EFFECT OF SUPPLEMENTING THE NON-NUTRIENT, NON-IMMUNOGLOBULIN FRACTION OF COLOSTRUM TO DAIRY CALVES

Thesis

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ABSTRACT

Colostrum has been considered essential primarily because of the role it plays in providing immunoglobulins (Ig's) for passive immunity in the neonatal calf. In addition, colostrum contains a significant amount of growth factors and hormones that have the capacity to affect nutrient absorption and possibly nutrient utilization. The objective of this study was to evaluate the effect of early life supplementation of the non-immunoglobulin factors in colostrum, using a commercially available colostrum extract, on calf performance from birth until post-weaning. A pilot study was conducted as a dose titration to determine a level of colostrum extract to supply in the larger study and to evaluate efficacy. In the pilot study calves were fed one of four dosing levels thirty minutes prior to the first feeding. In the pilot study, calves fed four doses of colostrum extract before colostrum supplementation versus two doses had the highest level of plasma protein (9.2 g dL^{-1} vs 6.3 dL^{-1}) and ADG was enhanced in calves fed at least four doses of the colostrum extract. For the larger study, calves were fed either four doses of colostrum extract prior to the first colostrum feeding (TRT B), or four doses over four days (TRT C) compared to a control group fed no colostrum extract (TRT A). Calves were all supplemented with colostrum replacer and fed the same milk replacer and housed in a greenhouse barn with ambient temperature. For the first 21 days calves were fed only milk replacer (Period 1) and then from day 22 to 14 days post-weaning calves were offered free choice starter in addition to milk replacer (Period 2). Calves on TRT C had significantly higher plasma protein compared to calves on TRT A (7.5 g dL^{-1} vs 6.3 g dL^{-1}). There was no significant difference in average daily gain, a significant decrease in dry matter intake for TRT C, and calves on TRT C had numerically modest increase in feed efficiency than TRT B overall (0.59 kg gain kg DMI^{-1} vs 0.57 kg d gain kg DMI^{-1}). The results of this study do not indicate a clear overall effect, however, they do support improved colostrum absorption

suggesting that the colostrum extract successfully increased the uptake of nutrients from the colostrum fed. Additionally, calves fed colostrum extract over four days exhibited an improved feed efficiency when consuming a diet of milk and dry feed. These data support the potential for colostrum extract and the non-immunoglobulin fraction of colostrum to have impact on nutrient utilization in the neonatal calf.

Keywords: calves, colostrum, lactocrine, hormones, efficiency

BIOGRAPHICAL SKETCH

Kaitlin Andrews was born on November 20, 1992 to Cathi Strain and Jon Andrews in Cambridge, NY. Katie grew up in Greenwich, NY, a small farming community and place where her dairy roots began. She attended Greenwich Central schools from kindergarten through high-school and following graduation and began her college career in a pre-med program at Stonehill College in Easton, MA. It was there that she discovered she missed the sights, smells and people of dairy farming and decided to return to her roots in agriculture. As a third year student, Katie transferred to Cornell University under the advising of Dr. Thomas Overton to pursue her undergraduate degree in Dairy Management. During her undergraduate studies at Cornell, she participated in several internships where she was able to experience calf management and dairy cattle nutrition which further developed her passion and led her to apply to a graduate program for dairy nutrition. Upon commencement, Katie began studies for her Master of Science degree under the guidance of Dr. Michael E. Van Amburgh. Her thesis research evaluated the effect of the low molecular weight fraction of colostrum on dairy calf growth and performance. Somewhere between calf trials, she escaped to the Adirondacks for a weekend and became engaged to her fiancé Samuel Steinberg. Upon completion of her M.S. degree she will be relocating to Eastern New York to marry Sam on September 24, 2016. Katie has accepted a position as a dairy nutritionist with Land O'Lakes - Purina and will begin working as a dairy cattle nutritionist in October 2016. In this position, she is excited to be able to work with producers at the farm-gate and have the opportunity to better the industry of dairy nutrition.

To my family for always encouraging me to have goals and dreams and for building a strong foundation of faith and confidence to go forward and achieve them. To my fiancé, Sam, without your unwavering love, support and encouragement, this degree and all the trials and tribulations that it entailed would have been practically impossible.

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LIST OF ABBREVIATIONS

AFC	Age at First Calving
CE	Colostrum Extract
EGF	Epidermal Growth Factor
eGP	Endogenous glucose production
FPT	Failure of Passive Transfer
GH	Growth Hormone
GIT	Gastrointestinal Tract
Ig	Immunoglobulin
IGF	Insulin Growth Like Factors
IGFBP	Insulin Growth Like Factor Binding Protein
IGF-I	Insulin Growth Like Factor I
IgG	Immunoglobulin G
MEg	Metabolizable Energy Allowable for Gain
MR	Milk Replacer

Chapter 1:

Review of the Literature:

This review will focus primarily on the current understanding of neonatal requirements, components of maternal-colostrum as it relates to physiological development in the neonate, as well as observed growth differences as an outcome of neonatal nutrition. These effects will be reviewed as they are seen as potential outcomes of long-lasting epigenetic programming in the dairy replacement heifer performance and profitability.

Why maximize the potential of the dairy replacement heifer?

Raising dairy heifer replacements is one of the costliest aspects of a dairy business and given the natural interval between birth and calving, there is a significant delay in the time to initiate payback. Recent evaluations of average age at first calving (AFC) indicated approximately 25 months of age (NAHMS, 2007) which is slightly older than the 24 months of age in the previous evaluation (NAHMS, 2002). For a more interactive evaluation of heifer rearing programs benchmarks have been determined as way-points for evaluation (DCHA, 2016), but implementation of such approaches is still an issue in the industry and contradictions still exist concerning best approaches to grow and manage replacements. The traditional approach yields heifers fed a low cost, nutrient restricted diet with the expectation of the highest quality heifer as an outcome. However, after numerous years of research and work in the area, more recently there has been interest from dairy producers in maximizing the growth and energy status of dairy calves pre-weaning. Ultimately this approach is designed to reduce the time to AFC without a negative effect on the quality of the animal entering the herd allowing for a more productive first lactation

and increase the profit margin of the dairy herd. Through the reduction in the time to AFC paired with a maximization of the genetic potential of the heifer, allows for reduced costs and possible increased profitability margins over the lifetime of the dairy cow. The focus of this literature review is to characterize factors that impact the long-term productivity of dairy cattle by evaluating the nutrition and management of them starting at birth. The overall outcome is to elucidate and reinforce strategies designed to maximize the productive potential of the dairy replacement heifer beginning at birth.

