Kafkas Univ Vet Fak Derg
23 (5): 763-768, 2017
DOI: 10.9775/kvfd.2017.17743

Kafkas Universitesi Veteriner Fakultesi Dergisi
Journal Home-Page: http://vetdergikafkas.org
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Research Article

Influence of Niacin Supplementation on the Metabolic Parameters and Lipolysis in Dairy Cows During Early Lactation

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Article Code: KVFD-2017-17743 Received: 13.03.2017 Accepted: 09.05.2017 Published Online: 06.06.2017

Citation of This Article

Hristovska T, Cincovic M, Stojanovic D, Belic B, Kovacevic Z, Jezdimirovic M: Influence of niacin supplementation on the metabolic parameters and lipolysis in dairy cows during early lactation. *Kafkas Univ Vet Fak Derg,* 23 (5): 763-768, 2017 *(in Press).* DOI: 10.9775/kvfd.2017.17743

Abstract

The objective of this study was to evaluate the effect of niacin on the metabolic parameters and lipolysis inhibition in dairy cows during early lactation. A total of 30 clinically healthy, multiparous Holstein-Friesian cows in late gestation were enrolled in the study (15 supplemented with niacin (120 g/d/cow) and 15 in the negative control group). Blood samples were taken weekly for 3 weeks after calving. The research results show that cows that received niacin indicated lower NEFA concentrations in all three weeks of the experiment. The NEFA concentrations did not change from weeks 0 to 2 after calving in the niacin group, whereas the NEFA concentrations in the control group were significantly increased (P<0.05). The administration of niacin exerted significant effects on the metabolic adaptations in cows during early lactation. Niacin significantly decreased BHB, MDA, total bilirubin, urea and phosphorus concentrations and liver enzyme activity (AST, ALP and GGT) and increased albumin, cholesterol, triglyceride and glucose concentrations. The administration of niacin significantly affected the correlation and regression between NEFA concentrations and other metabolic parameters, rendering the glucose, cholesterol, triglycerides, total bilirubin, AST, albumin, urea and phosphorus values less regressed against the NEFA values. In conclusion, niacin administration decreases lipolysis and metabolic adaptations proved to be less dependent on NEFA concentrations in niacin group compared to the control group.

Keywords: *Cow, Niacin, Lipolysis, Metabolic profile*

Erken Laktasyon Süresince Sütçü İneklerde Niasin İlavesinin Metabolik Parametreler ve Lipoliz Üzerine Etkisi

Özet

Bu çalışmanın amacı erken laktasyon süresince sütçü ineklerde niasinin metabolic parametreler ve lipolizi inhibe etme üzerine etkilerini araştırmaktır. Toplam 30 adet klinik olarak sağlıklı geç gebelik dönemindeki multiparous Holstein-Friesian inek (15'i 120 g/gün niasin takviyesi verilmiş ve 15'i negatif kontrol) çalışmada kullanıldı. Kan örnekleri doğumu takiben 3 hafta süresince haftalık olarak alındı. Çalışma sonuçları niasin alan ineklerde 3 hafta süresince NEFA konsantrasyonunun daha düşük olduğunu gösterdi. NEFA konsantrasyonu 0 ile doğumdan sonraki 2 hafta boyunca niasin grubunda değişmezken kontrol grubunda anlamlı oranda artma gösterdi (P<0.05). Niasin verilmesi erken laktasyon dönemindeki ineklerdeki metabolik adaptasyona anlamlı derecede etki etti. Niasin anlamlı oranda BHB, MDA, total bilirubin, üre ve fosfor konsantrasyonları ile karaciğer enzim aktivitesini (AST, ALP ve GGT) düşürürken albümin, kolesterol, trigliserid ve glikoz konsantrasyonlarını artırdı. Niasin verilmesi anlamlı oranlarda olmak üzere NEFA konsantrasyonları ile diğer metabolik parametreler arasındaki korelasyon ve regresyonu etkiledi. Glikoz, kolesterol, trigliserid, total bilirubin, AST, albümin, üre ve fosfor değerleri NEFA değerlerine göre daha az gerileme gösterdi. Sonuç olarak, niasin verilmesi lipolizi azaltırken metabolik adaptasyonun kontrol grubu ile karşılaştırıldığında niasin grubunda NEFA konsantrasyonuna daha az bağımlı olduğu gösterilmiştir.

