ABSTRACT OF THE THESIS OF

Jason Chamberlain for the degree of Master of Science in Animal Sciences presented on June 1, 2006.
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Abstract approved:

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An experiment was conducted with 27 multiparous Holstein and 27 multiparous Jersey cows to determine if nicotinic acid (NA) supplementation during the prepartum phase of the transition period decreases lipolysis and improves dry matter intake and to determine if Holstein and Jersey cows respond similarly to NA supplementation. Cows were blocked by expected calving date and assigned at random to one of three prepartum dietary treatments which were 0, 49, and 98 mg of NA/kg of body weight (BW). Cows were group housed in freestalls and fed individually via Calan® gates from 30 d prepartum to 21 d postpartum. Cows were offered a dry cow total mixed ration twice daily and NA was hand mixed in the morning feeding. Following parturition all cows received the same lactation total mixed ration. Data were analyzed as repeated measures using the MIXED procedure of SAS. Dry matter intake -3 wk prepartum was used as a covariate for analysis of prepartum dry matter intake. Prepartum and postpartum BW and body condition score (BCS) were similar for NA treatments. Body weight was greater for Holsteins compared to Jerseys; however BCS between breeds did not differ. Prepartum DMI was similar for NA treatments, but cows supplemented with 49 mg NA/kg BW had greater DMI following parturition. Prepartum DMI depression was greater for Holsteins compared with Jerseys, 32 and 14%, respectively. Prepartum NA treatment had no effect on prepartum or postpartum nonesterfied fatty acids (NEFA), β-hydroxybutyrate, and glucose. The magnitude of increase of NEFA as parturition approached was greater for Holsteins compared with Jerseys. Further, plasma NEFA of Jersey cows were lower than Holstein cows during the postpartum period (613 vs 862 µEq/L for Jerseys and Holsteins). Milk production

differed between NA treatments, with increased production from cows supplemented with 49 mg NA/kg body BW compared to other treatments. Milk composition was not affected by the supplementation of NA. In summary, supplemental NA during the last 3 wk of gestation did not affect DMI or plasma metabolites during the transition period. Lipid metabolism and prepartum feed intake depression does differ for the two major breeds of dairy cattle.

Key Words: dairy breed, transition cow, nicotinic acid

The Effects of Nicotinic Acid Supplementation During Late-gestation on Lipolysis
and Feed Intake During the Transition Period.

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Jason Chamberlain, Author

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CONTRIBUTION OF AUTHORS

Dr. Patrick French assisted in the statistical analysis, interpretation of data, and writing presented in "The effects of nicotinic acid supplementation during late-gestation on lipolysis and feed intake during the transition period."

TABLE OF CONTENTS

List of Figures

List of Tables

The effects of nicotinic acid supplementation during late-gestation on lipolysis and feed intake during the transition period.

Literature Review

Introduction

The transition period for the dairy cow is a very complex time. The metabolic status of the transition period cow is continually changing and results in high levels of stress for the cow. Ketosis, fatty liver, milk fever, displaced abomasums, negative energy balances, ration changes, and high energy demands are all potential challenges that could arise during the transition period. The transition period is three weeks prior to parturition to three weeks after parturition. Proper nutrition can be a very effective way of prevention or minimizing the effects of all of the previous mentioned challenges. While most of these challenges occur at or after the act of calving, the proper nutrition prior to parturition is just as vital if not more vital than the nutrition after the act of calving. For example milk fever prevention can occur with proper cation-anion balances during the dry period. Ketosis and fatty liver are both causes of excessive fat mobilization of the body reserves; quite often as the result of excessive body reserves build up during late lactation or dry period. With the proper nutrition during late lactation and the dry period the excessive build up of body reserves can be prevented; in addition, through proper nutrition prior to calving and during early lactation the excessive mobilization of fat can be prevented and mobilization can occur in a controlled manner. Genetic selection has had a major impact on the disorders and diseases that occur at parturition including fatty liver and ketosis. The selection of cows that will go through the act of parturition and then perform at high levels has impacted the importance of controlling metabolic disorders during this period. Naturally we have selected not the cows that have the least amount of

problems during this period, but the cows that performed at the highest level during this period.

Dry Matter Intake

Arguably the most important barrier to maximize high production is maintaining dry matter intake (DMI) during the transition period. For over three decades it has been known that DMI declines during the period leading up to parturition. Marquardt et al. (1977) observed DMI decreases of 25% during the last three weeks of gestation. In addition, 52% of the 25% decline in DMI occurred during the final 14 days of gestation. According to the NRC (2001) DMI decreases 32% during the last three weeks of gestation. The importance of dry matter decline becomes relevant when postpartum dry matter intake is considered. Grummer et al. (2004) found that when cows are fed ad libitum, there is a positive relationship between prepartum and postpartum dry matter intake. Declining dry matter may cause cows to enter into a negative energy balance which is compensated naturally by lipolysis of the adipose tissue. Heifers are more likely to experience a negative energy balance prior to parturition than mature cows; however, cows may enter a negative energy balance prior to calving if DMI decreases to level that are inadequate to supply needed energy (Grummer et al., 2004). Increased dry matter intake during early lactation results in a less severe negative energy balance; leading to decreased fat mobilization. The latter results in a return to positive energy balance sooner in lactation. Excessive fat deposits in the liver caused by increased lipolysis have been shown to increase days to first ovulation (Rukkwamsuk et al, 1999) and to decrease pregnancy rates (Jorritsma et al., 2000).

The relationship between feed intake and non-esterfied fatty acids (NEFA) is of great interest during the transition period; NEFA along with propionate are the main metabolic sources of fuel utilized by the ruminant liver (Oba et al., 2003). As parturition nears energy demands increase. To meet these increasing energy demands lipolysis rates are stepped up, resulting in an inflation of NEFA levels. The increase in NEFA levels could be one of the main contributing factors causing decreased DMI. Controlling NEFA levels during the transition period should allow for greater DMI to be maintained allowing cows to meet increased energy demands from the production of propionate and other volatile fatty acids. Dyke (1995) found that higher prepartum plasma NEFA concentrations were associated with greater incidences of dystocia, retained placenta, ketosis, displaced abomasums, and mastitis, but not hypocalcemia. Bareille and Faverdin (1996) reported increased plasma NEFA concentration and a decrease in dry matter intake occurred when cows were infused with a synthetic triglyceride emulsion while in a lipogenic state. Cows in a lipolytic state infused with the same triglyceride also had elevated NEFA levels but DMI remained constant. In both cases following infusion of triglycerides NEFA and DMI returned to normal levels by the following day. A second group of Cows were also infused with Clenbuterol a β_2-adrenergic agonist during either a lipolytic or lipogenic state. Cows in both lipolytic and lipogenic states had elevated NEFA and depressed DMI during the infusion. A negative correlation has been seen at Oregon State University between increased NEFA levels and decreased DMI (French, 2002). Perhaps more importantly than DMI is the total amount of energy consumed. Volatile fatty acids were intraruminally infused at a constant rate for 14 hours in mid-lactation dairy cows; with

propionate increasing in concentration by treatment. DMI was measured and then total metabolizible energy intake was calculated. As propionate infusion concentrations increased DMI decreased linearly (P<.01); also total energy intake decreased linearly (P<.05) (Oba and Allen., 2003). A second study was conducted by Oba and Allen (2003) with greater infusion rates; in the second study they found similar results with both DMI and total metabolizible energy intake decreasing linearly. Altered feeding behavior was seen with both experiments. The first experiment saw a tendency for longer intermeal meal intervals and decreased meal size as propionate levels increased. The second experiment saw a significant decrease meal size and significantly fewer minutes actually eating. While this experiment was to measure the effect of the production of propionate on highly fermentable diets, and found that propionate can have a negative effect if over production occurs, one could easily argue that since VFA are readily passed across the rumen wall that an increase in any type of fatty acid in the blood may have the same effect as over production of propionate. Since propionate and NEFA levels are the main metabolic fuels used by the liver and overload of NEFA in the system could have the same effect of over production of propionate by the rumen.

Nutritional management during the dry period affects susceptibility of cows to metabolic disorders and infectious diseases during the periparturient period (Grummer, 1995; Drackley, 1999). In a study to try to quantify the later statement Dann et al. (2005) used restricted feeding during the dry period in hope to induce metabolic disorders at calving. Interestingly enough while numbers (n=35) were small there was no difference in the occurrence of metabolic disorders for ad libitum versus restricted

fed cows. What they did find was that during the 7 days prior to calving DMI for ad libitum decreased by 31 percent while DMI only decreased 7 percent for restricted fed cows all of which occurred 1 day prior to calving. Furthermore, serum NEFA concentrations increased by 193% during the final 7 days of gestation for ad libitum fed cows and only 42% for restricted fed cows. In addition, at 1 day following calving ad libitum cows had more lipid accumulation in the liver than did restricted fed cows. The later results support that higher prepartum plasma NEFA concentrations leads to increased up-take of NEFA and increased triacylglycerol accumulation in the liver. Increased total lipid triacylglycerol concentrations in liver of periparturient cows have been linked to greater risk for health problems (Bobe et al., 2004).