Nutrient Supply and Productivity

Historically, dairy heifers have been viewed as a necessary cost that is void of return on the producers' investment. This approach has led to restricted feeding of calves to reduce the costs of raising, decrease incidence of disease such as scours and encourage dry-feed intake (Otterby and Linn, 1981, Anderson et al., 1987). This approach minimizes liquid-feed (milk or milk-replacer) intake and maximizes dry feed (starter grain/hay) in an effort to encourage consumption of lower cost feed-stuffs and accelerate rumen development. Evaluation of calf management data where calf rearing strategy was implemented have shown no significant reduction in time to weaning or a reduction in the incidence for scours or other disease (NAHMS, 2002, 2007, Soberon et al., 2012). When this feeding strategy is implemented it becomes inherently difficult for calves to meet their maintenance energy requirements year around and especially during the winter months. Maintenance energy is that portion of intake energy that is used to keep the calf alive by maintaining the animal's core body temperature and stable body weight (NRC, 2001); therefore to meet those requirements, calves require macronutrients such as fat and protein immediately after birth (Quigley and Drewry, 1998). Due to the nutrient composition of whole milk or milk replacer

as compared to starter grain and the lack of a functioning rumen, calves need to consume significantly greater quantities of grain to yield the same amount of metabolizable energy and protein they would receive from the same unit of liquid feed and prior to approximately 21 to 28 days of age that is relatively difficult. With calves having a dynamic maintenance cost, the challenge becomes accounting for the environmental effects on maintenance costs and adjusting the intake energy to ensure nutrients, especially energy are supplied in excess of the maintenance requirement.

Data exist that suggest there is potential for a profound impact on heifer performance, time to first lactation and milk production and this effect is dependent on nutrition and management of calves in the early stages of life. Feeding an ad-libitum amount as compared to a restricted amount of milk or milk-replacer in the pre-weaning phase of life demonstrated an increase in average daily gain (ADG) and subsequent pre-pubertal increases in gain to feed ratios in dairy heifers (Shamay et al., 2005, Terré et al., 2009). Calves that were followed and fed formulated diets up to and through first lactation had a decreased age to puberty and subsequently were younger at AFC (Shamay et al., 2005). In Soberon et al. (2012) intake above maintenance was analyzed to determine if there was a relationship between energy above maintenance and first lactation milk yield. The study evaluated first lactation milk yield as a function of ADG prior to weaning and found that for every 1 kg of pre-pubertal ADG an increase of approximately 850 kg of milk yield was observed in the first lactation (Soberon et al., 2012). Similarly, Moallem et al., (2010) and Heinrichs and Heinrichs (2011) found a positive correlation between dry matter intake (DMI) at weaning and milk yield in the first and subsequent lactations. Illness in the pre-weaning phase of life can have long-term negative effects on milk production. This can be seen as early as the first lactation and follow through the lifetime of the cow as increased time to first lactation and

decreased performance during lactation (Moallem et al., 2010, Heinrichs and Heinrichs, 2011). Outcomes like this have led to a desire for decreased illness and enhanced management practices in early-life to help maximize the potential of those calves once they enter lactation. Adopting feeding programs to meet and exceed the maintenance requirements of the neonatal calf and provide enough to achieve a high growth rate can have a profound impact on the health, growth and productivity of dairy replacements (Bar-Peled et al., 1997, Shamay et al., 2005, Moallem et al., 2010, Van Amburgh et al., 2011, Soberon et al., 2012, Soberon and Van Amburgh, 2013).

Neonatal Requirements and Colostrum

The adaptation from fetal to neonatal life is a major event that requires orchestration of physiological changes, nutritional provisions and adjustments in metabolic state. Upon parturition there is cessation of continuous maternal nutrient supply and the calf must metabolically shift to function autonomously utilizing nutrients provided in discontinuous feedings (Hammon et al., 2013). A calf is born with minimal energy reserves and a rapidly changing metabolism and has an intrinsic maintenance requirement that needs to continuously be met. The maintenance requirement is the basal energy level at which metabolic body weight is static and essential life processes can occur, therefore calves are in need of macronutrients such as fat and protein immediately after birth (Quigley and Drewry, 1998). The 2001 NRC outlines nutrients required for maintenance and nutrients needed for gain throughout the pre-weaning phase of life (NRC, 2001) and as the calf's environment changes, multiple physiological adaptations are necessary to develop their metabolism to provide continual absorption and utilization of dietary nutrients.

Evolutionarily colostrum has been designed to fit this neonatal need and provide the basis for the start of extra-uterine life. In-utero, nutrition was supplied mainly via maternal circulation until late gestation when the calf begins endogenous glucose production (eGP) (DiGiacomo and Hay, 1990, Fowden et al., 1998). In the final stages of development, calves develop some lactase enzymatic capacity and upon parturition and ingestion of colostrum, must begin utilizing lactase to digest lactose and hydrolyze it to its metabolically useful forms: galactose and glucose (Freund et al., 1995, Dudley et al., 1996). Colostrum provides a segue of nutritional provision from fetal to neonatal life and stimulates enzyme production that continues to have activity through the milk-feeding phase of life (Dudley et al., 1996, Jost et al., 1998).

Colostrum as the 'first-milk' is compositionally different than whole-milk produced after a few days and is the calf's first exposure to extra-uterine nutrients. There is a significantly higher protein to fat (2.1:1) ratio of colostrum as compared to whole-milk (0.8:1) and a multitude of immunoglobulins, hormones, growth factors, peptides and immune-factors present in colostrum at first milking post-calving and then dissipate over the first 3 to 4 days of lactation. Uniquely, these factors are entirely absent in whole-milk or present in minute amounts.

Due to the short lived but concentrated presence of these factors in colostrum, a look at colostrogenesis is relevant. Colostrum, consists of approximately 6.7% fat and 14% protein as reported by Kehoe et al. (Kehoe et al., 2007) and supplies metabolizable energy (ME) largely through fat and lactose, in addition to a variety of proteins (Akers, 2002, Patton, 2004). Much work can be found investigating how these macronutrients are synthesized and or arrive in the mammary gland for excretion in the milk. Beginning in the late stages of gestation, mammary tissue rapidly develops and in the weeks prior to parturition and colostrogenesis commences (Barrington et al., 2001). During the process of colostrogenesis, macronutrients, micronutrients

and other proteins that have come to be known as the low molecular weight fraction must all find their way from blood circulation or tissue into the mammary gland. While exact mechanisms are not elucidated for all components clear paths have been extensively researched and demonstrated for several components.

For this review, pathways of macronutrients will be highlighted first and working towards the non-nutritive factors. Lactose is largely the driver in the production of milk since it acts as the osmotic gradient to pull water in. Lactose is comprised from two units of glucose; one unit of glucose maintains structure as glucose, the second is converted via enzymatic action to galactose. The unit of glucose is then attached to the unit of galactose via lactose synthase and lactose is formed (Akers, 2002). Glucose can also be involved in the biosynthesis of milk fat by production of glycerol, although it is not as common in ruminants as milk fat synthesis from free fatty acids that are readily taken up from capillaries into the secretory cells. Fatty acids in milk are largely in the form of triglycerides which can have mainly three sources: glucose via glycolysis and conversion in the TCA cycle to acetyl CoA in the cytoplasm, from feedstuffs by way of chylomicra hydrolysis as well as de novo synthesis in the mammary gland itself (Akers, 2002). In the secretory cell, fatty acids and glycerol will become triacylglycerols in the presence of enzymes, becoming what is better known as milk fat (Akers, 2002, Patton, 2004). In the aqueous environment of the secretory epithelial cell, the triacylglycerols condense to form droplets and a larger hydrophobic molecule to protect against the polarity of their aqueous environment, migrating towards the lipid membrane of the cell. As the fat droplets grow and come into contact with the outer cell membrane, they begin to press outwards toward the lumen of the alveoli until they become enveloped by the membrane and released into the lumen where other secreted milk

begins to accumulate (Patton, 2004). Through these components, colostrum can meet the energy needs of the calf during this period and can also promote gluconeogenesis (Hammon et al., 2013).

