Prepartum supplementation of nicotinic acid: Effects on health of the dam, colostrum quality, and acquisition of immunity in the calf

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ABSTRACT

Nicotinic acid (NA) has been shown to reduce lipolysis, alter milk components and the ruminal environment, and increase blood flow. Increased blood flow to the mammary gland during colostrogenesis might increase nutrients and immunoglobulin concentration of colostrum. Twenty-six multiparous Holstein cows were housed in a tiestall barn. Cows were blocked by expected calving date and randomly assigned to 1 of 2 treatments 4 wk prepartum: (1) 0 g/d of NA (control, CON) or (2) 48 g/d of NA (NA). Total mixed ration amounts fed and refused were measured daily to determine dry matter intake. Blood samples were collected from dams every Monday, Wednesday, and Friday from the coccygeal vein or artery and were analyzed for glucose, nonesterified fatty acids (NEFA), and β -hydroxybutyrate (BHB). Colostrum was collected and weighed within 90 min of parturition. Colostral immunoglobulin G (IgG) concentration was analyzed using radial immunodiffusion assay. Calves were removed from their dams before suckling and weighed within 30 min after birth. Calves received 3 L of a lacteal-based colostrum replacer that provided a total of 225.8 g of IgG within 2 h of birth. Calf blood samples were collected via jugular venipuncture at 0 and 24 h of age and analyzed for IgG concentration and determination of apparent efficiency of absorption. Colostrum yield, dry matter intake, IgG yield, and fat and solids percentage of colostrum did not differ between treatments. Serum concentrations of glucose and BHB were not affected by treatment. We detected an effect of week on serum glucose concentrations at calving and on serum BHB concentrations at 1 wk postpartum. There was a treatment by week effect for serum NEFA concentrations

at 1 wk postpartum, where cows that received NA prepartum had higher serum NEFA concentration than CON cows, indicating that a NEFA rebound occurred. No differences were observed for calf body weight, 0- or 24-h serum IgG concentration, or apparent efficiency of absorption. Supplementation of NA increased IgG concentration in colostrum from 73.8 to 86.8 g/L. Results indicate that 48 g/d of supplemental NA during the prepartum period improved colostrum quality.

Key words: nicotinic acid, prepartum, colostrum, dairy calf, immunoglobulin G

INTRODUCTION

Effects of supplemental nicotinic acid (NA) on metabolism in pre- and postpartum cattle have been widely studied (Neihoff et al., 2009a), but little is known about its possible effects on colostrum quality or calf immunity, which are key factors for dairy farm success and profitability. Acquisition of immunity in the neonate is dependent on consumption of high-quality colostrum. A nationwide evaluation of colostrum quality in the United States found that >60% of colostrum does not meet industry recommendations of ≥ 50 g of IgG/L and a total plate count <100,000 cfu/mL (Morrill et al., 2012). The USDA National Animal Health Monitoring System (NAHMS, 2007) reported that one-fifth of heifer calves do not achieve successful passive transfer. Supplemental NA can increase blood flow, which may increase nutrients and immunoglobulin concentration in colostrum if supplemented during colostrogenesis.

Colostrogenesis is a unique stage in prepartum mammary gland development when maternal immunoglobulins are transferred from the blood into mammary secretions (Barrington et al., 2001). This distinct phase of development begins about 3 wk prepartum and ceases just before parturition and the onset of lactation (Brandon et al., 1971). Immunoglobulin G is the most abundant immunoglobulin present, accounting for 85 to 90% of total Ig (Butler, 1969; Sasaki et al., 1976; Larson et al., 1980). Due to the 6-layer synepi-

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theliochorial placenta in bovines, transfer of maternal immunoglobulins does not occur in utero, rendering the calf hypogammaglobulinemic (Lopez et al., 1988). For this reason, it is vital that calves receive high-quality colostrum as soon as possible after birth and within 24 h, before complete gut closure occurs (Arthington et al., 2000). Calves that do not receive colostrum will lack necessary antibodies and many other nutrients to fight disease and survive. At 24 h of age, calves should achieve a minimum of 10 g/L of IgG in plasma (Quigley and Drewry, 1998).

Proper nutrition in the prepartum period affects acquisition of immunity in the newborn calf (Burton et al., 1984; Hough et al., 1990) and colostrum quality (Fatahnia et al., 2012). During the last trimester, the developing fetus requires greater nutrients, as total fetal weight gain is greatest during this time (Bell, 1995). Proper feeding of the prefresh cow requires meeting the needs of both the dam and the developing fetus.