Metabolic Disorders

Metabolic disorder occurrence during early lactation is greater than any other point in lactation. While a wide variety of metabolic disorders occur during this time; lipid related disorders can be the most detrimental. Lipid related disorders such as ketosis and fatty liver usually occur for one of the following conditions: 1) Fatty liver occurs when the rate of triglyceride synthesis exceeds the rate of triglyceride hydrolysis plus triglyceride export as very low density lipoproteins (VLDL) (Grummer, 1993), 2) primary underfeeding ketosis because the cow is not offered enough "acceptable" feed; secondary underfeeding ketosis occurs because the cow's feed intake has been reduced as a result of another disease (Kronfeld, 1982). Two other types of ketosis as described by Kronfeld (1982) are alimentary ketosis and spontaneous ketosis. Alimentary ketosis results because intakes of fermented feeds containing ketogenic precursors such as butyrate are high; Spontaneous ketosis refers to a condition under which a cow has

elevated blood ketone bodies even though the diet appears to be nutritionally adequate. Ketosis, like fatty liver, occurs during periods of elevated plasma NEFA (Grummer 1993).

While most think of fatty liver and ketosis as a postpartum disorder there is evidence fatty liver actually is occurring in cows prior to calving. Grummer (1993) classified fatty liver as a periparturient metabolic disorder. In the 1960's Ford (1961) measured ether extract content of liver tissues in 20 day intervals starting 60 days prior to calving to 80 days following parturition. Ether extract was the highest the last 20 days of gestation. More recent Skaar (1989) observed a 2 to 17% increase in liver triglyceride during the last 17 days of gestation and 1 to 2 days postpartum. This period of time is also the same time that plasma NEFA levels start to elevate. Plasma NEFA increase approximately twofold between day 17 and 2 prior to calving and increase twofold again to peak calving (Grummer, 1993). In a review by Bobe et al. (2004) fatty liver is classified into three categories based on triacylglycerol levels in the liver; he further associated fatty liver severity with the occurrence of urinary ketones, feed intake and milk production, and health status and reproductive performance (Table 1). The estimated cost associated with fatty liver is approximately $60 million; this is assuming that ketosis and fatty liver are highly correlated and that there are 9 million dairy cows in the United States and occurrence is about 4.8% (Bobe et al., 2004).

Table 1. Categories of fatty liver in dairy cows. (Adopted from Bobe et al., 2004)

Liver Category	Liver TAG (% Wet Weight)	Urinary Ketones	Feed Intake, Milk production	Health and, Reproductive Status
Normal	<1%	0^2	0	0
Mild	1-5%	+	0	-
Moderate	5-10%	++	0	--
Severe	>10%	+++	---	---

*TAG=Triacylglycerol

**The symbols + and – Mean positive and negative association, respectively and the number of symbols represents slight, moderate, or strong association; 0 means no association

Evidence supports that fatty liver proceeds ketosis. The first evidence is that fatty liver is prevalent by 1 day following parturition, but cows are most susceptible to ketosis 3 weeks following calving (Grummer 1993). The exact mechanism for the onset of fatty liver is unknown. However, evidence supports that the reduction of liver triglyceride levels prior to calving and in early lactation and that controlling the ratio of liver triglyceride levels to glycogen may reduce the risk of cows developing fatty liver and ketosis (Grummer, 1993). Gerloff et al. (1986) found that cows prone to severe fatty liver had elevated concentrations of hepatic triglycerides prior to calving. The ability of ruminant animals to metabolize and export fatty acids in the form of VLDL is much lower than that of other animals (Kleppe et al., 1988; Pullen et al., 1990). Many enzymes and proteins that are involved in the synthesis and exportation of VLDL and LDL along with lipoproteins and enzymes responsible for the transportation of lipids are reduced in cows with fatty liver (Bobe et al., 2004). The main lipoprotein in which fatty liver has a detrimental effect on is high-density lipoprotein (HDL; Katoh, 2002). The decreased function of HDL results in a decreased synthesis of cholesterol esters. These esters are important in the synthesis of

steroids (Katoh, 2002); in addition HDL plays a vital role in the body of returning excess cholesterol back to the liver for metabolism or excretion. Beyond just immediate losses seen with fatty liver other possible consequences of fatty liver include poor reproductive soundness. Without the proper steroid availability some vital reproductive hormones could be limiting for optimal reproductive performance. Fatty liver has a negative effect on some vital metabolic pathways in the dairy cow. A reduction in energy precursors via decreased gluconeogenesis along with mixed effects on ketogenesis and β-oxidation and increased lipogenesis. Ureagenesis and the ability of insulin to decrease protein synthesis are also decreased with fatty liver (Bobe et al., 2004). Plasma BHBA and acetoacetate concentration increase with fatty liver; resulting in decreased β-oxidation, gluconeogenesis, and the citric acid cycle in hepatocytes (Bobe et al., 2004). The inability of dairy cattle and other ruminants to export fatty acids readily from the liver is definitely a contributor to fatty liver. The natural phenomenon of parturition could be the number one enemy of the animal scientist in their ability to alter triglyceride exportation from hepatocyte tissues. As parturition nears estrogen levels increase in non-ruminants; estrogen has inhibitory effects on fatty acid metabolism (Bertics et al., 1992) the same could be true of ruminants. Other factors that may play a role in fatty acid metabolism include: end products of ruminal fermentation and concentrations of malonyl-CaA. Manonyl-CoA is a critical factor regulating the entry of fatty acids into the mitochondria for oxidation (McGarry and Foster, 1980). Propionate has been shown to be antiketogenic (Grummer 1993). The exact mechanism for which the antiketogenic actions of

propionate affect fatty acid metabolism is not yet known, but one possibility is the inhibition of CPT-1 via methyl malonyl-CoA (Grummer 1993).

Cows that are at risk for fatty liver include those that have nutritional deficiencies or alterations that cause a change in liver metabolism, obese cows (BCS$\geq$4; Rukkwamsuk et al., 1998) and genetically prone cows. Cows that are in the periparturient period may fall into one or more of the three main areas of risk. The inability of cows to meet increasing nutritional demands during the prepartum period and meet energy demands through increased lipolysis automatically put themselves in a high risk category for fatty liver. In addition, many of these cows because of improper nutrition during late lactation or problems such as hard breeding, challenging early lactation, or high production that causes extend days in milk become or approach obesity during the dry period. To further elevate the probability of developing fatty liver cows that are obese cows experience a greater reduction in feed intake and reach a greater negative energy balance (Stockdale, 2001). The periparturient cow also challenges its immune system or develops a suppressed immune system which changes many bodily functions and metabolisms including those in the liver.

Niacin in Dairy cows

Niacin is used to describe pyridine 3-carboxylic acid otherwise known as nicotinic acid. A second form of niacin nicotinamide is equivalent to nicotinic acid in biological terms. The difference between the two lies in the R-group. Nicotinic acid has a carboxyl group (COOH) while nicotinamide has a $CONH_2$ in the place of the carboxyl group. Absorption of niacin from small intestine occurs by simple diffusion. In humans niacin absorption is absorbed with equal efficiency from the intestines and the

stomach (Pond et al., 1995); however in ruminants niacin is unstable in the rumen and becomes disassociated. Mean nicotinic acid concentrations were measured 1 hour prior to feeding to 11 hours after feeding. Cows that were supplemented with niacin had a greater concentration of nicotinic acid present in the rumen for a longer period of time than did controls cows; by 7 hours after feeding all cows had returned to pre-feeding concentrations (Campbell et al., 1994). Campbell et al. (1994) supplemented both nicotinic acid and nicotinamide; only nicotinic acid was detected in ruminal and duodenal fluids. This led to the conclusion that nicotinamide was converted to nicotinic acid in the rumen. In the same study the ability of niacin to enter the small intestine for absorption was measured. Using duodenal nicotinic acid concentrations and DM flow to the duodenum it was estimated that only 17% of supplemented niacin reached the small intestine; with cows that were supplemented with nicotinamide having slightly greater levels of nicotinic acid in the duodenum than cows supplemented with nicotinic acid (Campbell et al., 1994). These results are similar to results found in sheep by Harmeyer and Kollenkirchen (1989). They estimated that 20 to 30% of supplemented niacin reached the small intestine depending on the dosage. In non-ruminants the vitamin is considered an essential vitamin. Ruminants are able to synthesize niacin at high levels; therefore ruminants do not require supplementation of the vitamin. Miller et al (1986) and Zinn et al (1987) found that quantities of niacin appearing at the duodenum in steers exceeded that provided by feedstuffs. This supports findings from the mid 1940s that when diets relatively free of niacin were fed, the niacin concentration in ruminal digesta exceeded dietary concentrations (Schwab et al, 2005). However, the supplementation of niacin has shown to have positive

consequences these include: a reduction of plasma NEFA and ketone concentration, increased microbial protein synthesis and protozoal numbers in the rumen, and increase in milk protein percentages in early lactation. Small amounts of supplemental niacin have shown to increase niacin production in the rumen (Campbell et al., 1994). A possible explanation of the benefits that have been seen from supplemented niacin is that the high production demands have made niacin a limiting factor in the dairy cow more specifically in the rumen.