Anahtar sözcükler: *İnek, Niasin, Lipoliz, Metabolik profil*

INTRODUCTION

During the transition period, energy requirements exceed energy intake, resulting in negative energy balances (NEB) and marked catabolism [1,2]. Increased plasma non-esterified fatty acids (NEFA) concentrations occur as a result of lipid mobilization. Consequently, the high influx of NEFA to the liver exceeds its oxidative capacity, which results in triacylglycerol (TG) accumulation in the liver and ketosis [3]. Lipolysis (NEFA) and ketogenesis (β-hydroxybutyrate- BHB)

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exert a significant influence on the metabolic profile in cows during the periparturient period [4]. Proper nutrition and management of cows during this period benefits their future health and milk production.

The term *niacin* is a generic descriptor for two compounds performing the biological action of the vitamin: nicotinic acid and nicotinamide [5]. Another physiological effect of niacin is the potential to suppress lipolysis when administered in pharmacological doses [6,7]. Nicotinic acid, under certain conditions, reduces the NEFA release from adipose tissue, whereas nicotinamide does not exert the same effect [8]. Reduced NEFA concentrations lead to a lowered TG accumulation and ketone body formation in the liver [9]. The antilipolytic effect of niacin is mediated by the activation of G protein-coupled GPR109A receptors, which exist in a functional form in cattle [10]. Consequently, the inhibition of adenyl cyclase activity occurs, reducing the intracellular levels of cyclic adenosine monophosphate (cAMP) and resulting in the suppression of lipolysis [11].

In this research, it has been hypothesized that antilpolytic effects of niacin is taken into consideration, niacin may show beneficial effect metabolic and oxidative status in dairy cows during early lactation.

The objective of this study was to evaluate the effect of niacin on the metabolic parameters and lipolysis inhibition in dairy cows during early lactation.

MATERIAL and METHODS

Animals, Treatments and Blood Collection

A total of 30 clinically healthy, Holstein-Friesian cows in second and third lactation were enrolled in the study. Cows were 3 to 4 years old. Their health status was evaluated on clinical examination and no signs of illness were found. None of the cows had history of abortion. Cows were divided into two groups, 15 cows in the experimental and 15 cows in the control group. The experimental group was treated with niacin for 14 days prior to the expected calving date and for 14 days after parturition. Niacin was not in a rumen-protected form such as nicotinic acids (Rovimix®Niacin, F. Hoffmann-La Roche AG, Switzerland) and was administered per os with food, 120 g/d per cow (in order to ensure about 12 g of niacin in small intestine). The control group was not treated with niacin. Cows were feed twice a day. The diet suited the energy necessary for cows in late pregnancy and early lactation. The cows in late pregnancy were fed with a diet consisting of 6 kg lucerne hay, 15 kg maize silage (30% DM) and 3 kg concentrate (18% crude proteins, CP). The cows in early lactation were fed with a diet consisting of 7 kg lucerne hay, 20 kg maize silage (30% DM) and 5 kg concentrate (18% CP).

Blood samples were collected by venipuncture from the coccygeal vein before morning feeding and were taken three times, on the day of calving and during the first and second week after parturition. Blood samples for biochemical analysis were collected in sterile 10-ml vacuum tubes with gel separator (BD Vacutainer® SST II Advance, BD Plymoth, UK) and appropriately marked. After centrifugation of the blood samples at 4.000x g for 10 min, the plasma was obtained. The samples were kept in a dry pace and protected from light until laboratory analysis.

Measurements of Metabolic Parameters

Metabolic parameters such as NEFA (colorimetric method based on acylation of ACoA), BHB (BHB dehydrogenase), triglyceride (GPO-PAP method), cholesterol (cholesterol esterase method), glucose (glucose oxidase test, GOT), total protein (Biuret method), albumin (BCG/BCP methods), aspartate aminotransferase (AST) (modified IFCC method), alkaline phosphatase (ALP) (DEA method), gamma-glutamyl transferase (GGT) (colorimetric method with final 5-amino-2-nitrobenzoat), total bilirubin (Modified Jendrassik and Vanadate Oxidation), urea (kinetic method), malondialdehyde *(*MDA) (method with thiobarbituric acid), calcium (CPC/AMP method) and phosphorus (UV method) concentrations were determined using colorimetric test kits (Randox, UK and Pointe Scientific, USA) and a semi-automatic bio-chemistry analyzer (Rayto RT/1904cv, China).

Calculation and Statistical Analyses

The effects of niacin administration on the metabolic parameter values were analyzed during the first three weeks after calving (week 0, 1 and 2). The two-way ANOVA analysis and LSD tests indicated differences in the mean values of metabolic parameters between cows that received niacin and cows that did not receive niacin (the control group) in all three weeks of the experiment.

