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The relationship between ketosis and transitional nutritional diseases

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ABSTRACT

Ketosis is a highly prevalent nutritional condition that affects fresh dairy cows during the transition period. Ketosis occurs when there is a negative energy balance. Clinical findings of ketosis include excessive loss of body condition, decreased feed consumption (especially of concentrated feed), reduced milk yield, and nervous signs. Subclinical ketosis is a serious nutritional disease that may result in displaced abomasum, decreased milk yield, poor reproductive performances, early culling of herds, and economic losses, among other adverse effects. Ketosis is linked to nutritional disorders that are commonly observed after calving including, metritis, mastitis, milk fever, lameness, retained placenta, and displaced abomasum. The two most crucial strategies for preventing ketosis are reducing negative energy balance and increasing dry matter consumption. The density of triacyl-glycerides and non-esterified fatty acids in plasma is higher after calving. Non-esterified fatty acids are oxidized to ketone bodies. A cow starts to mobilize its body fat for energy when it reaches a negative energy balance. Live weight and body condition score fall under such circumstances.

Keywords: dairy cattle, ketosis, negative energy balance

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Introduction

Due to low feed consumption and high milk output, energy needs cannot be physiologically met at the start of lactation, leading to an energy deficit during this period. The body uses its fat reserves to make up for this deficit. Ketosis usually occurs in high milk producing cows at the start of lactation, when the energy balance is negative. However, it can also occur when dry matter intake is reduced and the diet lacks sufficient energy density in conditions such as displaced abomasum, mastitis, metritis, fatty liver syndrome, and retained placenta, which may reduce appetite and feed intake, increasing the risk of secondary ketosis (Atalay and Eseceli, 2015).

Ketosis is a nutritional disease characterized by liver degeneration, decrease in blood glucose concentration, and increase in ketone bodies in the blood and other body tissues particularly in the postpartum period. In a negative energy balance, the mobilization of body fat results in an increase in the concentration of free fatty acids in various tissues. Free fatty acids in the liver are limited by the oxidation capacity of the liver. When the capacity is surpassed, free fatty acids are converted to triglycerides, which accumulate in the liver. The incidence of ketosis increases when plasma free fatty acid concentrations exceed 1000 mEq/L (Arslan and Tufan, 2010b).

Dry matter consumption

Dry matter intake, milk output, and blood glucose levels have all been shown to be reduced in ketosis cows, although NEFA, BHBA, and serum total lipid levels are higher (Dann et al., 2005). Cows with subclinical ketosis had higher amounts of BHBA and NEFA, but lower levels of glucose than healthy cows (Zhang et al., 2010).

The following processes supply the glucose and metabolic energy required during the transition period due to low dry matter consumption: hepatic

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gluconeogenesis; lactic acid accumulated from anaerobic glycolysis in muscle tissue and transported to the liver; glucogenic amino acids released from protein catabolism; and glycerol released from lipolysis in adipose tissue (Arslan and Tufan, 2010a; Reynolds et al., 2003).

Obesity in cows during the parturition period leads to a significant decrease in dry matter consumption and an increased release of NEFA (Stockdale, 2001; Roche et al., 2009).

Subclinical acidosis is caused by the addition of easily digestible non-structural carbohydrates to the diet to balance energy and boost dry matter consumption. Subclinical acidosis quickly progresses to laminitis. The cow with laminitis prefers to rest rather than feed, thus dry matter consumption drops, and the negative energy balance further exacerbates (Kelley, 2014).

Dry matter consumption is one of the most key factors that influence milk output. Hormonal and metabolic changes during the transition phase may affect dry matter consumption (Ingvartsen and Andersen, 2000). Dry matter consumption decreases by more than thirty percent in the last three weeks of gestation (Hayırlı et al., 2002).

Numerous clinical indicators of ketosis are nonspecific, including decreased milk production and dry matter consumption as well as environmental indifference. Abnormal behaviours like aggression, lack of coordination, and chewing on nonfeed items are displayed by some cows. Ketone levels in milk, urine, or blood must be measured for a conclusive diagnosis. The value and accuracy of different tests have previously been reviewed (Tatone et al., 2016).

Nutritional diseases

High milk yielding cows experience decreased blood glucose levels, depleted liver glycogen stores, formation of ketone bodies from unesterified fatty acids in the body, and ketosis because of their high energy requirements during the transition period and their inability to meet these needs. Hypocalcemia, metritis, retained placenta, ketosis, and displaced abomasum may occur simultaneously. Abomasal atony is the biggest contributor to displaced abomasum. Atony is caused by RPT, ulcers, metritis, mastitis, retentio secundinarum, acidosis, elevated volatile fatty acids, and low blood calcium levels (Rukkwamsuk et al., 1999).