Nicotinic acid has been used in humans as an antilipolytic remedy (Carlson, 2005). It lowers triglyceride and low-density lipoprotein cholesterol levels and alters lipolysis via a G protein-coupled receptor (**GPR**) 109A (Lorenzen et al., 2001; Tunaru et al., 2003). Recent work by Titgemeyer et al. (2011) with cattle detected the presence of GPR109A in tail head, back, and perirenal fat, longissimus muscle, liver tissue, and 5 regions of the brain: hypothalamus, thalamus, cerebellum, cerebral cortex, and brain stem. When supplemented at pharmacological doses in cattle, NA inhibits lipolysis via stimulation of GPR109A (Tunaru et al., 2003; Benyó et al., 2006). Nicotinic acid reduces adenyl cyclase activity, causing inhibition of cyclic AMP (**cAMP**) production (Harvey and Ferrier, 2011). If cAMP concentrations fail to rise, protein kinase A will not be able to phosphorylate hormone sensitive lipase into its active form. If hormone sensitive lipase is inactive, it is unable to break down triglycerides in adipose tissue (Harvey and Ferrier, 2011), thus reducing the release of nonesterified fatty acids (**NEFA**) into the blood (Neihoff et al., 2009a; Kang et al., 2011; Morey et al., 2011).

Tissue requirements for NA in dairy cattle have not been determined experimentally (Neihoff et al., 2009a). In addition to NA supplied from feed, many mammals are able to synthesize NA from tryptophan or quinolinic acid, although dairy cattle are relatively inefficient at this conversion (Frye et al., 1991; Flachowsky, 1993). Microbial synthesis serves as another source of NA. Ruminal production of NA in a 650-kg cow producing 35 kg/d of 4% FCM was estimated to be 1,804 mg/d (NRC, 2001). However, it is speculated that ruminal bacteria do not synthesize more NA than is required for their own growth and function because de novo syn-

thesis of the vitamin is an energy-demanding process (Hannah and Stern, 1985; Abdouli and Schaefer, 1986; Doreau and Ottou, 1996).

A major drawback of NA supplementation in humans has been an unpleasant flushing response. Tunaru et al. (2003) and Benyó et al. (2006) found that the GPR109A receptor is also involved in a cutaneous vasodilation response. The GPR109A receptor is expressed in Langerhans cells, immune cells that densely populate the skin. Activation of the GPR109A receptor causes a classic response from these immune cells: activation of a G $\beta\gamma$ -mediated phospholipase C receptor (Benyó et al., 2006). Activation of this receptor causes a conformational change in membrane-embedded Ca²⁺ channels, leading to a temporary increase in Ca²⁺ concentrations in the cytoplasm. This increase in concentration activates the enzyme Ca-dependent phospholipase A₂. This enzyme catalyzes hydrolysis of phospholipids from membranes and lipoproteins, yielding arachidonic acid, a precursor of eicosanoids, such as prostaglandins. Prostaglandin E₂ and prostaglandin D₂ are released from the Langerhans cells and cause vasodilation in the skin (Benyó et al., 2005, 2006). Supplemental NA in the prepartum period could increase blood flow during colostrogenesis, resulting in a higher concentration of IgG in colostrum.

The objectives of this experiment were (1) to determine if supplementing NA during the prepartum period affects colostrum quality, DMI, or blood metabolites of the dam, and (2) to determine if NA supplementation to the dam affects IgG absorption in the calf via in utero effects. Our hypothesis was that supplemental NA during the prepartum period would increase colostrum IgG concentration and decrease serum NEFA and BHB concentrations in the dam.

MATERIALS AND METHODS

Experimental Design and Animal Management

This experiment was reviewed and approved by the University of New Hampshire Institutional Animal Care and Use Committee (Protocol #131103).

Twenty-six multiparous Holstein cows were blocked by expected calving date and randomly assigned to 1 of 2 treatments: (1) 0 g/d NA (control, **CON**) or (2) 48 g/d NA (NA), both with 52 g/d of corn meal as a carrier. Treatments were top dressed at each feeding, beginning 4 wk prepartum, and continued until calving. Cows were housed in a tiestall barn, and stalls had mattresses bedded with kiln-dried sawdust. Cows had access to water at all times via automated water bowls (DeLaval, Tumba, Sweden). Each cow had an individual wooden feed tub (90 × 90 × 90 cm) to allow

for measurements of daily feed intake. As cows neared calving, they were moved into individual maternity pens.

