demonstrate the effect of monensin on cholesterol.

Monensin is also known to affect protein metabolism, increasing blood urea concentrations, especially around the time of calving (7). The effect of a monensin CRC on urea has previously been reported in several studies. They have reported higher urea levels in monensin CRC-treated cows after calving (9, 11). In our study, the highest level of urea in cows that received a monensin CRC was found 1 week after calving, and this value was higher than in the other weeks ($P < 0.05$). The urea concentration in group M was increased 1 week after parturition compared to that in group C. The higher uremia detected in blood suggests that the monensin CRC could have increased the role of amino acids from muscle tissue in covering the energy deficit during a NEB because blood urea is partially derived from the deamination of muscle amino acids after they have been used as gluconeogenic sources (24).

The administration of a monensin CRC to dairy cows during the pre-calving period had no effect on milk yield, but led to significant changes, especially in BHBA, NEFA, glucose and urea concentrations. As a result, it has been concluded that the use of monensin as a glycogenic precursor during transition periods, in which metabolic changes are intense, may contribute to improved dairy cow management and economy in farms.

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