Niacin, Milk Production & Components

The use of Niacin in dairy cows is a relatively new journey. Research by Waterman and Schultz in 1972 opened the door to niacin research in the dairy industry. Since 1972 the research that has been done has shown few concrete results. The supplementation of niacin has ranged from a variety of time frames including over and entire lactation, during the transition period, or and during early lactation. All periods have resulted in mixed results. In a field study by researchers in Illinois 6 g/d of niacin during the first 10 wks of lactation increased milk production in high producing heifers, but response for older cows was nadir (Jaster et al., 1983). Muller et al (1986) reported increased milk production over all parity of cows during the same time frame. Drackely (1992) reviewed the use of niacin and reported that when all comparisons were considered niacin resulted in a slight (.36 kg/d) increase in milk yield; however when just considering the first 15 wks of lactation larger increases in milk yield and 4% fat corrected milk existed.

Fat supplementation can be used in the dairy industry as a very advantageous tool for increasing dietary energy intake especially during heat stress periods. A

consequence associated with fat supplementation can be decreased milk protein percentages (Jenkins and McGuire, 2006). This can be a negative association since many milk pricing systems are now on a formula based pricing system; where producers get paid based on the percent protein in milk. However, the ability of fat supplementation to increase or maintain milk production could potentially negate the decreased milk protein percent resulting in equal or slightly increased total milk protein. Horner et al (1986) reported increased milk protein percentages when 6 g/d of niacin was supplemented to cows fed whole cotton seed diets (15% of diet). A study by Driver et al (1990) compared heat treated soybeans versus heat treated soybean meal as dietary protein sources and the effect of 6 g/d of niacin. Cows that were fed heat treated soybeans had a diet containing 2.5% more lipids; cows that were fed heat treated soybeans had significantly reduced milk protein. However, cows that received 6 g/d of niacin had significantly higher milk protein percentages compared to those with out niacin. Niacin had no effect on cows fed heat treated soybean meal. The latter studies had a diet composition that was very high or all alfalfa based. Corn Silage based diets may pose different challenges; based on the amino acid profile and their interactions. Supplemental niacin may be limiting when heat treated soybeans are included in corn silage based diets; due to the reduction of tryptophan availability for the synthesis of niacin in the rumen (Bernard, 1995). Bernard (1995) found that niacin was not limiting when heat treated soybeans were fed with high corn silage based diets. There was no difference in milk production or components. Niacin supplementation unlike the study conducted by Driver et al. (1990) did not eliminate milk protein percent depression. However, the under roasting of soybeans fed in the diet in this

study may have confounded the results. Drackley et al. (1998) reported mixed results with the supplementation of Nicotinic Acid. In early lactation weeks 4 to 25 milk crude protein was not effected; however in weeks 4 to 43 milk crude protein was increased. Milk true protein was increased in cows fed diets with supplemental fat and nicotinic acid.

The economic basis for supplementation of niacin is important. Erdman (1992) reported that there was no economic benefit from the supplementation of nicotinic acid with diets containing fat even if milk crude protein increased; Drackley et al. (1998) taking into consideration the increased production of milk from supplemented fat and nicotinic acid reported that the economic benefits would have to be based on the effects of milk components and the pricing scheme for milk and milk components.

Milk yield has varied through niacin supplementation. Niacin supplementation in early lactation seems to be beneficial in increasing milk production and components (Drackley 1992). A review conducted by Schwab et al. (2005) reported that milk yield and 3.5% FCM yield did not change for cows fed 6 g/d of nicotinic acid. However, cows supplemented with 12 g/d had an increase in over all milk yield and 3.5 % FCM of .4 and .5 kg/d respectively over control cows. Similarly milk fat yield increased 25.8 g/d for cows supplemented with 12 g/d of nicotinic acid, but 6 g/d had no effect. The increase reported from cows supplemented 12 g/d of nicotinic acid could be due to increased milk production as milk fat percent did not increase. The latter statement is consistent with the findings of Drackley et al (1998). Jaster and Ward (1990) reported differences between 6 g/d of nicotinic acid and 6 g/d of nicotinamide versus control cows. Nicotinamide increased actual milk yield and 4% FCM milk during

weeks 9, 11 & 12 compared to controls; while nicotinic acid had no effect on milk yield during early lactation. Milk fat was also increased in cows fed 6 g/d of nicotinamide compared to controls in weeks 1 and 4. According to Campbell et al. (1994) nicotinamide is converted to nicotinic acid in the rumen and then passed to the small intestine for absorption; if this is true the effects of seen by Jaster and Ward (1990) would have to be a result of alteration of fermentation or increased efficiency of nicotinamide to pass through the rumen and be absorbed and alter lipid and energy metabolism. Possible explanation of the effect of nicotinic acid or nicotinamide on the rumen and energy metabolism have been described by Riddell et al (1981); increased stimulation of protein synthesis by rumen microbes could possible be the key to the benefits associated with feeding a form of niacin. Niacin functions as a coenzyme in the form of either an electron carrier (NAD) during oxidation reaction or many metabolic fuels such as acetate, β-hydroxybuteryrate (BHBA), glucose, and fatty acids; or as hydrogen donor $NADPH^+$ in functions such as fatty acid synthesis. Niacin has been shown to increase protozoa numbers in the rumen (Erickson et al, 1992). The increase in protozoa numbers could be in their ability to engulf starch granules and act in pH stabilization. Riddell et al. (1981) suggested niacin supplementation will have little effect in diets with readily available N such as NPN or diets that are high in rumen bypass protein. The diet composition that is most effective is uncertain. Schwab et al. (2005) reported that supplemental niacin may be the most beneficial when diets are lacking in the ability to synthesize niacin or ruminal microbial growth is not being maximized. Diets that have greater levels of dietary forages and non-fiber carbohydrates seem to increase ruminal niacin synthesis (Schwab et al., 2005);

therefore diets that are high in concentrates niacin supplementation may be beneficial in increasing milk production and milk composition.

Niacin & lipolysis

Exploration of production benefits to supplemental niacin has seen mixed results; the use of niacin to prevent excessive lipolysis from occurring during the late gestation and early lactation has been successful. The first research that demonstrated that niacin may be beneficial in reducing lipolysis was in 1972 by Waterman and Schultz. Pharmacological doses of 160 g given over an 8 hour period decreased plasma NEFA and ketone Body concentrations in dairy cows with clinical and sub-clinical ketosis. A rebound of plasma NEFA concentrations was seen after infusion of Niacin ceased. Day one following treatment also resulted in a return appetite and increased alertness, day 2 after treatment cow's appetite had decreased and this was the same period in which plasma NEFA and ketone bodies were increasing. Following the rebound stage just described appetite was returned to normal and plasma NEFA and ketone bodies started to return to normal levels. Lipolysis is the mobilization of triglycerides stored in adipose tissues to the liver for metabolism during times when the body energy demands are greater than the diet consumed is supplying. These triglycerides are mobilized and transported to the liver in the form of free fatty acids (FFA). About 25% of circulating FFA are taken up by the liver (Church, 1988). In normally fed sheep 35% of FFA taken up by the liver are metabolized into ketone bodies; this increases up to 81% in ketotic sheep (Bergman E.N, 1971). The increase in FFA being taken up by the liver would in return decrease the percent of FFA being esterified, but the total amount of FFA being esterified would still increase due to the large increase

in liver uptake. Further, blood triglyceride levels will decrease because liver lipid levels are higher than that of blood and abnormal release of lipids from the liver occur (Church, 1988). The abundance of FFA in the liver and in essences a deficiency of oxalacetate for oxidation of FFA results in free fatty acids being forced into ketogenesis and esterfication. The resulting factor of excessive lipid transport to the liver and depressed lipid transport out of the liver and an increase in ketogenesis and FFA esterifation is the onset of fatty liver and ketosis.

Fronk and Schultz (1979) fed 12 g/d of nicotinic acid to ketotic cows and saw a decrease in plasma NEFA and BHBA concentrations (P<.05). An increase in blood glucose concentrations were reported 7d after initiation of nicotinic acid treatments. In numerous other studies (Minor et al, 1998; Driver et al, 1990; Skaar et al, 1989) 12 g/d of nicotinic acid was not effective in reducing plasma NEFA concentrations. Grummer (1993) reported that NEFA levels are at their highest around the time of parturition. Recently French (2004) reported decreased plasma NEFA concentrations and liver triglyceride levels at calving and 1d following calving in Jersey cows fed 48 g/d of nicotinic acid 21 days prior to parturition compared to controls cows with no nicotinic acid supplementation. Niacin must be absorbed in to the blood stream to have beneficial properties in the control of lipolysis. NA lacks stability in the rumen and is not readily absorbed across the rumen wall. Campbell et al. (1994) reported that only 17-30% of supplemented NA reaches the small intestine for absorption. The possible reasoning for the later studies' success in controlling lipolysis and in return maintaining DMI is increased concentration on niacin allowed for greater amounts of niacin to reach the small intestine for absorption. Based on the success of found in

human medicine of 1-3 g of NA daily; and the lack of rumen stability cows would need 24-141 g daily. Although 48 g of NA supplementation showed positive results during late gestation lactation responses are unknown.

