Shaping her future – the colostrum contribution

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Abstract

Colostrum has long been valued as critical to newborn calf health, but its potential impact on the nutritional programming of the calf and consequently, her lifetime performance in milk production and health, are now areas of active research. New levels of importance and value are being attributed to colostrum, as scientists work to better understand the mechanisms and regulation of epigenetics, the influences of non-nutritional components of colostrum, and the impact of timely colostrum nutrition. Many of these benefits of colostrum were once attributed to passive transfer, but epigenetics and nutritional programming have revealed that there is much more in colostrum than IgG. Relaxin, leptin, insulin, IGF-I, IGF-II, prolactin, and lactoferrin are some of the nutritional and non-nutritional factors in colostrum that have a direct and indirect effect on the development and long-term gene expression of offspring. Researchers have shown that calves that received more colostrum at birth have higher average daily gains improved feed efficiency, higher dry matter intakes post-weaning, reduced time to conception and first calving, increased milk production during 2 lactations, and an increased survivability through second lactation.

Key words: cattle, calf, colostrum

Résumé

On reconnait depuis longtemps le lien fondamental entre le colostrum et la santé des nouveaux nés chez les bovins. Néanmoins, l'impact potentiel du colostrum sur le développement nutritionnel du veau et donc sur la santé et la production de lait durant la vie sont des domaines tout récents de recherche. On attribue maintenant de nouvelles valeurs et une plus grande importance au colostrum suite aux percées par des chercheurs sur la régulation et les mécanismes épigénétiques, l'influence des composantes non-nutritionnelles du colostrum et l'impact du moment où l'on administre le colostrum. Plusieurs des bénéfices du colostrum étaient attribués par le passé au transfert passif. Toutefois, l'épigénétique et les programmes de nutrition ont montré que les IgG ne sont pas les seuls éléments importants dans le colostrum. Plusieurs facteurs nutritionnels et non-nutritionnels du colostrum, comme la relaxine, la leptine, l'insuline, l'IGF-I, l'IGF-II, la prolactine et la lactoferrine peuvent avoir un impact direct ou indirect sur le développement et l'expression à long terme des gènes chez la progéniture. Les chercheurs ont montré que les veaux qui recevaient plus de colostrum à la naissance avaient un gain moyen quotidien plus élevé, une plus grande efficacité alimentaire, une plus grande prise alimentaire de matières sèches suivant le sevrage, un plus petit intervalle de temps avant la conception et le premier vêlage, une plus grande production de lait durant les deux premières lactations et une plus grande survie jusqu'à la seconde lactation.

Introduction

The conversation of what factors influence and impact lifelong health, performance, and growth has been a dialogue of great interest throughout history, but with recent scientific assessments and technologies coupled with new observations and perspectives, our understanding has increased, and with it, the ability to better quantify and isolate those factors. Colostrum has long been valued as critical to newborn calf health, but its potential impact on the nutritional programming of the calf and even lifetime performance in milk production and health, are just now receiving recognition. The idea that 1 meal, the first meal of life, can impact an animal for its entire life, generates discussion of how an environmental factor such as nutrition, can alter an animal's genome.

The modulation of gene expression through biochemical mechanisms that do not alter the DNA sequence but permanently alter their ability to be transcribed has gained the attention of the medical and scientific community as a means to better understand development, disease, and performance.

Nutritional programming has been reported in multiple species, including insects, birds and mammals, but particularly in mammals, it provides a mechanism for the mother to continue to influence the development of offspring after birth through her colostrum and milk. This regulation can only occur during specific windows of opportunity that, as we better understand, open the possibility to enhance the performance of productive species as well as the possibility to predict and reduce the probability of certain diseases later in life.

Epigenetics

The concept of epigenetics is attributed to Conrad Hal Waddington, who in 1953 described epigenetics as an animal's useful response to an environmental stress that persists even after the environmental stress is removed. In some instances, the trait or response becomes permanent in that animal, regardless of the environment.[22] Different terms have been used to describe some of the effects controlled through epigenetic mechanisms including imprinting, metabolic programming, and nutritional programming. Some of the environmental factors attributed in scientific literature for the generation of permanent epigenetic changes are temperature, grooming,[24] malnutrition,[12,15] and overnutrition.[9,13]