Colostrum Collection and Analysis

Cows that experienced difficulty calving were not used for this study. Within 90 min of calving, colostrum was collected from dams and weighed, and 2 aliquots were taken. One aliquot was sent to Dairy One Laboratory (Ithaca, NY) for analysis of fat (method 989.05), protein (method 991.20), and solids (method 990.20) percentages according to AOAC International methods (AOAC International, 2006). The second aliquot was frozen at -20°C until further analysis of IgG content by radial immunodiffusion (**RID**) assay (Triple J Farms, Bellingham, WA).

Cow Measurements

All cows were weighed (Cardinal, Northeast Scale Co. Inc., Hooksett, NH) before starting treatments, and every Monday thereafter until calving. Blood samples were collected from each cow before administration of treatments. Once cows were assigned to treatments, blood samples were collected every Monday, Wednesday, and Friday at 1130 h (3.5 h after feeding) via coccygeal vein or artery into 10-mL tubes (BD Vacutainer, Becton Dickinson, Franklin Lakes, NJ) containing sodium heparin. Blood samples were collected at calving and 24 h and 7 d postpartum. Samples were placed on ice until they were centrifuged at $1,278 \times g$ at 4°C for 20 min (5430R, Eppendorf, Hamburg, Germany). Serum was aspirated and stored at -20°C until further analysis for glucose, NEFA, and BHB. Serum glucose concentrations were measured in duplicate using Wako Autokit for Glucose (Wako Diagnostics, Mountain View, CA). Concentrations were read on a DU 520 spectrophotometer according to manufacturer's instructions (Beckman Coulter, Brea, CA). Serum NEFA concentrations were measured in triplicate using the Wako NEFA-HR (2) kit (Wako Diagnostics). Serum BHB concentrations were measured in triplicate using the β -hydroxybutyrate Colorimetric Assay Kit from Cayman Chemical (Ann Arbor, MI). Both serum NEFA and BHB concentrations were read using a plate reader (Chromate, Awareness Technology Inc., Palm City, FL) according to the manufacturer's instructions. Urine samples were also collected Monday, Wednesday, and Friday just before blood sampling until calving, and pH was analyzed using a portable pH probe (VWR Symphony, Thermo Scientific, Radnor, PA).

Calf Care and Blood Collection for IgG Assay and Apparent Efficiency of Absorption

Calves were removed within 30 min of birth and before nursing. Calves were weighed (A and A Scales, Prospect Park, NJ), placed into an individual pen in a naturally ventilated, enclosed calf room, and navels were dipped in 7% iodine. Pens had a mattress topped with kiln-dried sawdust. Calves remained on study until 24 h of age.

Calves were fed 3 L of a lacteal-based colostrum replacer that provided a total of 225.8 g of IgG (Saskatoon Colostrum Co. Ltd., Saskatoon, SK, Canada) within 2 h of birth. To determine whether NA supplementation to the dam had any effects on the calf in utero, calves were not fed maternal colostrum. If calves did not immediately consume the colostrum replacer, it was kept warm and reintroduced 1 h later. If the remaining colostrum replacer was still refused, it was fed via esophageal tube.

Blood samples were collected into 10-mL tubes (BD Vacutainer) containing sodium heparin via jugular venipuncture at 0 and 24 h of age. Samples were placed on ice and centrifuged at $1,278 \times g$ at 4°C for 20 min (5430R, Eppendorf). Serum was harvested and stored at -20°C until further analysis for IgG concentration by RID (Triple J Farms).

Apparent efficiency of absorption (**AEA**) at 24 h of age was estimated using the following equation according to Quigley et al. (1998) and adjusted for colostrum replacer according to Cabral et al. (2015):

$$\frac{[(24\text{-h plasma IgG (g/L)} \times \text{BW (kg)} \times 0.0825)]}{\text{IgG intake (g/L)}} \times 100.$$

Feed Analysis

All feed ingredients were analyzed at Analab (Fulton, IL) before the start of the experiment for ADF (method 973.18), NDF (method 2002.04), CP (method 990.03), starch (glucose was extracted from starch and analyzed by enzymatic methods from Trinder, 1969a,b), crude fat (method 920.39), ash (method 942.05), Ca, P, Mg, and K (method 98.01), and S (method 923.01) according to AOAC International methods (AOAC International, 1999). Diets were adjusted as needed based on DM of ingredients and nutrient analysis.