While carbohydrate and fat components are important and essential to the calf, protein is necessary in the form of immunoglobulins, hormones and growth factors and amino acids. Milk protein comes in a variety of forms, both nutritive and non-nutritive and has an array of functions in the neonate. Milk protein present in colostrum is largely transported into the secretory cell from maternal circulation. Some proteins will pass directly through the lactating epithelial cell and into the alveolar lumen unchanged, whereas others may undergo synthesis in the secretory cells from amino acid building blocks (Akers, 2002, Patton, 2004). In the case of colostrum, of interest are the non-nutritive factors that are present to help the neonate to utilize the components of colostrum to their fullest potential. Such factors include, but are not limited to: immunoglobulins, IGF-I, insulin, epidermal growth factor (EGF), transforming growth factor-alpha (TGF-α), TGF-β, leptin, growth hormone, relaxin, prolactin, estradiol, cortisol, and oligosaccharides (Blum and Hammon, 2000, Bonnet et al., 2002, Asakuma et al., 2007, Blum and Baumrucker, 2008). These factors have been far less extensively studied than lactose, fat or nutritive milk protein; however, there are data that provide insight into mechanisms that could allow for such an abundant arrival of these non-nutritive proteins in colostrum. Immunoglobulins generally take center stage in the discussion of colostrum. They provide passive immunity to the calf that has a naïve immune system at birth, and they are present in small amounts in milk, but in colostrum they have a substantial presence and constitute approximately 90% of the protein in colostrum (Butler, 1974, Larson and Fox, 1992). Due to the significant requirement of immunoglobulins, the mechanism for their entry into colostrum has been fairly well studied. During the last few weeks of gestation as colostrogenesis is taking place, immunoglobulins from circulation are transported into the secretory cell via IgG

receptors, where they enter the golgi apparatus. As they are processed via the golgi, they are enveloped in a vesicle and released into the cytoplasm. After release, the vesicle containing the immunoglobulin travels the length of the secretory cell towards the plasma membrane where it will eventually attach and release its immunoglobulin contents to the alveolar lumen (Patton, 2004). Immunoglobulins travel through the secretory cells, and not between them to arrive within the secretory cell and for processing to enter colostrum, this happens at increasing rates right up to the moments of parturition (Larson et al., 1980, Akers, 2002).

Hormones, growth and immune-factors are not as clearly established in the literature as to their origins, but nonetheless there are available data regarding their entry into colostrum. Within the structure of the mammary gland and in particular among the cells of the alveolus, there is an interstitial space that contains lymph fluid near the base of the mammary epithelial cells. The interstitial space is also in the same vicinity as the capillaries that flow through the alveoli lending to one proposed mechanism of colostrum synthesis in the interstitial fluid (Patton, 2004). During the days around parturition, blood flow to the mammary gland is increased, and as lymph vessels around the mammary gland flow in one direction, there is a hypothesis (Patton, 2004) that the hormones, growth and immune factors build up in the interstitial space, thought to belong to the lymph system, and are pushed through the secretory cells to allow for excretion via colostrum to rid of the build-up. Evidence that demonstrates an openness in the tight junctions between secretory cells pre-partum is supportive of that hypothesis. Work in this area has shown that the tight-junctions that form the milk-blood barrier during lactation are not yet fully established (Nguyen and Neville, 1998, Stelwagen and Singh, 2014) at the time of parturition and that allows for spilling of the hormones (Stelwagen et al., 1994), growth and immune-factors between the secretory cells and their subsequent accumulation in the alveolar lumen to be excreted via milking

(Anderson, 1985, Akers, 2002, Patton, 2004). Due to the high circulating levels of these bioactive components in late gestation (Edgerton and Hafs, 1973, Arije et al., 1974), and especially at the time of parturition, these hypotheses are both probable explanations of how colostrum becomes abundant with these proteins at the time of colostrogenesis and in secretion of the first milk. The variety of factors present in colostrum have previously been questioned as to their purpose and effect and are still presently being evaluated to further understand their potential in the neonate (Donovan and Odle, 1994, Blum and Hammon, 2000).

Epigenetic Impact of Colostrum

Much data can be found supporting the colostrum quality and quantity that calves should receive in the early hours of life to support adequate immunoglobulin (Ig) level intake and establishment of passive immunity. Colostrum quality becomes one of the most important factors in successful reduction of failure of passive transfer (FPT) to promote maximum Ig absorption and passive immune protection until the calf's naïve immune system has adequate time to develop (Godden, 2008, Beam et al., 2009).

While the Ig status of a calf is fundamentally very important to a calf program, the remainder review will focus primarily on this bioactive or non-nutritive fraction of colostrum and its implications on growth and development of the calf. Several studies have outlined the presence of this fraction in colostrum across various species and the length of time for which it is present in mammary secretions. Outcomes of research where the non-nutritive fraction was fed against a naïve control have shown increased gastrointestinal tract (GIT) growth rate, improved digestion and alterations of metabolism. Ingestion of these bioactive compounds has demonstrated various

effects resulting in direct or indirect promotion of anabolism in the neonatal calf (Baumrucker et al., 1994, Blum, 1997, Guilloteau et al., 1997, Bühler et al., 1998, Blum and Hammon, 2000, Kühne et al., 2000, Blättler et al., 2001, David et al., 2003, Norrman et al., 2003, Sauter et al., 2003, Bittrich et al., 2004, Sauter et al., 2004, Blum et al., 2005, Blum, 2006). With this data, there is opportunity to enhance productivity of the calf in the post-natal period by promoting an anabolic state of metabolism in the calf. This could be achieved through colostrum component feeding strategies which might also positively impact the growth potential of the calf. With so much emphasis in the early hours of life and focus placed on achieving passive transfer from dam to calf, it is easy to understand how the epigenetic impact of perinatal management practices might be more easily overlooked in day to day practice. Epigenetics, described by Waddington circa 1940, was said to encompass the environmental effect on the genes of a species and the phenotypic expression of those genes (Waddington, 1940, Waddington, 1942). While we are still aiming to understand the full impact that early-life management might have on the lifetime of the lactating dairy cow, there are published data in bovine and other species demonstrating the potential of the epigenetic effect on phenotypic expression of functions in several species. With better understanding of gene expression and environmental impact there is now evidence of the ability to turn on or off gene capacity by nutritional and non-nutritional factors (Waterland and Jirtle, 2004, Jirtle and Skinner, 2007). In 2008, Bartol, Wiley and Bagnell coined the term 'Lactocrine hypothesis' to help explain the effect that colostrum or first-milk has on the neonate. Their work in piglets demonstrated the effect of programming via maternal hormones resulting from ingestion of colostrum by neonates. The hypothesis describes the ingestion of milk-borne morphological factors as a way of extra-uterine communication (Bartol et al., 2008, Bartol et al., 2013). Supporting evidence for the lactocrine hypothesis can be found in the work of Baumrucker, et al.,