Niacin in Humans

The use of nicotinic acid in the treatment of lipid disorders in humans has been used since the 1950's. Nicotinic acid, otherwise known as vitamin B3 was found by Rudolf Altschul to have this unique ability to lower both serum cholesterol and also inhibit lipid deposits in the cholesterol fed rabbit (Carlson, 2005). In his first study in 1955, Altschul reported that nicotinic acid in gram doses lowered plasma cholesterol in the normal as well as the hypercholesterolamic subjects. In the same study Altschul reported that nicotinic acid's equivalent nicotinamide did not lower plasma lipid levels. While both nicotinamide and nicotinic acid are precursors to the coenzyme nicotinamide adenine dinucleotide; nicotinamide may not have the same inhibitory properties on lipolysis in adipose tissue. Soon after the studies by Altschul et al., Parsons and coworkers at the Mayo clinic reported positive effects in patients that took 3 g of nicotinic acid daily for twelve weeks. Seven patients with familial hypercholesterolaemia cholesterol levels were lowered on average by 16% from 9.2 to 7.7 mmol L^{-1} (Carlson, 2005). Studies by Parsons and Finn (1959) continued to get exciting results including: the lowering of the ratio of β to α1-cholesterol (LDL to HDL) declined from 9.0 to 5.6. Parsons also reported lowered cholesterol by up to 20%, and in increases of HDL of up to 44%.

For about a five to ten year period Altschul and Parsons established the ability of nicotinic acid to lower plasma cholesterol in the human body. The exact mode of

action at which nicotinic acid work in lowering cholesterol was still in question; theories about the subject manifested and it was not until the late 1950s that a promising discovery came about. Through a series of studies conducted by numerous individuals it was soon found that free fatty acid (FFA) mobilization from adipose tissues were precursors of hepatic and subsequently plasma triglycerides transported as very low density lipoproteins (VLDL), the precursor to cholesterol rich LDL. It was found that nicotinic acid administered at 200mg *per os,* lowered the arterial plasma concentration of FFA in fasting human subjects. The lowering was followed by a rebound within 1 hr (Carlson et al, 1963). In the same study Carlson also showed nicotinic acid supplemented as a pretreatment to a FFA infusion of noradrenaline almost completely inhibited the rise of plasma FFA, without affecting cardiovascular response. Since about 1968 the administration of nicotinic acid in the form of immediate release at 4 hour intervals to keep continued suppression of FFA has been widely used in the human medical field; 1g of nicotinic acid will suppress FFA levels for about 3 hours. The Recent studies by numerous individuals that identified a nicotinic acid receptor in adipose tissue helps to back the ideas by Carlson and others in the 1950's and 60's, that nicotinic acid is readily absorbed by adipose tissues and acts on the tissue leading to a decrease of plasma FFA.

The importance of lowering plasma cholesterol was known about the same time as Altschul started his series of experiments in the 1950s. The relationship that hypercholesterolaemia had with cardiovascular diseases especially coronary heart disease was being established. Carlson et al (1973) made the connection that not only did nicotinic acid reduce plasma cholesterol in hypercholesterolemia patients; but that

nicotinic acid also lowered both cholesterol and triglyceride levels in all 5 types of hyperlipidaemia patients. Table 2 shows a summary of his findings.

Table 2. Effect of nicotinic acid on plasma lipids in hyperlipidaemia types II-V. (Carlson et al., 1973)

	Type of hyperlidiaemia									
	II A		II B		III		IV		V	
	Chol	TG	Chol	TG	Chol	TG	Chol	TG	Chol	TG
Men										
Pretreatment[b]	12	1.7	9	2.9	16	9.3	7.7	6.9	20	81
% Decrease	8	29	21	40	50	62	16	55	73	94
Women										
Pretreatment[b]	12	1.7	9.6	2.4	-	-	8.2	5.4	-	-
% Decrease	25	36	25	42	-	-	26	59	-	-

[b]mean values (mmol L^{-1}). Effect of 1g of nicotinic acid three times daily for 1 month on fasting plasma concentrations of cholesterol and triglycerides in the different types of hyperlipoproteinaemia.

The relevance of nicotinic acid acting on not only cholesterol levels and on all five types of hyperlipidaemia, but also on triglyceride levels was further increased with the ability to distinguish between lipoproteins. The ability to distinguish between lipoproteins and there causality to coronary heart disease was also developed in the 1950s. LDL was recognized as a risk factor for coronary heart disease, however in the 1960's and 70's the role of the high levels of LDL and low levels of HDL and the role of high levels of triglycerides became relevant. Dyslipidaemia is the description given when the concentrations of one or more of the plasma lipoproteins is abnormal (Carlson et al., 2005).

Nicotinic acid was found to have positive results on lowering both VLDL (Very low density lipoproteins) and LDL. In addition, it was found that nicotinic acid increased HDL levels, and that nicotinic acids ability to lower plasma triglyceride levels was primarily do to the lowering of VLDL levels and the lowering of cholesterol was due to the lowering of LDL particles specifically the small dense particles (Carlson, 2005). Nicotinic Acid was found to have a huge effect on plasma HDL levels in the 1950's. The lack of knowledge concerning the benefits of increased

HDL concentrations led to a void of research concerning HDL concentrations. Later the benefits of having increased HDL concentrations for the export of cholesterol and triglycerides were discovered. An increase of 50% on HDL particles and 100% increase in HDL_2 particles by Carlson and co-workers (1989) made niacin the one of the most powerful drugs for increasing HDL and HDL_2 concentrations. The mechanism for which niacin works to increase HDL may be the most important mechanism from a health stand point for human nutrition. Increased levels of HDL are strongly associated with decreasing incidence of coronary heart disease, increased reverse cholesterol transport, and increases cholesterol elimination from the body (Carlson, 2005). Reverse Cholesterol transport is the removal of cholesterol from tissues and arteries back to the liver where they are exported out of the body.

Two possible mechanisms for which niacin reduces plasma LDL and VLDL concentrations are thought to exist. The first is modulation of triglyceride lipolysis in adipose tissue, and the second is modulation of triglyceride synthesis resulting in increased intracellular apo B degradation (Ganji et al., 2003). The control of lipolysis in adipose cells is thought to be the main mechanism for which nicotinic acid decreases VLDL and LDL levels. Adipose cells are specialized for synthesis and storage of triglycerides and for their mobilization as free fatty acids to the liver for metabolism in to a useable metabolic fuel. Carlson (1968) established that nicotinic acid decreases the mobilization of free fatty acids from adipose tissue by inhibiting the lipolysis of triglycerides. The lipolysis of triglycerides is controlled by cyclic AMP (c-AMP) mediated activation of hormone sensitive lipase. Aktories and co-workers (1980) found that niacin inhibited adenylate cyclase activity in adipocytes resulting in

reduced concentrations of c-AMP. The mechanism for which niacin inhibits c-AMP is by the activation of the nicotinic acid receptor that activates an inhibitory G-protein signal which reduces adipocyte c-AMP (Karpe and Frayn, 2004). The actual end result is seen in that FFA's mobilized to the liver are the main precursors for hepatic triglyceride synthesis. Hepatic triglycerides are the foundation for the formation of LDL and VLDL particles. Ganji et al. (2003) showed that niacin directly in a non-competitive type inhibited microsamal diacylglycerol acyltrasferase (DGAT). DGAT is a key rate limiting enzyme in hepatic triglyceride synthesis.

In summary nicotinic acid through the an inhibitory G-protein signal reduces c-AMP in adipose tissues decreases hormone sensitive lipase leading to decreased circulation of FFA and the conversion of FFA to hepatic triglycerides; which in turn causes a decrease in the catabolism of LDL and VLDL. Further, through reverse cholesterol transport increases HDL and the excretion of cholesterol and triglycerides. The dual mechanism of nicotinic acid has become one of the most powerful tools in the control of lipid disorders such as hyperlipidemia and coronary heart disease in humans. The ability of nicotinic acid to improve milk production and its components has been seen to be beneficial. Perhaps the key for the use of niacin is to increase the dose. With promising results in 12 g/d versus 6 g/d and positive results seen in lowering plasma NEFA levels using high levels such as 160g or 48g gives reason for further investigation of nicotinic acid supplementation in dairy cows.

The effects of nicotinic acid supplementation during late-gestation on lipolysis and feed intake during the transition period.