Total mixed ration amounts fed and refused were measured daily at 0800 h to determine DMI. Samples of TMR and orts were collected daily and frozen for later analysis. Frozen samples were thawed and dried in a forced hot-air convection oven at 55°C for 48 h to

determine DM (Binder, Bohemia, NY). Ort samples were composited weekly by cow, and TMR samples were composited monthly by cow. Samples were ground through a 1-mm screen using a Wiley mill (Thomas Scientific, Swedesboro, NJ). Samples were sent to Analab for analysis of ADF, NDF, CP, starch, fat, ash, Na, P, K, Mg, Ca, Mn, Fe, Cu, Zn, S, and Cl, as previously described.

Statistical Analysis

Serum glucose, NEFA, and BHB, DMI, and cow BW data were analyzed as a randomized complete block design with repeated measures using the MIXED procedure of SAS 9.4 (SAS Institute Inc., Cary, NC) according to the following model:

$$Y_{ijkl} = \mu + B_i + N_j + W_k + L_l + \beta X_{ij} + NW_{jk} + e_{ijkl},$$

where Y_{ijkl} = the dependent variable; μ = the overall mean; B_i = the random effect of block i ($i = 1, \dots, 13$); N_j = the fixed effect of the j th nicotinic acid level ($j = 0, 48$); W_k = the fixed effect of the k th week relative to calving ($k = -4, \dots, 1$); L_l = the fixed effect of the l th lactation ($l = 2, 3, 4, 7, 8$); β = the regression (covariate coefficient); X_{ij} = the covariate measurement; NW_{jk} = the fixed interaction between the j th niacin level and the k th week; and e_{ijkl} = the residual error $\sim N(0, \sigma_e^2)$.

In this model, the random effect of cow within block subclass was used as the error term for the effect of treatment. The residual errors are errors within cow across time and represent errors from repeated measurements in the experimental units (cows). All variables, except BW, were modeled using a first-order autoregressive covariance spatial structure. First-order autoregressive resulted in the smallest Bayesian information criteria of the 4 covariate structures tested: compound symmetry, unstructured, Toeplitz, and first autoregressive. Cow BW was modeled using compound symmetry covariance spatial structure as it resulted in the smallest Bayesian information criterion. Degrees of freedom were calculated using the Kenward-Roger approximation option of the MIXED procedure. Covariate P -values for NEFA, DMI, and milk production were >0.25 ; therefore, they were removed from the models.

Urine pH data were transformed into H^+ ion concentration (Murphy, 1982) and analyzed in a randomized complete block design using the GLM procedure of SAS 9.4 (SAS Institute Inc.) according to the following model:

$$Y_{ijk} = \mu + B_i + N_j + W_k + NW_{jk} + e_{ijk},$$

where Y_{ijk} = the dependent variable; μ = the overall mean; B_i = the random effect of block i ($i = 1, \dots, 13$); N_j = the fixed effect of the j th nicotinic acid level ($j = 0, 48$); W_k = the fixed effect of the k th week relative to calving ($k = -4, \dots, 1$); NW_{jk} = the fixed interaction between the j th niacin level and the k th week; and e_{ijk} = the residual error $\sim N(0, \sigma_e^2)$.

Colostrum IgG concentration and yield, colostrum volume, and protein, fat, and solids percentage data were analyzed as a randomized complete block design using the MIXED procedure of SAS 9.4 (SAS Institute Inc.) according to the following model:

$$Y_{ij} = \mu + B_i + N_j + \beta X_{ij} + e_{ij},$$

where Y_{ij} = the dependent variable; μ = the overall mean; B_i = the random effect of block i ($i = 1, \dots, 13$); N_j = the fixed effect of the j th nicotinic acid level ($j = 0, 48$); β = the regression (covariate coefficient); X_{ij} = the covariate measurement; and e_{ij} = the residual error $\sim N(0, \sigma_e^2)$. In this model, the random effect of cow within block subclass was used as the error term for the effect of treatment. Degrees of freedom were calculated using the Kenward-Roger approximation option of the MIXED procedure.

Calf BW, 0-h and 24-h IgG concentrations, and AEA data were analyzed as a randomized complete block design using the MIXED procedure of SAS 9.4 (SAS Institute Inc.) according to the following model:

$$Y_{ij} = \mu + B_i + N_j + e_{ij},$$

where Y_{ij} = the dependent variable; μ = the overall mean; B_i = the random effect of block i ($i = 1, \dots, 13$); N_j = the fixed effect of the j th nicotinic acid level ($j = 0, 48$); and e_{ij} = the residual error $\sim N(0, \sigma_e^2)$. In this model, the random effect of calf within treatment subclass was used as the error term for effect of treatment. Degrees of freedom were calculated using the Kenward-Roger approximation option of the MIXED procedure.