The metabolic adaptations of cows, relative to the degree of lipolysis, were determined by a regression analysis and correlation between the metabolic parameters and NEFA concentrations (using the general linear formula $Y = bXi + a$) in all the samples obtained from the experimental and control groups after calving (N = 45, 15 samples x 3 weeks). The effects of niacin on the metabolic adaptations of cows in early lactation were determined by testing differences in the correlation and regression coefficients obtained for certain metabolic parameters and NEFA concentrations in the experimental and control groups. Statgraphics Centurion (USA) and Microsoft Excel (USA) were used for statistical calculations and analysis. $P<0.05$ level was accepted statistically significant.

RESULTS

The research results show that cows supplemented with niacin indicated lower NEFA concentrations in all three weeks of the experiment. The NEFA concentrations did

Table 1. *Effects of niacin administration on the metabolic parameter values in cows during early lactation*

Parameter	Group	Week Postpartum			Influence of Niacin (P)	Influence of Week (P)
		0	1	2		
NEFA mmol/L	Niacin	0.30±0.09	0.35±0.1	0.39±0.1	<0.01	NS
	Control	0.47±0.09	0.67±0.1	0.76±0.1		<0.01
BHB mmol/L	Niacin	0.49±0.11	0.68±0.12	0.79±0.12	<0.01	<0.05
	Control	0.62±0.12	0.86±0.13	1.03±0.11		<0.01
Glucose mmol/L	Niacin	3.08±0.3	2.73±0.29	2.51±0.3	<0.01	<0.05
	Control	2.53±0.29	2.11±0.25	1.97±0.2		<0.05
Triglycerides mmol/L	Niacin	0.12±0.008	0.12±0.009	0.10±0.01	<0.01	<0.01
	Control	0.11±0.007	0.097±0.008	0.087±0.01		<0.01
Cholesterol mmol/L	Niacin	2.53±0.15	2.41±0.16	2.02±0.13	<0.01	<0.05
	Control	2.05±0.12	1.95±0.17	1.64±0.14		<0.01
MDA μmol/L	Niacin	1.42±0.12	1.63±0.15	1.8±0.14	<0.01	<0.01
	Control	1.89±0.3	2.36±0.25	2.6±0.35		<0.05
T. bilirubin μmol/L	Niacin	6.31±1.2	7.82±0.95	9.18±1.2	<0.01	<0.01
	Control	8.35±1.1	10.85±1.1	13.1±0.99		<0.01
AST U/L	Niacin	83±9.5	101±10.5	107±9.9	<0.01	<0.01
	Control	93±10.1	121±12	130±10.8		<0.01
ALP U/L	Niacin	68±9	72±14	74±15	<0.01	NS
	Control	99±12	106±13	108±10		NS
GGT U/L	Niacin	15±2.5	17±2.1	18±2.6	<0.01	<0.05
	Control	18±2.2	21±2.3	22±2.4		<0.05
Total protein g/L	Niacin	77.1±4.1	72.5±4.3	71.1±4.1	NS	<0.05
	Control	78.9±4.2	74.1±4.4	72.7±4.1		<0.05
Albumin g/L	Niacin	41.7±3.5	38±3.2	37±3.5	<0.01	NS
	Control	34.6±3	31.5±3.7	30.7±3.3		NS
Urea mmol/L	Niacin	3.5±0.6	3.3±0.7	3.5±0.6	<0.01	NS
	Control	5.1±0.9	4.8±0.9	4.6±0.9		NS
Ca mmol/L	Niacin	2.25±0.25	2.16±0.24	2.13±0.22	NS	NS
	Control	2.1±0.23	2.07±0.25	2.04±0.24		NS
P mmol/L	Niacin	2.17±0.21	2.08±0.23	2.07±0.2	<0.05	NS
	Control	2.43±0.25	2.33±0.24	2.31±0.22		NS

not change from weeks 0 to 2 after calving in the group that received niacin, whereas the NEFA concentrations in the control group were significantly increased. The administration of niacin exerted significant effects on the metabolic adaptations in cows during early lactation. Cows supplemented with niacin were found to exhibit significantly lower BHB concentrations, higher cholesterol and triglyceride concentrations, lower MDA concentrations, higher glucose concentrations, decreased total bilirubin concentrations and liver enzyme activity (AST, ALP and GGT), higher albumin concentrations, and lower urea and phosphorus concentrations. The changes in metabolite values were also tested in all weeks of the experiment. The results are shown in *Table 1*.