1994 where through direct work and review, they demonstrated a physiological effect of increased gut maturation in calves that were fed supplemental IGF-I subsequent colostrum feeding when compared to IGF-I absent milk replacer (MR) fed calves (Baumrucker and Blum, 1993). Subsequent studies demonstrate significant results of oral IGF-I supplementation via colostrum or in addition to milk replacer on increased quantity of IGF binding proteins (IGFBPs) and intestinal receptor populations (Baumrucker et al., 1994). In this time of accelerated GIT growth and development, IGF-I is one of the growth factors in the non-nutritive fraction that can act locally in the GIT facilitating growth and maturation of the GIT (Hammon and Blum, 2002). Some parameters that have been established in monitoring the effect of IGF-I on intestinal development are crypt cell proliferation (Blättler et al., 2001) and villus height in the GIT (Roffler et al., 2003). Both of these measurements have been evaluated in various studies and shown to increase in quantity and efficiency of absorption in the days after exposure to IGF-I in the colostrum or when given as part of an extract (Roffler et al., 2003).

While each hormone of the non-nutritive fraction has different physiological targets within species, in the neonatal calf we strive to understand how they work harmoniously in the promotion of an anabolic state primarily in the first few days of life. Earlier work shows that dietary IGF-I can enter blood circulation (Baumrucker et al., 1992) and the investigators suggest that IGF-I appears in neonatal blood as a result of rapid uptake in the small intestine; arriving in the gut in a biologically active form with a stimulatory effect on intestinal growth (Baumrucker and Blum, 1993). Insulin and IGF-I have a transient relationship after the first feeding of colostrum and supporting data show that calves fed a first meal absent in IGF-I have higher plasma insulin concentrations than an IGF-I + control (Baumrucker and Blum, 1993). Though this effect can only be seen after the first feeding, there is evidence in other species where rh-IGF-I infused across the

pancreas causes suppression in insulin secretion (Leahy and Vandekerkhove, 1990). Combining the effect of insulin suppression and increased uptake of glucose by metabolism of lactose are supportive of the idea that the calf has a system present at birth that promotes anabolism.

Much like IGF-I, insulin is a key factor in the early development of metabolism in the neonate and is well established in its ability to be absorbed across the GIT (Pierce et al., 1964, Shen and Xu, 2000). Primarily, insulin is thought to maintain glucose homeostasis, and there is a significant amount of insulin in colostrum in the first day of secretion. Much work done by various researchers outlines a relationship between calves that are fed intact colostrum (inclusive of the non-nutritive fraction) compared to milk replacer (naïve of the non-nutritive fraction) and their subsequent quantity of GIT IGF and insulin receptors (Hammon and Blum, 2002) as well as their circulating status of these hormones (Steinhoff-Wagner et al., 2011). In the paper by Steinhoff-Wagner et al. 2011, the authors were able to demonstrate that calves receiving colostrum versus a formula that was equal in nutrient content but void of the non-nutritive fraction maintained higher circulating glucose and are more insulin-responsive over the first four days of colostrum feeding. Endogenous glucose production was also measured in this study, and the insulin in colostrum did not inhibit glucose production in the neonatal calf; notably, the glucose absorption increased in response to a colostrum feeding vs a formula feeding. Soberon, (2011) made similar observations in response to colostrum feeding where calves were fed high and low levels of pooled colostrum. In the study by Soberon (2011), the calves fed a high level of colostrum had subsequently higher circulating insulin levels, but also higher circulating glucose levels. These data are supportive of an unpaired relationship between insulin and glucose in the neonate encouraging a more anabolic state and positive energy balance.

When connecting the neonatal dairy calf management period to heifer performance, calves that had a higher status of colostrum also had higher ADG when allowed access to 12 L MR per day. Data from Faber et al. 2005 also showed that the amount of colostrum fed at birth had a significant effect on pre-pubertal ADG and a trend for increased milk yield through the second lactation however due to the study design, it was not possible to determine if this was through greater feed intake, higher feed efficiency or a combination of both (Faber et al., 2005).

In order to understand the impact of the first meal, Jones et al. (2004) fed two groups of calves, one with a maternal intact-colostrum and another with a serum-based colostrum replacer (most likely naïve of the non-nutritive fraction) with iso-immunoglobulin status. Following this, each group was divided again – one to receive a milk replacer with animal plasma and the other without. As a result of this study, all calves had nearly identical Ig status and calves fed maternal colostrum had significantly higher feed efficiencies primarily in the first week, but the effect was pronounced enough that it could be detected at weaning (Jones et al., 2004). The results of this work provide support that independent of immunoglobulin, colostrum is providing something with influence on metabolic status of these calves. The implication here is that there may be influence throughout the lifetime of the dairy cow on feed efficiency dependent on their first meal. Current research is still working to evaluate the potential carry-over effect of dietary exposure to the non-nutritive fraction in the first and subsequent meals.

Outcomes on replacement programs

With evidence that AFC can be positively manipulated by achieving differing growth rates (Van Amburgh et al., 1998) a reasonable goal can be set to achieve the best performance in

lactation at the lowest AFC. There is opportunity for dairy farmers to positively impact profitability when examining evidence that colostrum fed calves show higher feed efficiency than their colostrum-replacement fed herd-mates (Jones et al., 2004) and heifers that receive a higher amount of the non-nutritive fraction in early life may have an additional opportunity to be more profitable as an outcome of increased milk yield (Faber et al., 2005). A 2015 analysis performed by Akins and Hagedorn highlights the cost to raise a dairy replacement in Wisconsin at $2,510 (Akins, 2015). This is a significant cost that can be reduced by shortening the interval from birth through breeding. For example, calves with higher feed efficiency need less nutrients to achieve the same unit of body mass gain; additionally, when fed to maximize this potential, the time required to meet biological benchmarks (Fox et al., 1999; NRC, 2001) can be reduced (Van Amburgh et al., 1998). With a reduction in the heifer rearing time period, subsequent heifer rearing costs will be decreased allowing the heifer entering the first lactation to have a better opportunity to be more profitable because of reduced cost.