For all variables, significant treatment and interaction effects were noted at $P \leq 0.05$ and trends were noted at $0.05 < P \leq 0.1$.

RESULTS

Diet Composition

Diet composition and nutrient analysis of the TMR is presented in Table 1. The diet was formulated to meet or exceed the nutrient requirements for prepartum dairy cows (NRC, 2001). Acid detergent fiber analysis

Table 1. Ingredient and chemical composition (% of DM unless otherwise noted; $\pm$ SD) of the prepartum diet

Item	Value
Dietary ingredient	
Corn silage	37.4
Grass haylage	30.0
RUP mix (Provaal Elite) ¹	2.1
Dry cow mix ²	30.4
Nutrient content	
CP	27.4 $\pm$ 1.8
ADF	40.6 $\pm$ 2.7
NDF	14.0 $\pm$ 1.3
NFC	35.6 $\pm$ 3.2
Starch	17.1 $\pm$ 2.4
Fat	2.7 $\pm$ 0.2
Lignin	3.6 $\pm$ 0.2
Ash	8.8 $\pm$ 0.5
Na	0.2 $\pm$ 0.04
Mg	0.6 $\pm$ 0.04
P	0.3 $\pm$ 0.02
S	0.4 $\pm$ 0.05
K	1.6 $\pm$ 0.1
Ca	0.7 $\pm$ 0.2
Cl	0.8 $\pm$ 0.1
Mn (mg/kg)	81.6 $\pm$ 5.3
Fe (mg/kg)	282.7 $\pm$ 62.1
Cu (mg/kg)	15.8 $\pm$ 2.1
Zn (mg/kg)	89.9 $\pm$ 6.3

¹RUP mix (Provaal Elite, Perdue, Kings Mountain, NC) contained 93% CP, 1.1% fat, 1.3% ash, 0.2% Ca, 0.1% P, 0.2% Mg, 0.3% Cl, 0.2% K, 0.2% Na, 1.4% S, 8.9 mg/kg Cu, 2,315 mg/kg Fe, 8.7 mg/kg Mn, 0.2 mg/kg Se, 35 mg/kg Zn, and 4.8% Arg, 5.4% His, 1.2% Ile, 12.6% Leu, 8.8% Lys, 3.9% Met, 6.8% Phe, 3.4% Thr, 1.2% Trp and 6.3% Val (% as CP).

²Dry cow mix (Poulin Grain, VT) contained 19.8% CP, 13.8% ADF, 21.6% NDF, 34.8% NFC, 7.2% RUP, 15.9% starch, 7.6% sugar, 2.5% fat, 1.9% Ca, 0.3% P, 1.2% Mg, 1.1% K, 0.9% S, 1 mg/kg Se, 0.6% Na, 1.6% Cl, 444.8 IU/kg of vitamin E.

of ort samples was 27.8 ± 1.9 for CON and 27.9 ± 2.1 for NA. Neutral detergent fiber analysis of ort samples was 43.1 ± 3.0 for CON and 42.1 ± 2.2 for NA. Crude protein analysis of ort samples was 13.5 ± 1.0 for CON and 14.1 ± 1.6 for NA. These data indicate that this NA dosage did not result in sorting of the TMR.

Cow Measurements

Average days on study were 28.9 ± 4.7 for CON and 25.8 ± 4.5 for NA. Initial BW of all cows were similar: 798.3 ± 5.8 kg for CON and 791.5 ± 6.1 kg for NA. Initial serum concentrations of BHB, glucose, and NEFA were similar: 0.49 ± 0.02 mmol/L for CON and 0.45 ± 0.02 mmol/L for NA; 60.9 ± 2.3 mg/dL for CON and 64.3 ± 2.3 mg/dL for NA; 122.3 ± 76.1 μ Eq/L for CON and 139.7 ± 75.6 μ Eq/L for NA, respectively.

Treatment for ketosis was administered to 4 CON cows and 2 NA cows. Treatment for udder edema was administered to 1 CON cow and 1 NA cow. One NA cow was diagnosed and treated for milk fever. Retained placenta occurred in 2 CON cows and 1 NA cow. These metabolic disorders occurred independently of one another to individual cows.

Nicotinic acid did not affect DMI or urine pH (Table 2). Week effects were noted for serum glucose and BHB concentrations (Table 2). We detected a week effect for serum BHB concentrations due to elevated levels 1 wk postpartum (Table 2), and a treatment by week effect for serum NEFA concentrations at 1 wk postpartum. Cows that received supplemental NA in the prepartum period had higher serum NEFA concentrations than CON cows ($P = 0.003$, Table 2, Figure 1), indicating a NEFA rebound.