Introduction

The transition period for the dairy cow is a very complex time. The metabolic status of the transition period cow is continually changing and results in high levels of stress for the cow. Ketosis, fatty liver, milk fever, displaced abomasums, negative energy balance, ration changes are all potential challenges that can arise during the transition period.

Arguably the most important barrier to maximizing production and minimizing health disorders is maintaining dry matter intake (DMI) during the transition period. For over three decades it has been known that DMI declines during the period leading up to parturition and is suppressed after parturition. Marquardt et al. (1977) observed DMI decreases of 25% during the last three weeks of gestation. In addition, one-half of the decline in DMI occurrs during the final 14 days of gestation. According to the NRC (2001), DMI decreases 32% during the last three weeks of gestation. The importance of DMI decline becomes relevant when postpartum DMI is considered. Grummer (2004) found that when cows are fed ad libitum, there is a positive relationship between prepartum and postpartum DMI.

Numerous factors have been implicated with prepartum DMI depression, including increasing fetal size, changes in reproductive hormones, and circulating concentrations of plasma nonesterified fatty acids (NEFA). French (2006) suggested that the concomitant fall in DMI and rise in NEFA are associated, with the exponential rise in plasma NEFA the leading cause of peripartum DMI depression. However, the most widely held theory is that declining DMI causes cows to enter into negative energy balance which is naturally compensated by lipolysis creating an influx of plasma NEFA to be used as a fuel source.

In the dairy industry cows have been selected cows to produce at high levels following parturition further increasing the demand and energy requirements need in early lactation.

There is evidence to support that increased lipolysis depresses DMI. The infusion of a β-antagonist during lipolytic state increased plasma NEFA and decreased DMI (Bareille & Faverdin, 1996). In addition, force-feeding cows during late gestation did not negate the rise in plasma NEFA (Betrics et al, 1992). The increase in lipolysis may be in response to the natural phenomena of a mother producing milk for her young.

Uptake of NEFA by the liver is directly proportional to the circulating concentration of plasma NEFA. When the capacity of the liver to oxidize NEFA and/or export lipid is exceeded the lipid is stored in the liver and the condition known as fatty liver develops. Excessive fat deposits in the liver caused by increased lipolysis have been shown to increase days to first ovulation (Rukkwamsuk et al, 1999) and to decrease pregnancy rates (Jorritsma et al., 2000). Dyk (1995) found that higher prepartum plasma NEFA concentrations were associated with greater incidences of dystocia, retained placenta, ketosis, displaced abomasums, and mastitis.

Nicotinic acid has been used for decades to control lipid related disorders in humans and therefore may be beneficial to the dairy cow. Although NA has been the most researched B-vitamin in the dairy cow, results have been mixed. In early research, Fronk and Schultz (1979) fed 12 g NA /d to ketotic cows and reported a decrease in plasma NEFA concentrations. Others have supplemented NA during the transition period, but have not seen similar results (Minor et al, 1998; Driver et al, 1990; Skaar et al, 1989). Recently, French (2004) reported decreased plasma NEFA concentrations and liver triglyceride levels at calving in Jersey cows fed 48 g NA /d the last three weeks of gestation compared to controls cows with no NA supplementation. Niacin must be absorbed into the blood stream to control lipolysis. Nicotinic acid lacks stability in the rumen and is not readily absorbed across the rumen wall. Campbell et al. (1994) reported that only 17-30% of supplemented NA reaches the small intestine. The reason French (2004) reported positive results from supplementing NA may have been due to the amount supplemented. Based on the common dose of 1-3 g NA/d in humans, lack of rumen stability, and the body weight difference; the human equivalent

dose in diary cows would be 24-141 g daily. Although 48 g NA/d showed positive results during late gestation, responses after parturition are unknown.

The objectives of this study were to 1) determine if NA supplementation during the transition period decreases lipolysis and improves DMI in Holstein and Jersey cows, and 2) determine if Holstein and Jersey cows respond similarly to nicotinic acid supplementation.

Materials & Methods

Animals and Diets

The Oregon State University Institutional Animal Care and Use Committee approved all procedures involving animals. Twenty-seven multiparous Jerseys and 27 multiparous Holsteins cows were selected from the Oregon State University Dairy Center. Cows were blocked by expected calving date and assigned at random to one of three prepartum dietary treatments beginning four weeks prior to expected calving date. The experimental design was a randomized complete block with factorial arrangement of treatments. Main effects were breed and niacin supplementation, and were balanced for parity and previous lactation milk production. Data was collected beginning 21 d prepartum and ended 21 d postpartum. Cows were group housed in a freestall barn and fed individually using Calan® gates (American Calan, Northwood, NH).

Nicotinic acid was supplemented in the prepartum diet at one of three levels: 0, 49, or 98 mg /kg BW. Assuming 25% of supplemental niacin escapes ruminal degradation, these supplementation levels are similar to a human dose of 0, 1 or 2 g/d for 0, 49, or 98 mg /kg BW, respectively. This is based on an average BW of 490 and 700 kg for Jerseys and Holsteins, respectively, and an 82 kg body weight for humans. The

resulting supplementation rates per day were 0, 24, 48 g for Jerseys and 0, 34, 68 g for Holsteins.

Cows entered the Calan® gates (American Calan, Northwood, NH) system 28 d prior to their expected calving date. Cows were given a 5 d adaptation period prior to data collection. Cows were fed a TMR twice daily at 0630 h and 1400h. Orts were recorded once daily at the morning and maintained at <5% (as-fed). All cows received the same basal diet prior to calving; niacin supplementation was the only difference between dietary treatments. Ground corn (227 g) was used as a carrier for the NA. The NA premix was top dressed and mixed in during the morning feeding; morning orts of <2 kg of feed (as-fed) were maintained to ensure consumption of the niacin premix. Supplementation occurred 24 days from their expected calving date to calving. Ingredient and diet composition is shown in Tables 3-5. The basal diet for prepartum cows consisted of corn silage, alfalfa hay, grass hay, anionic supplement and a vitamin & mineral premix. Following parturition all cows received a lactating cow TMR consisting of corn silage, grass silage, alfalfa hay, and grain mix.

Feed samples were collected weekly and dried at 55°C in a forced-air oven for DM determination and diets were adjusted to maintain consistent ingredient proportions throughout the experiment. Weekly feed samples were ground through a 1-mm screen in a Thomas Wiley Mill (Thomas Scientific, USA), composited by month, and stored for later analysis. Monthly composites analyzed for CP (AOAC, 1997), ADF (AOAC, 1997), and NDF (Van Soest et al., 1991). Neutral detergent fiber was measured using the ANKOM A200 (ANKOM Technology Corp., Fairport, NY) filter bag technique. Mineral levels were measured using the Perkin Elmer 3300 XL ICP (AOAC, 2000).

Sampling and Analysis

Blood samples were collected from the jugular vein at 1300h on days -23, -20, -17, -14, -11, -9, -7, -5. -4. -3, -2, -1, 0, 1, 3, 5, 7, 14, and 21. Immediately following collection blood was put on ice until transported back to the lab and plasma was separated after centrifugation at 2000 x g for 15 min at 5°C, and frozen until analysis. Collection of blood on 0 d was within six hours of calving. A subsample consisting of days -21, -14, -11, -7, -5, -3, -1, 0, 1, 3, 5, 7, 14, 21 were used for analysis. Blood plasma was analyzed for Non-esterfied fatty acid (NEFA) (NEFA-C, WAKO Pure Chemical Industries, Richmond, VA), β-hydroxylbuterate (BHBA) (Procedure 2440, Stanbio Laboratory, Boerne, TX), Glucose (Procedure 1070, Stanbio Laboratory, Boerne, TX), Aspartate Aminotransferase (AST) (Procedure 2920, Stanbio Laboratory, Boerne, TX). Liver triglyceride content was determined using the procedure described by Piepenbrink et al. (2004) and a commercial kit (Procedure No. 2150; Stanbio Laboratory, Boerne, TX).

Liver biopsies occurred 21 days prior to the cows expected calving date, within 24 hours of calving, and 21 days following calving. Biopsies were performed using the procedures described by Veenhuizen et al., (1991). Biopsy samples were approximately 3 g in size; the procedure had no lasting effects on the cows. Some cows experienced slightly depressed afternoon DMI on the day of sampling, but had complete recovery by the following feeding.

Cows were weighed and body conditioned scored on the same day weekly prior to afternoon feeding. There was no difference in starting body condition scores and body

weights between treatments. Cows were milked twice daily at approximately 0400h and 1800h; milk weights were recorded daily. Milk was analyzed for fat, protein and SCC on two consecutive milkings each week by Willamette Valley DHIA (Salem, OR). The day of calving (day 0) was omitted from all statistical analysis as some cows were milked only once on day 0 and some milked 2X on day 0 depending on time of calving.