Epigenetics refers to the modification of DNA that results in changes in DNA expression but does not change the nucleotide sequence itself. Epigenetic changes are normal, natural phenomena that function through both short-term/temporary and long-term/permanent changes in gene expression. Some of these gene expression regulators can be inherited. Epigenetic mechanisms are used for gene regulation throughout fetal development, but are not limited to that period of time; normal events such as hibernation, pregnancy, and starvation use epigenetic mechanisms for homeorhesis. Scientists have been particularly interested in those changes to the epigenetic code, also known as the epigenome, that occur at 1 specific point in time during development, yet have future phenotypical implications.[1,9,12,13,15,19,24] For example, the amount of grooming a rat received from its mother as a pup has been shown to modify the adult rat's stress response. Pups that were groomed more by their mothers had higher methylation of the first exon of the promoter region for glucocorticoid receptor; this modification persisted for life and resulted in a greater affinity for NGFI-A as an adult rat.[24]

A well-researched event that has further illuminated the effects of nutritional programming is the famine during the Dutch Hunger Winter. Towards the end of the Second World War, Germany imposed a food restriction on the western part of Holland during what proved to be a particularly cold winter. Researchers have used this event to follow up and study the individuals that were conceived or in their mothers' womb during this period. Drastic nutritional restrictions during critical developmental stages in utero led to permanent effects on the methylation of the children's DNA, and was especially linked to the regulation of IGF-II. Individuals exposed to the famine during their peri-conception or mother's gestation, exhibited an increased risk for glucose intolerance, impaired insulin secretion, obesity, stress sensitivity, coronary heart disease, schizophrenia, anti-social behavior, and addiction[12] later in life.

Another well-studied example of nutritional programming is provided by honey bees. All bees in a hive share the same genetic composition. However, when there is time to produce a new queen, the larva selected to become the queen is fed a 'royal honey'; moreover, it is fed 10 times more than other larvae. This difference in nutrient intake during a critical developmental stage changes the epigenome of that 1 bee and instead of becoming a common worker, she grows twice as fast, will have a life expectancy 20 times higher than any other bee, and becomes the only female to develop her female reproductive organs.[9]

Epigenetics has now been proposed as a potential integral component in future disease diagnosis but equally importantly, it has provided a deeper understanding of the well-known environmental influence on genotypic performance. As more information becomes available, the possibility for programming desirable traits in production animals will open a new chapter in animal science and agricultural production.

The Traditional Attributes of Colostrum

Colostrum has traditionally been recognized as critical for adequate transfer of passive immunity in the newborn calf. It is well documented that calves with <10 mg/mL IgG in blood plasma (5.2 g/dL protein) during the first 2 days of life experienced higher rates of pre-weaning morbidity and mortality.[8] In an attempt to explain the effectiveness of colostrum against *Escherichia coli* infections in the gastrointestinal tract, researchers provided calves with either colostrum followed by *E. coli*, colostrum combined with *E. coli*, or *E. coli* alone. The calves that were administered *E. coli* alone had high levels of *E. coli* attachment in the intestine as well as *E. coli* present in the lymph; when colostrum and *E. coli* were administered simultaneously, there was no attachment of *E. coli* in the gut, but there were low levels of passive transfer. Finally, when colostrum had been fed prior to the *E. coli* challenge, there was no bacterial colonization in the gut and high levels of circulating antibodies.[23] These IgG benefits of colostrum may last for as long as 3 weeks, but eventually, the calf must depend on its own immune system. While colostrum is a valuable source of immunoglobulins, increasing amounts of literature are suggesting that factors in colostrum other than immunoglobulins are important for long-term productivity and feed efficiency in dairy calves.

Colostrum Beyond IgGs

Proper colostrum administration has consistently been measured through IgG plasma concentration in the calves. Using this assessment, many studies have compared the performance of calves with high versus low levels of passive transfer. This has led to the assumption that IgGs are the cause or promoters of long-term effects associated with feeding proper levels of quality colostrum. However, with new understandings of the potential implications of nutritional programming and its long-term effects, it is now crucial to evaluate colostrum for all of its constituents and not restrict its value to that of passive immunity. The long-term effects reported in scientific literature of feeding an increased quantity as well as higher quality of colostrum include increased average daily growth up to at least 180 days,[17,25] reduced time to first calving,[23] and increased milk and fat production during first lactation.[7,11] Most of these studies have sorted calves into different treatment groups based on their IgG plasma concentration; however, a few studies have evaluated the direct effect of quantity of colostrum rather than the passive transfer of IgGs.