Summary and Hypothesis

From the reviewed data, a question remains concerning the performance of calves when fed the non-nutritive fraction of colostrum and are provided iso-immunoglobulins and enough nutrients from milk or milk replacer to at least double their birth weight: what are the expectations for calves that receive more of these factors, increased ADG or enhanced feed efficiency? From the work cited in this review, there is a basis of understanding that the non-nutritive fraction has a stimulatory effect on growth of the GIT and ultimately promotion of anabolism in the newborn. However, given the design of many of these studies, the same calves were not monitored all the way through the pre-weaning phase of life. That leaves open the opportunity to explore if feeding

additional components of the non-nutritive fraction at birth might have impact on the GIT development early in life and absorption of other components might alter feed intake and metabolism of the calf. And if so, can this effect be modified by increasing the amount of the non-nutritive factors in colostrum to affect development of the calf?

With further investigation, the effects of additional feeding of the non-nutritive fraction in the early days on neonatal life could be evaluated in its effects on ADG, feed efficiency, AFC and first lactation milk production. Insight into these effects would better help the dairy industry to understand the most effective way to increase marginal profitability in their herds through heifer rearing.

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CHAPTER 2

EFFECT OF SUPPLEMENTING THE NON-NUTRIENT, NON-IMMUNOGLOBULIN FRACTION OF COLOSTRUM TO DAIRY CALVES

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ABSTRACT

Colostrum has been considered essential primarily because of the role it plays in providing immunoglobulins (Ig's) as a source of passive immunity in the neonatal calf. In addition, colostrum contains a significant amount of growth factors and hormones that have the capacity to affect nutrient absorption and possibly nutrient utilization. The objective of this study was to evaluate the effect of early life supplementation of those factors in colostrum, using a commercially available colostrum extract, on calf performance from birth until post-weaning. A pilot study was conducted as a dose titration to determine a level of colostrum extract to supply in the larger study and to evaluate efficacy. In the pilot study calves were fed one of four dosing levels thirty minutes prior to the first colostrum feeding. In the pilot study, calves fed four doses of colostrum extract before colostrum supplementation versus two doses had the highest level of plasma protein (9.2 g dL^{-1} vs 6.3 dL^{-1}) and ADG was enhanced in calves fed at least four doses of the colostrum extract. For the larger study, calves were fed either four doses of colostrum extract prior to the first colostrum feeding (TRT B), or four doses over four days (TRT C) compared to a control group fed no colostrum extract (TRT A). Calves were all supplemented with colostrum replacer and fed the same milk replacer and housed in a greenhouse barn with ambient temperature.

For the first 21 days calves were fed only milk replacer (Period 1) and then from day 22 to 14 days post-weaning calves were offered free choice starter in addition to milk replacer (Period 2). Calves on TRT C had significantly higher plasma protein compared to calves on TRT A (7.5 g dL^{-1} vs 6.3 g dL^{-1}). There was no significant difference in average daily gain, a significant decrease in dry matter intake for TRT C, and calves on TRT C had numerically modest increase in feed efficiency than TRT B overall (0.59 kg gain kg DMI^{-1} vs 0.57 kg d gain kg DMI^{-1}). The results of this study do not indicate a clear overall effect, however, they do support improved colostrum absorption suggesting that the colostrum extract successfully increased the uptake of nutrients from the colostrum fed. Additionally, calves fed colostrum extract over four days exhibited an improved feed efficiency when consuming a diet of milk and dry feed. These data support the potential for colostrum extract and the non-immunoglobulin fraction of colostrum to have impact on nutrient utilization in the neonatal calf.

Keywords: calves, colostrum, lactocrine, hormones, efficiency

INTRODUCTION

The adaptation from fetal to neonatal life is a major event that requires orchestration of physiological changes, nutritional provisions and adjustments in metabolic state. Upon parturition there is cessation of continuous maternal nutrient supply and the calf must metabolically shift to function autonomously utilizing nutrients provided in discontinuous feedings (Hammon et al., 2013). The first hours and subsequent days of life can have a significant impact on the life of the calf and can potentially affect the performance of the animal over its lifetime thus appropriate

management practices should be focused on optimizing the growth and health of the calf (Soberon et al., 2012, Soberon and Van Amburgh, 2013). The presence of non-nutritional factors in colostrum and their effects have been described and evaluated as early as the 1960s (Pierce et al., 1964). Cattle, pigs and other species produce colostrum as the first mammary secretions and the first colostrum is usually the richest in nutrients, immunoglobulins, growth factors and hormones and these non-nutrient factors have the ability to impart a significant effect on the neonate (Hammon and Blum, 1998, Steinhoff-Wagner et al., 2011, Frankshun et al., 2012). Immunoglobulins are well known for their establishment of passive immunity (Godden, 2008), but non-nutritive factors present in colostrum such as, insulin (65 µg/L), IGF-I (310 µg/dL), growth hormone (1.4 µg/dL), TGF-α (210 µg/dL) have all demonstrated effects on gastrointestinal tract development and nutrient uptake and metabolism in the neonate (Grosvenor et al., 1993, Blum and Baumrucker, 2008, Steinhoff-Wagner et al., 2011, Hammon et al., 2013). In the first few days after birth, the calf has glucose transporters present on the mucosal side of the small intestine that can be influenced by the consumption of colostrum (Shirazi-Beechey, 1995, Steinhoff-Wagner et al., 2014) and these transporters have been shown to increase glucose uptake without increasing the quantity of transporters in the presence of colostrum feeding (Steinhoff-Wagner et al., 2014). In an experiment evaluating a non-immunological outcome of colostrum intake, calves were fed colostrum harvested over the first four days of lactation for four days compared to calves fed an iso-nutrient formula. The calves fed colostrum demonstrated significantly greater circulating plasma glucose and higher plasma insulin, suggesting that the non-nutritive components of colostrum were positively impacting glucose absorption from the gastrointestinal tract (Steinhoff-Wagner et al., 2011).

The delivery of factors other than nutrients through mammary secretions is a form of communication from the dam to the offspring and this has been termed the Lactocrine Hypothesis (Bartol et al., 2008, Bartol et al., 2009) and this term captures the concept of continued communication to the offspring once extra-uterine life has begun. Accordingly, colostrum components have the potential to influence the productivity of calves through enhanced growth, feed efficiency and milk yield (DeNise et al., 1989, Faber et al., 2005, Soberon et al., 2012).

Colostrum replacers are now widely available and some of the colostrum products have been differentiated into the various components of colostrum for other uses (Elfstrand et al., 2002, Poulsen et al., 2010, Cabral et al., 2013). It is now possible to use processes like reverse osmosis to remove or concentrate proteins and other low-molecular weight compounds in milk (Korhonen et al., 2010) and this provides an opportunity to evaluate these extracts for bio-activity.

Our hypothesis was that supplementation of additional non-nutritive, non-Ig factors present in colostrum, by way of a colostrum extract would have the potential to positively affect the performance and nutrient utilization of the calves. This study evaluated the effect of supplementing a commercially available colostrum extract on the feeding behavior, growth and feed efficiency of calves that received the same colostrum replacer and milk replacer over the first 63 days of life.

MATERIALS AND METHODS

All protocols involving the use of animals were reviewed and approved by the Cornell University Institutional Animal Care and Use Committee under protocol number 2012-0072.

Table 2.1. The nutrient and hormone profile of the colostrum extract. Each dose of colostrum extract contained 1.3 g of dry matter.