Supplemental NA increased colostral IgG concentration from 73.8 to 86.8 g/L ($P = 0.01$, Table 3). Nicotinic acid had no effect on colostrum yield, IgG yield, or fat and solids percentage (Table 3). Nicotinic acid tended to increase protein percentage of colostrum ($P = 0.09$, Table 3).

Calf Measurements

One CON cow had twins and 2 NA cows had twins. Mean initial IgG concentration was 0.41 and 0.72 g/L

Table 2. Cow DMI, BW, urine pH and blood metabolites in prepartum cows fed either 0 or 48 g/d of nicotinic acid

Item	Treatment (Trt) ¹		SEM	P-value		
	CON	NA		Trt	Week	Trt $\times$ Week
DMI, kg/d	16.0	14.6	0.6	0.15	<0.001	—
BW, kg	812.0	809.3	4.7	0.69	<0.001	—
Urine pH ²	6.9	7.1	4.17×10^{-8}	0.51	0.43	—
Glucose, mg/dL	69.5	70.6	0.99	0.40	<0.001	—
NEFA, ³ μ Eq/L	305.9	378.2	72.3	<0.001	<0.001	0.003
BHB, mmol/L	0.50	0.43	0.02	0.23	<0.001	—

¹Treatments: CON = control, basal TMR with 0 g/d of nicotinic acid; NA = nicotinic acid, basal TMR with 48 g/d of nicotinic acid.

²Urine pH standard error in H⁺ concentration.

³Nonesterified fatty acids.

Table 3. Colostrum composition data of cows fed either 0 or 48 g/d of nicotinic acid

Item	Treatment ¹		SEM	<i>P</i> -value
	CON	NA		
Colostrum yield, L	10.6	9.5	0.6	0.19
Protein, %	14.7	17.9	1.3	0.09
Fat, %	5.5	4.7	0.8	0.45
Solids, %	23.9	22.9	1.9	0.70
IgG yield, g	749	773.8	81.6	0.80
IgG, g/L	73.8	86.8	3.1	0.01

¹Treatments: CON = control, basal TMR with 0 g/d of nicotinic acid; NA = nicotinic acid, basal TMR with 48 g/d of nicotinic acid.

for calves of CON and NA cows, respectively. One of the 29 calves on study had failure of passive transfer; the 24-h IgG concentration was 7.8 g/L. This calf was a twin born from a NA cow, and her twin obtained passive transfer with a serum IgG concentration of 14.1 g/L at 24 h. The calf with failure of passive transfer was >2.5 standard deviations from the mean, deemed an outlier, and therefore removed from the statistical analyses. In total, 14 calves born from CON cows and 14 calves born from NA cows were used. Nicotinic acid supplementation of dams did not affect 0- and 24-h serum IgG concentration, AEA, or calf BW (Table 4).

DISCUSSION

The hypothesis of this experiment was that supplemental NA in the prepartum diet would increase colostrum

Table 4. Calf BW, 0- and 24-h serum IgG concentration and apparent efficiency of absorption (AEA) data of calves born of cows fed either 0 or 48 g/d of nicotinic acid

Item	Treatment ¹		SEM	<i>P</i> -value
	CON	NA		
Calf BW, kg	46.0	44.8	1.3	0.51
0-h IgG, g/L	0.4	0.7	0.3	0.49
24-h IgG, g/L	15.9	16.1	0.6	0.75
AEA, %	26.4	25.9	1.0	0.71

¹Treatments: CON = control, basal TMR with 0 g/d of nicotinic acid; NA = nicotinic acid; basal TMR with 48 g/d of nicotinic acid.

²AEA = [(24-h plasma IgG (g/L) × BW (kg) × 0.0825)/IgG intake (g/L)] × 100; Quigley and Drewry (1998), as modified by Cabral et al. (2015).

trum quality and decrease lipolysis, potentially leading to a decrease in metabolic disorders around calving. The effects of NA on the factors measured varied and agreed with our hypotheses in some cases.

Dry matter intake was not affected by NA. No effect on DMI was reported when feeding 12 g/d NA to late-lactation dairy cows (Erickson et al., 1990, 1992; Campbell et al., 1994). In contrast, a 3.6% increase in DMI was observed when feeding 12 g/d NA (Di Costanzo et al., 1997).

Cow BW was not affected by NA supplementation, but we noted an effect of week. Average BW increased until 2 wk prepartum. Fetal growth is greatest during the last trimester (Bell, 1995), which most likely contributed to the increase in BW of the dam.