Using Brown Swiss cattle, Faber et al measured the long-term effects of supplying 4 quarts versus 2 quarts of colostrum during the first feeding. Other than the amount of colostrum followed by the feeding of transition milk, all calves were treated the same. Calves that consumed 4 quarts of colostrum had an average daily gain (ADG) of 0.4 lb (0.18 kg) or 22% greater gain than those calves that received only 2 quarts; there were no significant differences in calving age, but by the end of the calves' second lactation, the survival rate of calves that had consumed 4 quarts of colostrum was 12% higher (87% vs 75%). Moreover, of the cattle that survived to the end of second lactation, cows that had consumed more colostrum at birth produced 2,265 lb (1,029 kg) more milk than those that consumed less colostrum.[11]

The amount of colostrum consumed at birth was thought to have an interactive effect with the amount of milk or milk replacer (MR) offered during the pre-weaning period. In order to better understand this interaction, Soberon and Van Amburgh conducted a 2x2 experimental design where calves were offered either 4 quarts or 2 quarts of colostrum at birth, after which all calves were fed in a commingled pen with an automatic feeder. Half of the calves on each colostrum treatment were allowed to consume up to 12 quarts of milk replacer per day and the other half of the calves from each treatment were offered 5 quarts per day. Results from this study are presented in Table 1. It is important to highlight for the purpose of this discussion that in this study every calf had plasma IgG levels above the 10 mg/mL, and only 2 out of 125 calves had IgG levels below 12 mg/mL; thus, in any other study, all of these calves would have been considered as having proper passive transfer. When calves were limit-fed 5 quarts per day, ADG pre-weaning, weaning weight, ADG to 80 days, and milk replacer consumption was not significantly different among colostrum treatments. However, when milk replacer was not restricted and calves were allowed to drink sufficient nutrients from milk replacer, calves that received 4 quarts of colostrum had higher ADG pre-weaning, higher weaning weights, higher milk replacer consumption, higher hip height gain by 80 days, and higher ADG post-weaning. In addition, regardless of the milk replacer treatment they were in, calves that consumed 4 quarts of colostrum had higher dry matter intake (DMI) post-weaning compared to calves that consumed only 2 quarts of colostrum.[19]

The incidence of clinical health events in this study was not different among treatments, which suggests the

Table 1. Weights, heights, average daily gains, and post-weaning dry matter intakes for calves (n = 125) fed either 4 quarts of colostrum and up to 12 quarts of MR (HH), 4 quarts of colostrum and 5 quarts of MR (HL), 2 quarts of colostrum and up to 12 quarts of MR (LH), or 2 quarts of colostrum and 5 quarts of MR (LL). Means and standard deviations shown.

Treatment	HH	HL	LH	LL	
	Mean	Mean	Mean	Mean	Std dev
N	34	38	26	27	
Days on treatment	84.3	83.3	82.8	82.8	0.7
Birth wt, lb	97.1	95.8	92.2	95.5	1
Birth hip height, in	31.7	31.6	31.5	31.9	0.6
IgG concentration, mg/dl[§]	2,746[a]	2,480[b]	1,466[c]	1,417[c]	98
Weaning wt, lb	172.4[a]	140.0[b]	159.1[c]	137.7[b]	1.9
Weaning hip height, in	36.61[a]	34.89[b]	36.04[a]	35.27[b]	0.6
ADG pre-weaning (0 to 52 d), lb	1.74[a]	0.93[b]	1.48[c]	0.86[b]	0
ADG birth to 80 d, lb	1.72[a]	1.30[bc]	1.46[b]	1.17[c]	0
Total milk replacer intake, lb DMI[§]	97.9[a]	45.2[b]	90.2[c]	44.1[b]	1.2
Grain intake pre-weaning, lb[*§]	5.5[a]	26.5[b]	4.6[a]	21.4[b]	1.5
Feed efficiency pre-weaning[†*]	0.61	0.61	0.65	0.61	0
Hip height gain, pre-weaning, in/d	0.098[a]	0.063[b]	0.091[a]	0.063[b]	0
Hip height gain, birth to 80 d, in/d	0.083[a]	0.063[b]	0.071[c]	0.059[b]	0
ADG post-weaning[‡], lb	2.36[a]	2.14a[b]	1.94[b]	2.03[b]	0.1
DMI post-weaning[‡], lb/d	6.37[ab]	6.37[a]	5.69[c]	5.87[bc]	0.1
Feed efficiency post-weaning	0.33	0.34	0.34	0.36	0