Energy required for maintenance, pregnancy, and milk production was computed using NRC (2001). Animals were assumed to have reached mature body weight and calf birth weight used was 45 kg for Holsteins and 23 kg for Jerseys. Estimated energy balance prepartum was calculated on a weekly basis as energy balance = net energy intake - (net energy for maintenance + net energy for pregnancy) and postpartum energy balance was calculated on a weekly basis as energy balance = net energy intake – (net energy for maintenance + net energy for milk production).

Statistical Analysis

Data analysis were analyzed as repeated measures using the MIXED procedure of SAS (SAS User's Guide, 2001).

Cow within block by niacin supplementation level was defined as the subject. For equally spaced repeated measures, AR(1) covariance structure was used. Akaike's information criteria was used to select the best covariance structure from one of three spatial structures [SP (POW) (spatial power law), SP (GAU) (Gaussian), and SP (SPH) (spherical)] for unequally spaced repeated measures. Prepartum and postpartum data were analyzed separately. Dry matter intake differed by niacin supplementation -3 wk prepartum. This was due to animal differences and not NA; therefore DMI for d -21 to

-15 were averaged by cow and used as a covariant in the analysis of prepartum DMI. Dry matter intake was converted to a percentage of BW prior to analysis. Energy balance -3 wk prepartum was used as a covariant in the analysis of prepartum energy balance.

Model used was $Y_{ijklm} = \mu + Cov_o + B_i + H_j + T_k + HT_{jk} + C_{(ijk)l} + R_m + HR_{jm} + TR_{km} + HTR_{jkm} + e_{ijklm}$ where μ = overall mean, Cov_o = oth regression coefficient for –3 wk prepartum DMI or energy balance (used only for prepartum DMI and energy balance), B_i = ith block (1,2,…9), H_j = jth breed (Holstein or Jersey), T_k = kth niacin supplementation level (0, 48, or 98 mg/kg BW), $C_{(ijk)l}$ = lth cow within the ith block, the jth breed, and the kth niacin level, R_m = mth day or week (repeated measure), and e = residual error. Trends over time for equally spaced repeated measures were determined using the orthogonal contrasts: linear, quadratic, and cubic. Results in tables are reported as least squares means. Significance was declared at $P \leq 0.05$.

Table 3. Chemical Composition of forages (DM basis).

Nutrient	Corn Silage	Grass Hay	Prepartum Alfalfa Hay	Postpartum Alfalfa Hay	Grass Silage
Crude Protein, %	7.6	6.1	20.3	21.2	10.6
ADF	18.0	33.4	25.5	24.4	29.7
NDF	38.8	61.0	35.3	33.8	50.5
Ca	0.23	0.37	1.37	1.50	0.42
P	0.20	0.21	0.31	0.31	0.35
Mg	0.17	0.17	0.37	0.38	0.18
K	1.00	1.45	2.79	2.69	3.07
Na	0.01	0.18	0.19	0.17	0.08
Fe, mg/kg	262	366	635	743	654
Mn	32.8	102	41	43	114
Zn	26.1	28.0	33.1	30.3	35.3
Cu	2.6	4.5	9.8	10.3	16.2

Table 4. Chemical composition of concentrates (DM basis).

Nutrient	Ground Corn	Anionic Supplement	Postpartum Grain Mix[2]	Prepartum Mineral/Vitamin[3]
Crude Protein, %	8.8	48.2	18.9	
ADF	2.4	18.5	7.2	
NDF	10.1	21.5	18.0	
Ca	0.05	0.11	0.81	19.61
P	0.30	0.76	0.60	2.65
Mg	0.15	0.31	0.44	0.75
K	0.41	1.39	0.99	0.99
Na	0.02	1.69	1.49	0.26
Fe, mg/kg	54	116	193	3088
Mn	11	90	67	523
Zn	32.80	62.7	118.7	919.4
Cu	2.2	4.7	24.3	726.5

[1]BioChlor® (Church & Dwight Co. Inc., Princeton, NJ)

[2]Contained 26.0% (as-fed) steam rolled barley, 26.0% steam flaked corn, 16.0% whole cottonseed, 14.7% ethanol distillers' dried grains, 13.0% soybean meal, 2.0% sodium bicarbonate, 1.6% calcium carbonate, 0.3% salt, and 0.4% vitamin and trace mineral premix. Formulated for 20.4% (DM) CP, 0.88% Ca, 0.53% P, 0.35% Mg, 196 mg/kg Fe, 42 mg/kg Mn, 70 mg/kg Zn, 20 mg/kg Cu, 0.88 mg/kg Se, 2 mg/kg biotin, 7.8 kIU/kg A, 2.5 kIU/kg D, and 80 IU/kg E.

[3]Contained 46.4% limestone, 38.1% (as-fed) ethanol distillers' dried grains, 12.3% CaH_2PO_4, 1.0% mineral oil, 0.5% vitamin E (50%), 0.9% $FeSO_4(H_2O)_7$, 0.3% $CuSO_4(H_2O)_5$, 0.3% MgO, and 0.2% other trace minerals and vitamins. Formulated for 19.8% (DM) Ca, 2.7% P, 0.16% Mg, 2625 mg/kg Fe, 300 mg/kg Mn, 702 mg/kg Zn, 720 mg/kg Cu, 7 mg/kg Se, 185 kIU/kg A, 55 kIU/kg D, and 2480 IU/kg E.

Table 5. Ingredient and calculated chemical composition of diets (DM basis).

	Prepartum	Postpartum
Ingredients		
Corn Silage	35.35	17.67
Grass Hay	15.37	
Prepartum Alfalfa Hay	14.94	
Postpartum Alfalfa Hay		17.67
Grass Silage		17.67
Ground Corn	22.5	
BioChlor®	8.64	
Postpartum Grain Mix		47
Prepartum Mineral/Vitamin	3.22	
Chemical Composition		
Crude protein, %	12.8	15.8
ADF	17.1	16.1
NDF	31.1	30.2
Ca	0.99	0.76
P	0.37	0.43
Mg	0.22	0.34
K	1.24	1.65
Na	0.22	0.75
Fe, mg/kg	268	384
Mn	44	64.7
Zn	31.9	72.0
Cu	4.5	16.6

Results & Discussion

Body Weight and Condition Score

Least square means for NA treatments and breeds are shown in Tables 6 and 7, respectively. Prepartum and postpartum BW ($P > 0.05$) and BCS ($P > 0.05$) did not differ ($P > 0.05$) between dietary treatment groups. Prepartum BCS (Table 7) for Holstein and Jersey cows ($P > 0.05$) and postpartum BCS (Table 7; $P > 0.05$) were similar across breeds. As expected, Holstein cows where heavier compared to Jerseys ($P < 0.001$). Postpartum BCS decreased (linear; $P < 0.001$) and BW decreased (linear and quadratic; $P < 0.05$) for all cows.

Dry Matter Intake

Initial analysis of prepartum DMI without the covariant revealed that there was a linear decrease in DMI with increasing NA ($P < 0.05$; data not reported). French (2004), fed similar levels of NA as in the current trial (98 mg/kg of BW) found that NA supplemented cows had increased DMI in late gestation compared to control cows. Cows in the study by French (2004) received NA supplementation as a top dressed mixed into the entire days diet and cows were fed once daily, whereas in this study NA was top dressed and mixed into the morning feeding So, NA concentration in the morning feed of the current study was 2x that of French (2004). In addition, molasses was fed in the trial by French (2004) to increase palatability and minimize sorting. Niacin has a bitter taste (Drackley, 1992) and the use of the molasses may have negated the bitter taste. To test whether NA was causing a decrease in DMI, DMI 3 d prior to NA supplementation was compared to that of the first 3 d after NA supplementation. There was no change in DMI after NA supplementation began ($P > 0.05$). Therefore, prepartum DMI was affected by animal and not treatment, and as a result DMI -3 wk prepartum was used as a covariant in the analysis of prepartum DMI. After inclusion of the covariant, prepartum DMI was similar ($P > 0.05$) for NA treatments. These results are similar to the findings of Minor (1997) who supplemented 12 g NA/d, but differ from that of French (2004).

During the final 2 wk of gestation Holstein DMI declined more than 2x that of Jersey cows with Jerseys declining 14 % while Holsteins declined 32% (Figure 1).