Nicotinic acid supplementation to the dam did not affect any of the calf parameters measured, including 0- and 24-h serum IgG concentration, AEA, and calf BW. Previous research has found that IgG absorption is reduced in calves fed maternal colostrum from protein- or feed-restricted dams (Burton et al., 1984; Hough et al., 1990). However, in this study, to determine if NA supplementation to the dam had any effects on the calf in utero, calves were fed a commercial colostrum replacer, rather than maternal colostrum. Based on our results, NA supplementation to the dam did not affect IgG absorptive capacity or efficiency in the calf.

Urine pH was not affected by NA (Table 2). Normal pH of urine is around 8.2 when dairy cows are fed high-cation diets during lactation. Anionic salts are fed prepartum to prevent postpartum hypocalcemia by increasing mobilization of calcium from the bone (Riond, 2001). When administered properly, anionic diets should decrease urine pH to a range of 6.2 to 6.8 (Riond, 2001). Although urine pH was higher than the suggested range, we observed minimal incidence of metabolic disorders around calving. Ketosis treatment was administered to 4 CON and 2 NA cows, and milk fever treatment was administered to 1 NA cow.

Figure 1. Weekly serum nonesterified fatty acid (NEFA) concentration for cows fed either 0 (CON) or 48 (NA) g/d of nicotinic acid. *Treatment × week interaction (*P* = 0.003).

Serum glucose concentrations were not affected by NA, but we noted an effect of week (Table 2). Supplementation of NA did not affect glucose concentrations with NA supplementation in some cases (Erickson et al., 1990; Zimmerman et al., 1992; Yuan et al., 2012). However, increased serum glucose concentrations were observed with 14 g/d NA (Karkoodi and Tamizrad, 2009) and 6 g/d NA (Aschemann et al., 2012). Several studies corroborated this result (El-Barody et al., 2001; Neihoff et al., 2009b; Pescara et al., 2010). It is not known whether the effect of increased glucose concentration in the blood with NA supplementation is due to increased gluconeogenesis due to greater availability of coenzymes (NAD and NADP) and propionate, decreased extra-hepatic removal of glucose, or endocrine changes promoted by inhibiting lipolysis (Zimmerman et al., 1992; Di Costanzo et al., 1997; El-Barody et al., 2001).

Prepartum serum NEFA concentrations were not affected by NA supplementation (Table 2). During the prepartum period, DMI is typically reduced and this is accompanied by an increase in energy demand for colostrum and milk production. This results in a negative energy balance state, causing mobilization of adipose tissue and subsequent increase in serum NEFA. Supplemental NA has been shown to reduce lipolysis in some studies (Fronk and Schultz, 1979; Erickson et al., 1990; Pires et al., 2007), but not in others (Erickson et al., 1992; Drackley et al., 1998; Neihoff et al., 2009b). We detected a treatment by week interaction for postpartum serum NEFA concentrations (Table 2). At 1 wk postpartum, cows that were supplemented with NA prepartum had greater serum NEFA concentrations than CON cows (Figure 1), indicating that lipolysis was not reduced by NA. This result is the classic rebound effect that has previously been observed when NA was supplemented to dry cows (Waterman et al., 1972). The rebound effect was observed by Oh et al. (2011), where continuous infusion of NA in rats decreased NEFA, but once administration ceased, levels rebounded to more than twice the preinfusion levels. Those authors found that NA altered gene expression of phosphodiesterase, an enzyme responsible for degrading cAMP in adipocytes. Decreased expression of phosphodiesterase may have led to the sudden increase in lipolysis. In the current study, ceasing supplementation of NA at calving most likely exacerbated lipolysis, causing the increase, or rebound, of NEFA concentrations. This rebound is avoided when NA supplementation continues through positive energy balance (Morey et al., 2011).

Serum concentrations of BHB were not affected by NA supplementation; however, we noted an effect of week (Table 2). The threshold for subclinical ketosis

is 1.4 mmol of BHB/L (Berge and Vertenten, 2014). Concentrations in the current study were below this threshold, indicating that cows were not in severe negative energy balance at 1 wk postpartum. Elevated serum BHB concentrations around parturition are common due to the increase in energy demand that cannot be met by diet alone. In an attempt to meet energy needs, cows will mobilize adipose tissue. When adipose tissue is mobilized too quickly, the liver is overloaded with NEFA. β -Oxidation in the liver is unable to keep up, causing an increase in ketone production (Harvey and Ferrier, 2011). For this reason, changes in levels of BHB typically follow closely behind changes in NEFA concentrations, which was observed in this study. β -Hydroxybutyrate is also an agonist for the GPR109A receptor, indicating that a negative feedback mechanism exists where high levels of BHB could reduce lipolysis (Taggart et al., 2005).