[*]Data from 5 wk during the pre-weaning period was used in the analysis
[†]DMI includes milk replacer intake and grain intake from birth to weaning
[‡]Measured during 3 weeks after a 1-week adaptation period to pens
[§]Data is only reported for calves in the second block
[abc]Values within the same line with different superscripts differ $P < 0.05$

mechanism that triggered the increase in performance is more than can be attributed solely to passive transfer. Bartol et al coined a term that is very useful in understanding the possible mechanism working through colostrum; it is the *lactocrine hypothesis*.[1]

The Lactocrine Hypothesis

The 'lactocrine hypothesis' attributes the effects of milk-born factors, including colostrum, to the epigenetic development of specific tissues or physiological functions.[1] It has been described in multiple species including neonatal pigs, primates, and calves.[2,3,4,10,13,15,16] The term was first used by Bartol et al when his group was able to track the direct effects of relaxin found in sow milk on the development of the uterus. They showed an increased reproductive efficiency in sows that had been fed colostrum vs formula-fed sows.[1]

Other evidence for non-nutritional factors present in colostrum was presented by Burrin et al when they examined the effects of feeding colostrum, milk or formula with similar nutrient composition to colostrum to newborn piglets. Piglets that consumed colostrum had higher rates of skeletal protein synthesis as well as higher rates of protein synthesis in the jejunum.[5]

The evaluation of colostrum intake in calves showed significantly higher plasma levels of glucose in calves fed colostrum vs formula. This was due to an increased absorptive capacity since the gluconeogenic ability did not differ among the 2 groups of calves.[20] These results were further supported by an increased glycogen concentration in liver in colostrum-fed calves. Researchers also tested calves after a 15-hour feed deprivation period and observed that colostrum-fed calves had higher levels of circulating glucose and lower plasma urea concentrations, indicating lower levels of protein catabolism in colostrum-fed calves.[20]

The effects previously mentioned in this paper observed by Faber et al in Brown Swiss and those described by Soberon and Van Amburgh using Holstein calves that were fed either 2 or 4 quarts of colostrum at birth are most likely explainable through the lactocrine hypothesis, where non-nutritional factors present in colostrum might be responsible for the increase in feed efficiency, increased DMI, increased average daily growth, increase in milk production, and increased survival.

There are others that suggest these effects might be directly attributed to nutrient intake; this hypothesis is supported by data from Soberon et al that suggests that long-term effects such as increased milk production are a consequence more related to nutrient intake and pre-weaning growth rates than a single milk-born factor.[18] In most cases, the studies that support nutrient intake as the main factor for increased future productivity analyzed differences in intake during the first 30 to 60 days of life; therefore, the question remains as to the interaction of both nutrient intake levels and non-nutritional factors, given that each are provided within the right window of time or at the proper developmental stage.

Last Remarks on Colostrum

Colostrum is a highly concentrated source of nutrients and non-nutritional factors that are produced by the periparturient dam to be the first feed their progeny consumes. Colostrum, when compared to milk, is higher in fat (6.7% vs 3.7%), total protein (14% vs 3.2%), and IgG (3.2 vs 0.06 g/100 mL). Even though it is impressive to have 60 times more IgGs in colostrum than in milk, there is 155 times more IGF-I in colostrum than in milk. Colostrum also contains 18 times more prolactin, 100 times more insulin, 90 times more leptin, and 19 times more relaxin than milk. These are only a few of the non-nutritional factors that may have long-term implications in the development of newborn calves.

Conclusions

Colostrum has traditionally been valued for the passive transfer that it provides to calves. Although passive transfer is a valuable attribute of colostrum, it is now known that other factors present in colostrum, not directly related to immunity, have a great impact on the future performance of calves. Non-nutritional factors in colostrum are potential factors influencing the epigenome of newborn calves. The benefits of providing 4 quarts of colostrum within the first hour of birth have been observed to include improvements in ADG, increased DMI, reduced time to first breeding, reduced time to first calving, increased milk production, and increased survivability to second lactation. Colostrum is still important for passive transfer of immunity but its long-term benefits add to its value, making colostrum the 1 most important step in shaping the future of dairy cows.

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