Hayirli et al. (2003) reported a 32% decline in DMI during the prepartum period for multiparous Holstein cows. This is in agreement with French (2006) who reported that Holstein cows had a DMI depression of 35% compared to 17% for Jersey cows during late gestation. Postpartum DMI differed for NA treatments with cows supplemented with 49 mg NA/ kg BW consuming more than other treatments (Table 6; $P < 0.01$). Dry matter intake as a percentage of BW was greater for Jersey cows compared to Holsteins ($P < 0.05$). For all cows postpartum DMI increased (cubic; $P < 0.05$) over the 21 d postpartum period.
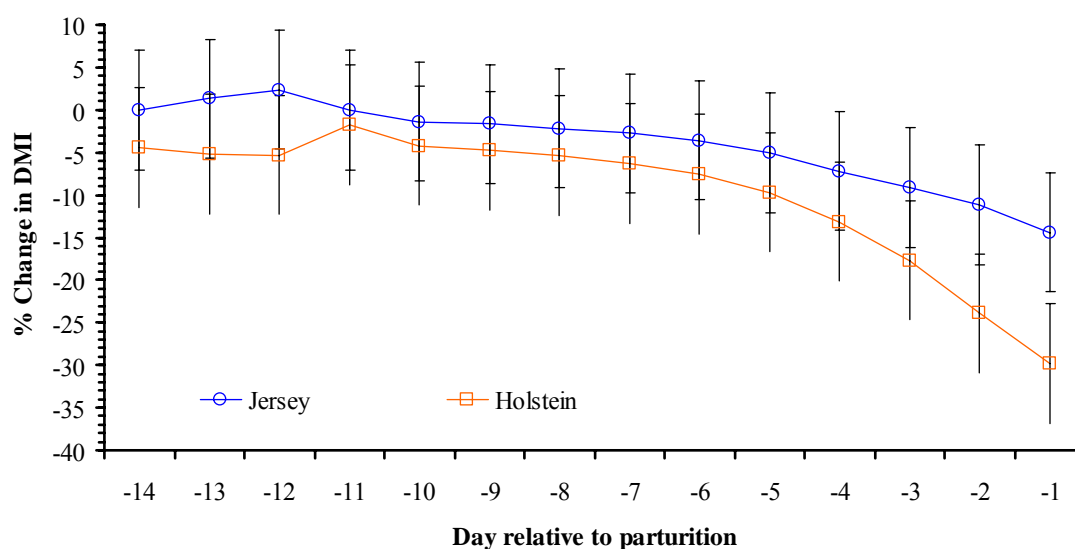

Figure 1. Jersey vs Holstein DMI % decline relative to week -3 DMI averages (Breed x Day interaction P < 0.05; SE = 0.07)

Blood Metabolites & Liver Triglyceride

Dietary treatment had no effect on prepartum or postpartum plasma NEFA. Fronk and Schultz (1979) reported decreased NEFA concentrations when 12 g NA/d was fed to ketotic cows. French (2004) reported decreased NEFA levels in Jersey cows supplemented with 48 g NA/d. In addition, Waterman and Schultz (1972) infused 160g of NA over an 8 hour period and reported a decrease in plasma NEFA concentrations while cows were receiving the NA infusion. In contrast, in a review by Schwab (2005) it was reported that 12 g/d of supplemental NA was not effective in reducing plasma NEFA concentrations. Supplementation at 12 g NA/d may be too low

to elicit a NEFA response. Campbell et al. (1994) reported that 17% of supplemental NA reaches the small intestine and Santschi et al. (2004) reported ruminal disappearance rates of 98.5% for NA. If the later is correct, it may explain the lack of response in this study and others. If 1.5 % of supplemental NA reaches the small intestine; cows in this study on the highest level of NA would have received approximately 1 g NA/d. Although this is in the range of 1-3 g/d human dose, the body weight of dairy cows is 8-10x greater than that of humans.

Grummer (1993) reported that NEFA levels are at their highest around parturition. The magnitude of increase in NEFA as parturition approached was greater for Holsteins compared with Jerseys (breed x day interaction; $P < 0.001$). As shown in Figure 2, Jersey cows had lower NEFA concentrations compared to Holsteins at d -3 (273 versus 520 µEq/L) and d -1 (755 versus 371.5 µEq/L). In addition, plasma NEFA concentration was lower for Jerseys compared to Holsteins during the postpartum period (613 vs 862 µEq/L for Jersey and Holstein, respectively; $P < 0.01$). Postpartum NEFA levels were highest at calving (1097 µEq/L) and decreased linearly and quadratically to 576 µEq/L at 21 d ($P < 0.01$) for all cows. Rastani et al. (2001) reported that Jersey cows had lower plasma NEFA concentrations during the first wk of lactation compared to Holstein cows. The reason for decreased lipolysis in Jersey cows compared to those of Holsteins is unknown. However, French (2006) suggested that the differences in plasma NEFA may be due in part to pretranslational or posttranslational mechanisms regulating hormone-sensitive lipase activity. Another possible mechanism that may explain or partially explain the differences between breeds and plasma NEFA concentrations may be differences in fatty acid metabolism in the liver. Ruminant animals have been reported to have decreased ability to metabolize and export FFA in the form of VLDL (Kleppe et al., 1988; Pullen et al., 1990); perhaps there are genetic differences between Holstein and Jersey cows which allow the Jersey liver to become more effective in the conversion and exportation of lipids out of the liver.
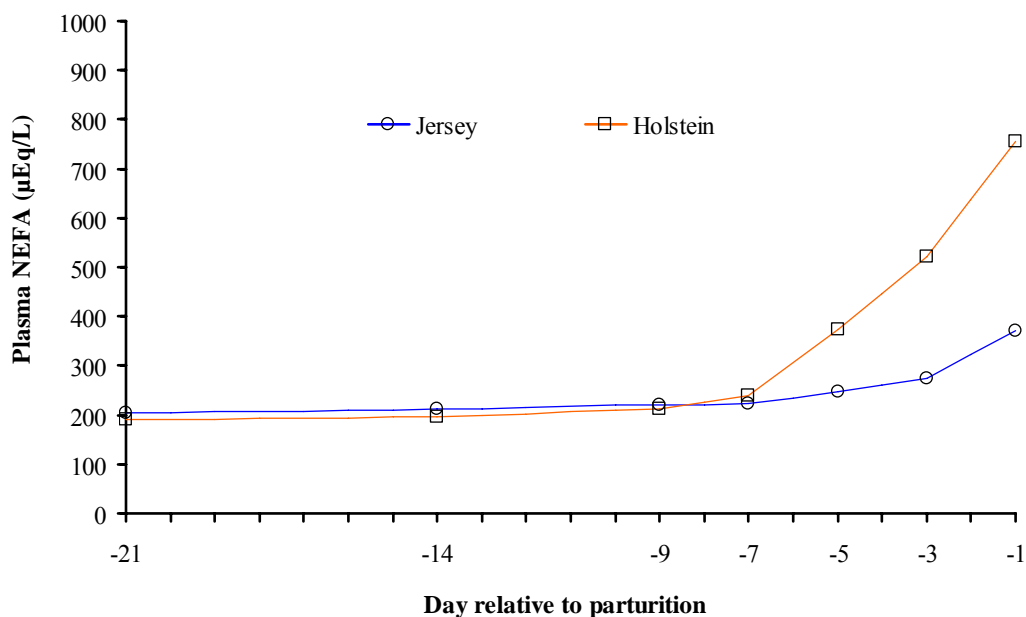
Figure 2. Least Square Means Plasma NEFA by day relative to parturition for Holstein and Jersey cows. Interaction Breed*Day was significant at the level of $P < 0.01$ (SE = 60.70; n = 27) from days -3 to -1.

There were no differences across NA treatments or breeds for prepartum or postpartum liver triglyceride levels ($P > 0.05$). This is expected since plasma NEFA did not differ. Skaar et al., (1989) reported no change in liver triglycerides prepartum or postpartum with the supplementation of 12 g/d of niacin from 17 days prior to parturition through 15 wks of lactation. Since Jerseys had lower plasma NEFA than Holsteins, lower liver triglycerides would be expected in Jerseys. However, liver triglyceride did not differ between breeds ($P > 0.05$). Lower NEFA in Jerseys should result in less NEFA being taken up by the liver and converted to triglycerides.

There were no NA treatment differences for prepartum and postpartum plasma β-hydroxybuterate (BHBA) and glucose concentrations ($P > 0.05$). Contrary to this data, Drackley (1992) reported that niacin tended to increase blood glucose compared to control cows. The increase in glucose along with the decrease in NEFA concentrations is important in the ability for niacin to reduce the incidence and effects of sub-clinical or clinical ketosis. Prepartum BHBA concentration differed between breeds With Jersey having higher plasma BHBA concentrations compared to Holsteins ($P < 0.01$). With lower levels of NEFA in the blood it would be expected that Jersey cows would have lower plasma BHBA concentrations compared to Holstein cows. Bergman (1970)

reported that when lipid mobilization increases and insufficient carbohydrate metabolism occurs the hepatic pathway for utilization of NEFA in the liver is shifted from the utilization to that of ketogenesis. Following parturition plasma BHBA concentration increased linearly ($P < 0.01$). The increase in BHBA following calving would be considered normal since ketogenesis increases in the weeks following parturition as energy demands increase and mobilization of body reserves increases. In a review by Grummer (1993), it was reported that the majority of ketosis occurs at 3 wk of lactation.

Aspartate aminotransferase (AST) is one of the many enzymes that can be used as a measure of liver dysfunction. Aspartate aminotransferase is released into plasma and becomes elevated when the liver, heart, kidney, or muscle is damaged. Long term NA supplementation in humans has been associated with liver damage. In the current trial, NA supplementation did not alter plasma AST concentration ($P > 0.05$).