In the niacin group, the metabolic adaptations proved to be less dependent on NEFA concentrations compared to the control group. With increased lipolysis, the administration of niacin significantly reduced the degree of ketogenesis *(Fig. 1)*. Increased NEFA concentrations greatly impeded the increase in MDA concentrations in cows that received niacin *(Fig. 2)*. In addition to ketogenesis and lipid peroxidation, the administration of niacin significantly affected the correlation between NEFA concentrations and other metabolic parameters, rendering the glucose, cholesterol, triglycerides, total bilirubin, AST, albumin, urea and phosphorus values less regressed against the NEFA values *(Table 2)*.

DISCUSSION

A typical metabolic profile of cows a week postpartum is characterized by reduced plasma concentrations of

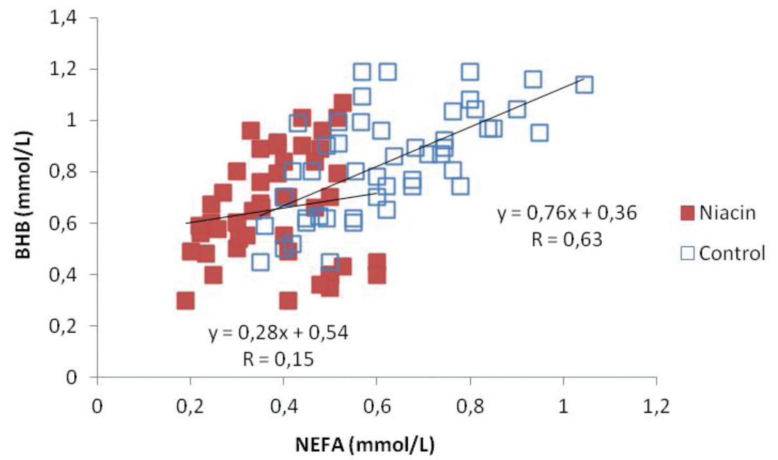

Fig 1. Regression and correlation between the NEFA and BHB concentrations in the group of cows supplemented with niacin and the control group

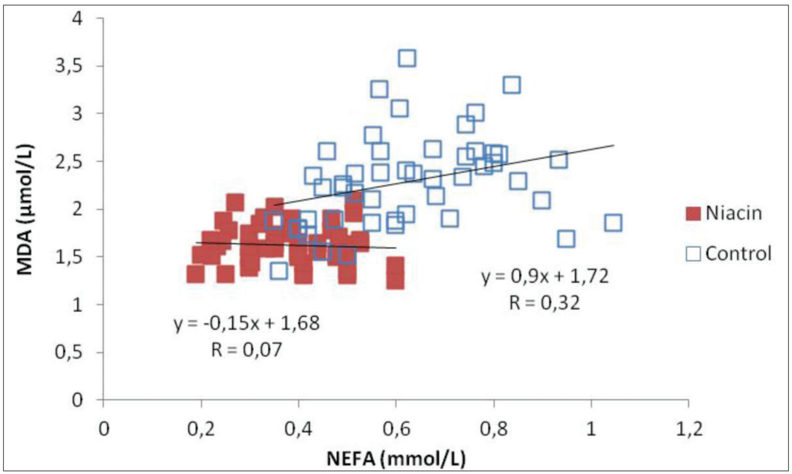

Fig 2. Regression and correlation between the NEFA and MDA concentrations in the group of cows supplemented with niacin and the control group

Table 2. *Effects of niacin administration on the regression and correlation between the metabolic parameters and NEFA concentrations*

Blood Parameters	Correlation with NEFA		P	Regression Against NEFA		P
	Niacin	Control		Niacin	Control	
BHB	0.15	0.63	<0.01	0.28	0.76	<0.01
Glucose	-0.17	-0.57	<0.01	-0.64	-1.16	<0.05
Triglycerides	-0.2	-0.72	<0.01	-0.02	-0.05	<0.05
Cholesterol	0.06	-0.69	<0.01	0.14	-0.87	<0.01
MDA	0.07	0.32	<0.01	-0.15	0.9	<0.01
T. bilirubin	0.06	0.61	<0.01	0.97	8.2	<0.01
AST	0.02	0.57	<0.01	3.3	63.1	<0.01
ALP	0.26	0.33	NS	15.5	20	NS
GGT	0.2	0.3	NS	6.37	5.38	NS
Total protein	0.05	0.4	<0.01	-2.4	-12.6	<0.01
Albumin	0.33	0.52	<0.05	17.7	-11	<0.01
Urea	~0	~0	NS	~0	~0	NS
Ca	0.06	0.07	NS	-0.15	-0.19	NS
P	~0	~0	NS	~0	~0	NS