Item	
Protein, % DM	55
Fat, %DM	7
Ash, %DM	8
Lactoferrin, mg/g	4.82
IGF-I, µg/g	2.06
Insulin, ng/g	12.53
Relaxin, ng/g[2]	5.04

values as labeled
[2] as measured

Sterling Technologies, Brookings, SD

Pilot Study:

Eighteen Holstein calves (9 male and 9 female) born at the Cornell University Ruminant Center (Harford, NY) were randomly assigned to one of four treatments at birth from August to October, 2015. The colostrum extract (CE) (Immu-prime, colostrum extract, Sterling Technologies, Inc., Brookings, SD) used in the pilot study was in the form of a liquid suspension in a tube similar to an antibiotic treatment for mastitis. Calves assigned to TRT A received two doses of colostrum extract (CE), TRT B received three doses, TRT C received four doses and TRT D received six doses. Each dose of CE contained 1.3 g of what is referred to as the non-immunoglobulin, non-nutritive fraction of colostrum. After 30 min, all calves were given 4L of colostrum replacer (240g IgG replacement, Sterling Technologies Inc., Brookings, SD) via esophageal tube within 2 h of birth and a second feeding of two liters of colostrum replacer (120g IgG replacement, Sterling Technologies Inc., Brookings, SD) 12h later. Due to a mis-communication, each package of colostrum replacer used in this trial contained a dose of the colostrum extract in a dry, powdered form. Thus, all calves received two unplanned doses of colostrum extract at the time of the first feeding and this has been accounted for in the treatments doses described below. Absorption related to the addition of the CE was evaluated on a plasma protein measurement on a digital refractometer at 48 hours after the first colostrum feeding as a proxy for immunoglobulin uptake.

Main Trial:

Forty-eight Holstein calves (11 male, 37 female) born at the Cornell University Ruminant Center were randomly assigned to one of three treatments at birth from January to March of 2016 and balanced by treatment for sex of calf and dam parity. Each calf was separated from the dam,

placed in a straw bedded box stall equipped with radiant floor heat and over-head heat lamps to provide warmth. The calf was then dried and colostrum extract was administered orally according to treatment. The first meal of colostrum was given thirty-minutes later and consisted of 4L of colostrum replacement via esophageal tube.

The colostrum replacer fed for the first and second feedings of was sourced from the same lot (Sterling Technologies Inc., Brookings, SD) and was a dried whole-colostrum replacement product with no added colostrum extract. Each packet consisted of 120g of IgG and was reconstituted to two liters total volume per packet with 46^0C water. All feedings were mixed to twenty-eight percent solids and fed at 39^0C within the first two hours of life.

All calves were given 4L of colostrum replacer (240g IgG replacement, Sterling Technologies Inc., Brookings, SD) via esophageal tube and a second feeding of two liters of colostrum replacer (120g Ig replacement, Sterling Technologies Inc., Brookings, SD) 12h later. TRT A served as the control group and did not receive anything additional to their colostrum feedings. Calves on TRT B were given four oral doses of 12mL each of CE (Immu-prime, colostrum extract, Sterling Technologies Inc., Brookings, SD) thirty-minutes prior to the first colostrum feeding and TRT C calves were given a total of four 12mL doses of CE. The first dose for TRT C was given thirty-minutes prior to the first colostrum feeding, the subsequent three doses were each given thirty-minutes prior to the morning milk feeding on days two, three and four of life. All doses of CE were sourced from the same lot during the pilot and main trials and the composition of the CE. The nutrient and hormone profile is from the manufacturer except for Relaxin (Table 2.1).

Calves remained in the box stall until after consuming the second colostrum feeding, and then they were weighed, measured for stature and moved to an individual pen in a greenhouse style calf barn. The wire panel pens were three square meters in area and deep bedded with straw. Calves

were maintained in the same pen for the duration of the study and at 64 days of age were removed and continued on in the farm's heifer raising system.

Once calves were in the greenhouse barn, their diet consisted of a 30% protein, 32% fat milk replacer (Bovine Innovation Group, 30/32 milk replacer, Keystone Mills, Romulus, NY) mixed at 15% solids for 62 days. Milk replacer mixing temperature and concentrations were measured and recorded at each feeding to ensure consistency. Milk replacer concentration was evaluated using a digital refractometer (Misco Digital Dairy Refractometer, Model DD3, Solon, OH). The calves were stepped up and offered up to 10.5 L of reconstituted milk replacer per day. On day 22, calves were offered ad-libitum access to a 60:40 blended starter grain mix of consisting of a commercially available 24% CP flavored calf grain (Calf Manna, Manna Pro, Chesterfield, MO), respectively. Fresh, clean, warm water was offered three times daily by bottle until day 21 and free-choice by bucket from day 22 through the end of the study at 63 days. All milk replacer offered and refused was weighed and recorded at each feeding for calculating intake. Also, any starter grain offered and refused was weighed and recorded three times daily.

Daily temperature and relative humidity was monitored and measured every fifteen minutes by three resident Hobo environmental data loggers (Onset Computer Corporation, Bourne, MA) installed around the barn. These data were recorded and used to aid in the calculation of maintenance energy costs of the calves to determine energy intake over maintenance. Measurements were made weekly of BW, and hip and wither height. All BW were taken by scale (WayPig 300 Digital scales, RayTec Mfg., Ephrata, PA) and height was evaluated with a level measuring stick.

A blood sample taken at 48 hours after the first feeding of colostrum and analyzed for hematocrit and total plasma protein concentration using a digital refractometer (Misco

Refractometer, Solon, OH). Blood samples were collected weekly from birth through weaning, placed immediately on ice and then centrifuged at 3,000 g. Plasma was allocated into five microfuge tubes and frozen at -20 °C until analyzed. All blood samples were collected 4-6 hours after the morning milk replacer feeding.

Relaxin was measured using a quantitative sandwich ELISA kit (Mybiosource.com, San Diego, CA). In short, 50µl of sample was added to each well, followed by 100µl of HRP-conjugate and incubated for 60 minutes at 37^0C. The contents were then aspirated, the plate was washed and 50µl of Chromagen A solution was added to each well, mixed and allowed to incubate in the dark for 15 minutes at 37^0C, allowing color to develop. Immediately following incubation, stop solution (50µl) was added and optical density was read at 450nm using a microplate reader. Other hormones and growth factors are present in the colostrum extract, however, resources did not allow for a comprehensive evaluation of the product.

Further analysis of plasma metabolites is ongoing.

Statistical Analysis:

Pilot Study:

Individual hematocrit-corrected total plasma protein levels were evaluated using fit of least squared means within JMP Pro 12 (SAS Inst. Inc., Cary, NC). The statistical model had an outcome of total plasma protein and evaluated the main effect of treatment. Using a mixed model for ADG, a regression was developed using measured BW for each calf over the 3 week study and the slope was used to evaluate daily gain based on the main effect of treatment. Significance was declared at $P < 0.05$.