Milk Production & Energy Balance

Cows supplemented with 49 mg NA/kg BW had greater milk production compared to control and cows supplemented with 98 mg NA/kg BW ($P < 0.001$). Muller (1986) reported cows supplemented with 6 g NA/d had increased milk production over the first 10 wks of lactation. Drackley (1992) in a review concluded that the supplementation of NA slightly increased milk production. Others (Jaster et al., 1983; Driver et al., 1989) have reported no increase in milk production of multiparous Holstein cows supplemented with NA. The increase in milk production from the 49 mg NA/kg BW cows was due to increased DMI during the postpartum period. Milk production increased cubically ($P < 0.001$) during the first 21 d of lactation for all cows. Holstein cows had superior milk production compared to Jersey cows ($P < 0.001$).

Nicotinic acid supplementation prior to parturition did not affect milk composition. Cows supplemented with 49 mg NA/kg BW had greater protein yield compared to control or cows supplemented with 98 mg/ kg BW of NA. This response can be explained by the greater milk yield of cows supplemented with 49 mg NA/kg BW. Jersey cows had higher milk protein percentage than Holstein cows ($P < 0.001$). Holstein cows, as expected, had greater protein yield than did Jersey cows ($P < 0.001$).

In addition, milk protein percentage decreased linearly ($P < 0.01$) and protein yield increased linearly for both Holstein and Jersey cows through the first 3 wk of lactation. Horner et al (1986) reported increased milk protein percentages when 6 g NA/d was supplemented during early lactation. Jersey cows had higher milk fat percentage compared to Holstein cows ($P < 0.05$). This result was expected due to the genetic difference between Holstein and Jersey cows. However, Holstein cows had greater milk fat yield during the first 3 weeks of lactation. Milk fat yield also increased linearly over the first three weeks of lactation for all cows ($P < 0.001$).

Energy balance did not differ between NA treatment groups during the prepartum or postpartum period. Jersey cows were in a more positive energy balance compared to Holstein cows at one week prior to parturition (Figure 3; $P < 0.001$). The pattern of energy balance by Holstein and Jersey cows followed the patterns of NEFA increases leading up to parturition and DMI declining. Holstein cows exhibited more severe negative energy balance compared to Jersey cows postpartum ($P < 0.001$). Rastani (2001) reported that Jersey cows exhibited a less severe negative energy balance postpartum and remained in a negative energy balance for a short period of time compared to Holsteins. The more positive energy balance exhibited by Jersey cows was likely due to the decreased plasma NEFA levels and greater DMI both prepartum and postpartum. Jersey cows have a slightly lower energy requirement than do Holsteins. However, Jersey cows also consumed more Mcal/d relative to body weight.
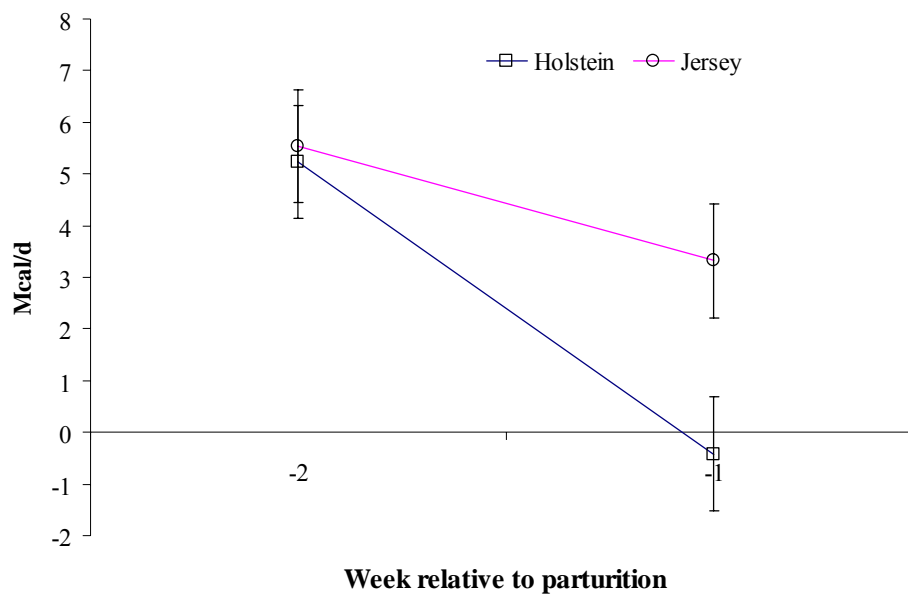
Figure 3. Least Square Means prepartum energy balance for Holstein and Jersey cows.

Table 6. Least square means for body condition score, body weight, dry matter intake, milk production and composition, and plasma metabolites of cows supplemented with varying levels of nicotinic acid during the prepartum period.

Prepartum	C[1]	L	H	Pooled SE	P <
BCS, units	3.74	3.61	3.59	0.14	0.37
BW, kg	680	669	672	31	0.89
DMI, % of BW	1.54	1.531	1.54	0.11	0.99
NEFA, µEq/L	249	356	302	91	0.34
BHBA, mg/dL	7.21	6.71	6.82	0.72	0.66
Glucose, mg/dL	79.5	77.2	78.0	2.9	0.60
Energy Balance, Mcal/d	4.76	3.05	2.45	1.54	0.19
Postpartum					
BCS, units	3.46	3.31	3.22	0.15	0.14
BW, kg	602	598	600	29	0.98
DMI, % of BW	2.59	2.78	2.38	0.15	0.01
Milk, kg	29.7	33.3	29.9	0.6	0.001
Milk fat, %	5.3	5.2	5.3	0.38	0.87
Milk fat, kg	1.53	1.63	1.52	0.13	0.49
Milk protein,%	3.8	3.8	3.5	0.25	0.17
Milk protein, kg	1.04	1.23	1.0	0.07	0.01
NEFA, µEq/L	750	753	715	70	0.77
BHBA, mg/dL	11.3	11.3	10.3	2.1	0.77
Glucose, mg/dL	78.3	74.9	86.5	16.0	0.64
Liver TAG[2], µg/µg DNA	7.4	7.6	9.7	4.3	0.76
AST[3], mg/dL	15.3	16.3	20.1	3.8	0.27
Energy Balance, Mcal/d	-13.7	-14.6	-14.1	2.4	0.89

[1]C= No supplemental nicotinic acid (NA), L=49 mg NA/kg BW, H=98mg NA/kg BW
[2]TAG= Triglyceride
[3]AST= Aspartate Aminotransferase

Table 7. Least Square Means for BCS, BW, DMI, milk production and composition, and plasma metabolites of Holstein and Jersey cows.

Prepartum	Holstein	Jersey	Pooled SE	*P* <
BCS, units	3.66	3.65	0.09	0.75
BW, kg	814	534	20	0.001
DMI, % of BW	1.45	1.62	0.07	†
NEFA, µEq/L	355	250	61	†
BHBA, mg/dL	6.22	7.61	0.48	0.01
Glucose, mg/dL	78.2	78.3	1.9	0.60
Energy Balance, Mcal/d	2.41	4.43	.99	‡
Postpartum				
BCS, units	3.28	3.38	0.10	0.30
BW, kg	714	486	43.27	0.001
DMI, % of BW	2.45	2.72	0.10	0.05
Milk, kg	38.20	23.69	1.78	0.001
Milk fat, %	4.95	5.95	0.27	0.015
Milk fat, kg	1.82	1.31	0.60	0.001
Milk protein,%	3.42	4.02	0.18	0.001
Milk protein, kg	1.25	0.93	0.52	0.001
NEFA, µEq/L	860.94	617.87	48.08	0.001
BHBA, mg/dL	10.67	11.28	1.45	0.65
Glucose, mg/dL	78.52	81.23	10.78	0.79
Liver TAG[1], µg/µg DNA	9.58	6.81	2.89	0.31
AST[2], mg/dL	16.4	18.1	2.5	0.48
Energy Balance, Mcal/d	-18.32	-9.95	1.64	0.001

[†] Breed*Day interaction significant; P < 0.01
[‡] Breed *Week interaction significant; P < 0.001
[1]TAG= Triglyceride
[2]AST= Aspartate Aminotransferase

Conclusion

Nicotinic acid supplementation had no affect on feed intake, blood metabolites, or milk production. However, these results corroborate differences in feed intake and lipolysis between Holstein and Jersey cows during late gestation and early lactation. The exact mechanism of this breed difference is unknown but regulation of hormone sensitive lipase or G-protein availability resulting in decreased levels of adipocyte cAMP appears a logical explanation. Nicotinic acid may have the ability to increase DMI and milk production in early lactation. However, like other studies the current experiment did not show a positive benefit from supplemental NA. Additional research is needed to determine if a level of supplemental NA, other than that examined in this experiment, can reduce lipolysis and improve intake during the time around parturition.

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