glucose, protein, albumin, cholesterol and calcium, as well as high plasma concentrations of NEFA, BHB, bilirubin and liver enzymes [12,13]. Pharmacological doses of niacin have the ability to inhibit lipolysis, thereby reducing the hepatic uptake of NEFA, improve the metabolic profile of the transition cow and prevent energy-related metabolic disorders associated with excessive mobilization of fat reserves [6,14]. Havlin et al.[15] concluded that effects of niacin in dairy cows dependent on dose level and feeding duration and low level of niacin feeding did not reduced blood serum NEFA concentration but it did result in a decreased prevalence of ketosis. In this study, cows that received niacin indicated decreased plasma NEFA and BHB concentrations in all three weeks of the experiment alongside a strong but lower correlation between the NEFA concentrations and metabolic parameters in comparison with the control group. Niacin was shown to reduce the dependence of the metabolic adaptations on the degree of lipid mobilization in cows during early lactation. Pires and Grummer [6] showed that a single abomasal infusion of niacin inhibits lipolysis and reduces plasma NEFA concentrations, followed by a rebound in plasma NEFA concentrations upon the termination of infusion and Rauls et al.[16] showed that niacin-supplemented cows had lower NEFA concentration in week 1 of lactation than non supplemented niacin cows but niacin had no effect if the cows are in late lactation. In our study, the niacin group did not indicate significant changes in the NEFA concentrations in all weeks of the experiment, which proved the antilipolytic effect of niacin and the importance of continuous niacin administration during the transition period. Serum levels of glucose, triglyceride, total cholesterol, total protein, albumin and urea are indicators of hepatic function [17,18], and a decrease in the plasma concentration of these metabolites may occur provided endogenous liver synthesis is reduced. In this study, the concentrations of triglyceride, cholesterol, glucose and albumin were higher in the niacin group, which emphasizes a better hepatic function. In human medicine the niacin is used as broad-spectrum lipid drug and has ability to reduce cholesterol concentration in plasma thereby inhibits diacylglycerol transferase, enzyme that is a key in hepatic synthesis of triglycerides. The niacin causes reduced catabolism rate of LDL (low-density lipoprotein) and VLDL (very low density lipoprotein) [19,20]. But metabolism in ruminates is different than metabolism of other mammals by having diminished capacity to form VLDL from cholesterol and to secrete VLDL from the liver [21,22]. There is negative correlation between cholesterol and NEFA [23] and the effect of niacin on triglyceride and cholesterol may be due to the action of niacin on NEFA. Further research is needed to established the direct effect of niacin on cholesterol in dairy cows.

When fat infiltrates the liver, a lesion appears in the hepatic tissues and the levels of enzymes indicating the liver injury (AST and GGT) are generally augmented [24]. Lower liver damage in the niacin group can be detected by a lower activity of liver enzymes (AST, ALP and GGT) and a lower concentration of total bilirubin. Plasma NEFA concentrations increase a few days before parturition and rise to higher levels in the week after calving [25,26]. In our study, cows supplemented with niacin were found to exhibit a reduced degree of ketogenesis upon increased lipolysis, which may be due to pharmacological doses of niacin administered. Niacin decreased the NEFA release from adipose tissue, leading to a reduced hepatic uptake of NEFAs and lowered BHB formation, i.e. an improved hepatic function. In the niacin group, less regression was recorded between the values of MDA and NEFA concentrations, which indicates that the administration of niacin may exert effects on lipid peroxidation. Moreover, Yuan et al.[9] speculate that niacin may have the antioxidant potential via inhibiting lipolysis, and thus decreasing the amount of fatty acid substrates available for lipid peroxidation.

Glucose concentrations change in early lactation in same manure in both of niacin and control group. Higher concentration of glucose in niacin group could be consequence of greater gluconeogenic activity, decrease removal of glucose or increased hepatic glucose production [7,27-29].

The administration of niacin affects the indicator values of carbohydrate metabolism, fats, proteins, as well as the functional status of hepatocytes and ions. Niacin decrease ketogenesis and oxidative stress in cows during early lactation.

In conclusion, niacin reduces the dependence of the metabolic adaptations on the degree of lipid mobilization in cows during early lactation.

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