Main Study:

The study was designed with two periods: period 1 (P1) days 2-21 where calves were fed exclusively milk replacer and period 2 (P2) where calves were fed up to 10.5 L of milk replacer and offered ad-libitum starter grain. One calf died of causes unrelated to the study and was therefore excluded from analysis. For all calves, individual growth rates were determined by regression of each calf's body weight over the days on treatment; the slopes of the regressions were considered the average daily gain (ADG). Data were analyzed using a mixed model and fitting least square means in JMP Pro 12 (SAS Inst. Inc., Cary, NC). The model included birth weight as a covariate where applicable. Fixed effects were TRT, Period and the interaction of Period and TRT where applicable. Significance was declared at $P < 0.05$ and a trend was declared at $P < 0.1$.

RESULTS AND DISCUSSION

Pilot Study:

The effect of the components of colostrum or CE has been investigated (Blättler et al., 2001, Roffler et al., 2003, Steinhoff-Wagner et al., 2011), however, most of those investigators collected their own extract and had not utilized a commercially available version nor had they evaluated varying doses. In order to have a foundation for the main trial, a dose titration was necessary to understand the effect of varying amounts of CE.

Calves fed 4 doses (TRT C) at birth had higher TPP levels compared to calves fed 2 doses (TRT A) ($P = 0.04$) (Table 2.2), thus 4 doses was chosen as the level to administer as a treatment for the main trial. At 3 weeks of age, calves showed no difference in ADG between treatments and due

to a computer malfunction with the auto-feeder mixing concentration, the result was an ADG of 0.27 kg/d, lower than what was previously evaluated under similar conditions (Soberon and Van Amburgh, 2012) and due to the undetected mixing error. Given the study protocol, bull calves left the study at 21 days, however weaning weights of heifer calves were used to evaluate ADG w at weaning. Calves fed 7 doses (TRT D) at birth had higher ADG from birth to weaning than calves fed 2 doses (TRT A), however, due to limited number of calves at the time of weaning this was not evaluated for statistical significance.

Main Study:

Each calf received 240g of IgG in the first colostrum feeding and a total of 360g of IgG within the first 24 hours of life. The colostrum extract contains no Ig's, therefore all calves were administered iso-Ig first and second meals. To evaluate blood parameters in calves, we elected to correct all values for hematocrit due to the possible variation in plasma volume of a calf (Quigley and Drewry, 1998, Bachmann et al., 2012). Given the possible fluctuation due to amount and timing of fluid consumed and ambient temperature, it seemed prudent to account for this measure when evaluating plasma concentrations of proteins, metabolites, nutrients and other factors, especially when studies are conducted over time, among seasons and when small concentration differences can be important. Although not directly evaluated, an example of the potential range in hematocrit can be seen between the pilot study and the main study, where the overall mean range was from 22% to 33%, a 50% difference from the lowest to the highest value, and an individual calf range from

Table 2.2. ***Pilot Study:*** Total plasma proteins (TPP) and average daily gain (ADG), for all treatments and periods. Treatment A – control, 2 doses Colostrum Extract (CE), B – 3 doses of

CE, C – 4 doses of CE. D – 6 doses of CE. All CE was given prior to the first colostrum feeding. Means and standard errors are shown.

	Units	2 doses	3 doses	4 doses	6 doses	SEM
n		5	5	4	4	
Days on TRT		21	21	21	21	
TPP	g/dL	6.34[a]	7.24[a]	9.15[b]	8.24[b]	0.65
Hematocrit	%	30	25	22	24	1.87
ADG 3-wk	kg/d	0.31	0.20	0.32	0.25	0.07
n		3	4	3	2	
ADG Wean	kg/d	0.61	0.66	0.72	0.84	0.07

[ab]within a row, values with the different superscript differ by $P < 0.05$

Table 2.3. ***Main Trial****:* The total plasma proteins (TPP), average daily gain (ADG), dry matter intake (DMI) and feed efficiencies for all treatments and periods. Treatment A - control, B – 4 doses of colostrum extract (CE) prior to the first colostrum feeding, C – 1 dose of CE prior to the first colostrum feeding and the remaining doses on days 2, 3 and 4 of life prior to the morning milk replacer feeding. Means and standard errors are shown.

	Units	Control	4x at one feeding	4x over four days	SEM
n		16	16	16	
TPP	g/dL	6.3[a]	7.0[ab]	7.5[b]	0.37
Hematocrit	%	33	29	28	1.33
n		16	16	15	
DMI P1	kg/d	0.94	0.97	0.96	0.06
DMI P2	kg/d	1.45[ab†]	1.49[a]	1.32[b†]	0.05
DMI overall	kg/d	1.29[ab]	1.32[a]	1.20[b]	0.04
ADG P1	kg/d	0.50	0.47	0.53	0.06
ADG P2	kg/d	0.86	0.91	0.83	0.04
ADG Overall	kg/d	0.75	0.77	0.73	0.03
Feed Efficiency P1	kg gain/kg DMI	0.52	0.47	0.54	0.05
Feed Efficiency P2	kg gain/kg DMI	0.60	0.61	0.62	0.02
Feed efficiency overall	kg gain/kg DMI	0.58	0.57	0.59	0.02

[ab]within a row, values with the different superscripts differ by $P < 0.05$

[†]differ by $P < 0.10$

18% to 48%, thus not adjusting to a common value would skew the plasma concentrations and lead to false positives for TPP concentrations.

The plasma TPP concentrations measured in the 48 h blood sample after the first colostrum feeding yielded a difference (P = 0.04) between the calves fed no CE (TRT A) compared to calves fed one dose per day over the four days (TRT C) (6.30 g dL^{-1} vs 7.53 g dL^{-1} respectively) (Table 2.3). This suggests that the proteins in the CE are available to the calf and there is a positive effect of supplementation on protein absorption. Evaluating TPP has been used as a proxy for IgG status and allowed for rapid evaluation of colostrum status within this study (Naylor and Kronfeld, 1977, Tyler et al., 1996). A common benchmark for achieving passive transfer using a refractometer is 5.5 g dL^{-1} (Godden, 2008, Beam et al., 2009) and all calves within this study exceeded that benchmark and thus had adequate passive immunity, and demonstrated the colostrum replacer was effective at providing IgG's.

Overall, the calves performed well on this study except for the period associated with the low ambient temperatures and a diagnosed rotavirus outbreak. Both of those issues were transient, but did impact several calves per treatment. Within Period 1 DMI and ADG were not different and subsequently, feed efficiency was also not different. Over the first period DMI averaged about 1 kg d^{-1} and ADG was approximately 0.50 kg d^{-1} and predictions for ADG from the Dairy NRC (NRC, 2001) were 0.89 kg d^{-1} (Table 2.4). The observed performance was consistently about 0.4 kg d^{-1} lower than the predictions from the calf model in the 2001 Dairy NRC (data not shown) and the discrepancy for this difference in predicted vs observed was not identified, but suggests that maintenance requirements were greater than predicted by the model calculations and also suggests the rotovirus affected many of the calves although not clinically. Although feed efficiency was expected to be higher, energy intake above maintenance was reduced due to the lower ambient

temperatures in the early period of the study and rotavirus present in the calves might have hindered nutrient absorption from intake. However feed efficiency was similar to previous studies conducted in the same barn through similar environmental conditions (Diaz et al., 2001, Tikofsky et al., 2001).