Yield of colostrum and fat percentage of colostrum were not affected by treatment (Table 3). These results are in agreement with previous work, where NA did not affect yield or fat percentage of milk (Campbell et al., 1994; Di Costanzo et al., 1997; Nielsen and Ingvarsen, 2003; Morey et al., 2011). However, other work did observe an increase in milk fat percentage with NA supplementation (Belibaskakis and Tsirgogianni, 1996). Although colostral lactose was not measured in this study, NA has not been shown to increase lactose content in milk. Solids percentage of colostrum was not affected by NA, which is in agreement with other work (Belibaskakis and Tsirgogianni, 1996; Morey et al., 2011). Yield of IgG was also not affected by NA treatment.

Colostrum protein percentage of cows supplemented with NA tended to be higher ($P = 0.09$; Table 3), which may be due to an increase in IgG concentration or to an increase in microbial protein production. Riddell et al. (1981) found a slight increase in milk protein percentage when cows were supplemented with NA in mid lactation, which the authors attributed to the greater microbial protein synthesis. Similar results were observed in early- and mid-lactation cows supplemented with NA (Erickson et al., 1992; Karkoodi and Tamizrad, 2009). Nicotinic acid supplementation may spare tryptophan, allowing more to be incorporated into milk protein (Flachowsky, 1993). However, several studies have reported no effect on milk protein with NA supplementation (Riddell et al., 1981; Dufva et al., 1983; Erickson et al., 1990).

Supplementation of NA increased colostral IgG concentration from 73.8 to 86.8 g/L ($P = 0.01$). Immunoglobulin G concentration may have been improved in 1 of 2 ways: (1) NA supplementation has been shown to

cause vasodilation through activation of the GPR109A receptor, as previously described (Tunaru et al., 2003; Benyó et al., 2006). Therefore, by supplementing NA during colostrogenesis, blood flow to the mammary gland may have been increased, thus more IgG would be transferred into colostrum; or (2) NA supplementation has been shown to increase protozoa numbers in the rumen, specifically *Entodinia* species (Erickson et al., 1990; Doreau and Ottou, 1996; Aschemann et al., 2012). *Entodinia* species engulf starch particles, which results in a slow release of acetic acid that maintains ruminal pH (Williams and Coleman, 1992; Dehority, 2003). Stable rumen pH enhances proliferation of bacteria and therefore may increase microbial protein reaching the small intestine of the dam. Microbial protein synthesized in the rumen provides the majority of absorbable amino acids to the small intestine in the cow (Fatahnia et al., 2012). Therefore, an increase in amino acids could lead to an increase in IgG production.

Failure of passive transfer has been associated with increased risk of morbidity and mortality, increased veterinary costs, decreased growth rates, decreased milk production in the first and second lactations, and increased risk of being culled from the herd (Robison et al., 1988; DeNise et al., 1989). In the United States, 20% of calves do not achieve successful passive transfer (NAHMS, 2007) and >60% of colostrum in the United States fails to meet industry standards (Morrill et al., 2012). Clearly, improvements can and need to be made in this area. Proper health, growth, and development in early life are critical to subsequent growth, development, and production of dairy heifers. A diseased calf cannot utilize ingested nutrients exclusively for growth and development; nutrients must be allocated to fight and repair any damages from pathogens. By improving colostrum quality and calf immunity, healthier heifers can be raised to become more successful and profitable dairy cows.

CONCLUSIONS

Supplemental NA in the prepartum period increased colostral IgG concentration by 18%. Dry matter intake, urine pH, colostrum yield, yield of IgG, and colostrum fat and solids percentage were not affected by NA. Serum glucose and BHB concentrations were not affected by NA. Prepartum serum NEFA concentrations were not affected by NA, indicating that lipolysis was not reduced. However, serum NEFA concentrations increased dramatically 1 wk postpartum in cows that received NA during the prepartum period, indicating that ceasing NA supplementation at calving caused a rebound effect. Calf BW, 0- and 24-h IgG concentration, and

AEA were not affected by NA supplementation in the dam. More research is necessary to elucidate possible mechanisms for the increase in colostral IgG concentration, such as microbial protein production and blood flow. These results suggest that dairy producers should feed NA to prepartum cows to improve colostrum quality.

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