During Period 2, DMI was significantly different between TRT B and C (1.49 and 1.32 kg. d^{-1} respectively) and TRT C tended to be different from TRT A (1.45 kg. d^{-1}). The ADG and feed efficiency were not significantly different and averaged approximately 0.87 kg d^{-1} and 0.61 kg gain kg DMI^{-1}, respectively. Due to the differences in DMI and consistent ADG, feed efficiency in the calves was expected to be different between treatments, but might have been affected by the reduced energy above maintenance due to lower ambient temperatures as well as a potential reduction in nutrient uptake caused by presence of rotavirus. The modest but positive difference suggests there might be a small effect of the CE on calf performance. Previous data demonstrated a positive effect of colostrum intake on growth through weaning and puberty (Faber et al., 2005; Soberon, 2011) that was not observed in this study most likely due to cold stress and the presence of the virus.

Overall, ADG measurements indicated there was no effect of CE supplementation in this larger study. The lack of difference in performance was different than a previous study that evaluated the amount of intact colostrum fed to calves at birth and over the first 12 h of life (Soberon and Van Amburgh, 2012). A possible explanation for the differences between the study of Soberon and this study was amount of hormones and growth factors supplied in this from the CE versus whole colostrum. Assuming an insulin concentration of 65 µg/L for intact colostrum, Soberon fed 4 L at birth and an additional 2 L by 12 h of life for an approximate insulin supply of 390 µg whereas the calves in this study received an additional 65 µg above whatever level might have

been present in the colostrum replacer. Thus, it is possible that the amount offered was not adequate enough to elicit the response as observed in the study of Soberon. Similarly, in another experiment unrelated to the current study, human insulin (1,000 IU) was added to a commercially available colostrum replacer and fed to calves within 2 h of birth and compared to non-supplemented calves. Significant increases in plasma concentrations of both insulin and glucose were observed (Lopez, 2012) suggesting that a higher feeding rate of the CE might be necessary.

An additional possibility of lack of difference between treatments ADG could be due to the temperatures in which this study was conducted. The average temperature during this study was 7^0C, where the lower critical temperature for young calves is approximately 20^0C and the barn environment reflects ambient temperature, thus, the calves less than 3 to 4 wk of age were below the lower critical temperature. Nutrient intake was designed to provide nutrients far beyond maintenance, however there were a few periods were metabolizable energy (ME) available for growth was limiting (Table 2.4). It is unlikely to detect an effect to a treatment if the nutrient supply is not adequate to allow for the response and this is consistent with other studies where intake over maintenance was limiting.

Feed efficiency was evaluated among treatments by period using weight gained per period divided by the DMI for given period. Overall, there was no difference among treatments, however, TRT C maintained a modestly increased feed efficiency compared to TRT A and B throughout each period (Table 2.3). These data suggest that there might have been a subtle response to the CE for better nutrient utilization by these calves.

Table 2.4: The average barn temperature, average daily gain, and metabolizable energy allowable gain (MEg) predicted by the Dairy NRC (2001) for calves during P1. The prediction of MEg was calculated using the calf model from the 2001 Dairy NRC for the main trial. Ambient temperature as monitored in the greenhouse calf barn are represented as the average temperate and kg/d of allowable gain as calculated by NRC 2001 equations amd observed ADG as evaluated by scale weights are also shown. All data are for the Period 1 averages throughout the duration of the study.

	Week of Study				
	1	2	3	4	5
Observed gain (kg/d)	0.33	0.38	0.56	0.57	0.57
Average Temp. (°C)	3.0	3.1	-7.9	0.2	3.9
Predicted metabolizable energy allowable gain (kg/d)	0.67	0.74	0.91	1.04	1.08

The available data has shown an increased capacity for glucose or xylose absorption from nutrient intake (Blum, 1997, Rauprich et al., 2000, Steinhoff-Wagner et al., 2011) and over time if the effect persists that should translate into enhanced growth or feed efficiency as observed in Faber et al. (2005) and Soberon and Van Amburgh, (2012).

There was an unfortunate rotavirus challenge present, an unintended outcome might have been a reduced nutrient uptake from the small intestine. Rotavirus damages mature enterocytes at a higher rate than which they can be replaced, thus reducing villus height and subsequent capacity for nutrient uptake (Torres-Medina et al., 1985; Merck Veterinary Manual, 2016 #2953). However, even with presence of rotavirus during this study calves performed remarkably well with only one death and calves gained approximately 0.75kg d^{-1} overall the treatments.

There is a robust literature concerning the role of colostrum components on gastrointestinal tract development, nutrient intake and nutrient utilization (Blättler et al., 2001, Roffler et al., 2003, Steinhoff-Wagner et al., 2011, Soberon et al., 2012, Hammon et al., 2013). Each of these studies has shown an enhanced absorption of nutrients, primarily glucose or glucose analogues, when an extract of colostrum or whole colostrum was fed. In the pilot study, there was an increase in overall ADG at the time of weaning and an increase in plasma protein in the calves fed 7 doses of colostrum extract. However, in the main trial we only saw the increase in plasma proteins and no difference in average daily gain. The approach we used for supplementing the CE raises questions and suggest more work is needed to better understand how to best evaluate the CE. In the pilot study, the CE was fed 30 minutes prior to colostrum feeding as a liquid suspension, but it was also unintentionally fed as a powder reconstituted in the colostrum. There is a possibility that when the colostrum extract is fed together with the colostrum there is a synergy and this promotes a larger increase in the uptake of the components present in the CE or the component of colostrum

(Roffler et al., 2003). In a different study, a plasma derived extract was added to a colostrum supplement and resulted in a reduction in absorption of colostrum components (Hammer et al., 2004) suggesting that in the case of that particular extract, separate administration might have been better. Further, additional evaluation with the commercially available CE might be required to fully appreciate how much is required to elicit a functional response. The increase in TPP demonstrated that the calves were responding to the supplemented colostrum components and the subtle changes in feed efficiency suggest achieving a greater intake would result in a more pronounced change in growth.

CONCLUSION:

Providing oral supplementation of colostrum extract in the first four days of life has significant impact on the increase of TPP status of calves above and beyond industry standards. Further effect of supplementing colostrum extract was found in a slight increase in feed efficiency during the second period when calves were fed milk and ad-libitum grain and maintained the same rates of average daily gain as their peers. These effects further substantiate others' work in suggesting an implication of the non-nutritive, non-Ig fraction of colostrum on nutrient utilization and feed efficiency in calves (Faber et al., 2005, Soberon and Van Amburgh, 2012). Further research is necessary to better understand if these effects are long-term beyond the scope of weaning and the interaction between timing of the extract feeding and colostrum administration.

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