BHBA > 1.2 mmol/ L is linked to abomasum displacement, mastitis, metritis, and increased milk loss in cows experiencing ketosis in the first one or two weeks postpartum (LeBlanc, 2010). The cut-off value for subclinical ketosis in blood BHBA is 1-1.4 mmol/L (Ospina et al., 2010). The likelihood of displaced abomasum, clinical ketosis, and metritis is 2.6–8 times, 3–6 times, and 1–5.8 times higher, respectively, if BHBA levels are elevated in cows during the first two weeks following calving (Dubuc et al., 2010). Metabolic diseases are frequently associated with low blood glucose levels as well as high blood NEFA and BHBA levels, both of which suggest negative energy balance. Increased ketone bodies in the blood raise the possibility of left-displaced abomasum. Ketone bodies can disrupt the activities of milk and blood immune system cells (Graber et al., 2010). Negative energy balance is linked to diseases including mastitis, metritis, and retained placenta, which are not metabolic diseases (Grummer et al., 2004).

It is critical to assess the prevalence of ketosis in the herds in the enterprise. The occurrence of ketosis is influenced by a variety of factors, including geographical location, temperature, barn structure, roughage structure, pasture structure, season, and lactation number. There is a negative correlation between ketosis prevalence and herd size during lactation. It has been suggested that feeding with Total Mix Ration minimizes the risk of ketosis. The highest prevalence of ketosis was reported in cows calving during the second quarter of the year (April-June). Low consumption of concentrated feed has been linked to an increased risk of ketosis due to reduced energy consumption. Cows that had only one calving showed the lowest levels of ketosis. Cows in the second lactation are reported to have a higher prevalence of ketosis, whereas cows in the third to seventh lactation have the highest prevalence of ketosis. It has been stated that ketosis in the first week after calving is linked to increased abomasum displacement, metritis, and mastitis. Another study indicates a significant link among ketosis, mastitis, and clinical laminitis (Berge and Vertenten, 2014).

Fatty liver is a major risk factor for abomasal displacement, ketosis, and immune dysfunction. In contrast, if these disorders reduce dry matter intake and induce a more severe negative energy balance, they may increase the likelihood of developing fatty liver. Obesity is a significant risk factor for developing fatty liver (Bobe et al., 2004). In the early postpartum period, fatty cows consume less dry matter than cows in proper body condition, which results in higher mobilization of body fat (Stockdale, 2001).

Hormonal change

Insulin levels in cows have been reported to be low after calving (Holtenius et al., 1993). Lactating cows produce only half the insulin that non-lactating cows do (Lomax et al., 1979). Insulin resistance develops in

peripheral tissues during early lactation (Holtenius and Holtenius, 1996). Insulin levels vary during the transition period. Low insulin levels after parturition decrease glucose uptake in insulin-sensitive organs, such as muscle and adipose tissue. This condition favors glucose uptake in the mammary gland, which is not influenced by insulin action. Thus, the concentration of triglycerides in the liver rises in response to adipose tissue mobilization in the body (Aschenbach et al., 2010).

The mammary gland does not require insulin for glucose metabolism (Komatsu et al., 2005). NEFA circulating freely during negative energy balance contributes to milk fat formation (Bauman and Griinari, 2001). In a lactating cow experiencing negative energy balance, milk fat concentration tends to increase, while milk protein concentration tends to decrease. The fat to protein ratio expresses negative energy intensity and the risk of metabolic disease. Milk samples should be evaluated within 9 to 30 days to estimate the risk factors for metabolic diseases (Duffield et al., 1997; Toni et al., 2011).

Insulin inhibits the mobilization of fatty acids from adipose tissue and reduces blood glucose levels by increasing glucose absorption into tissues. Insulin resistance refers to a decrease in the tissues' response to insulin actions. As insulin resistance in adipose tissues increases, so does fatty acid mobilization and the concentration of non-esterified fatty acids in the blood. The body condition score used in determining energy balance provides information regarding the change in live weight. It has been stated that one unit change in body condition score corresponds to an 80 kg change in live weight. The fatty tissues that are mobilized or the live weights that are regained are located in the abdominal, intramuscular, and subcutaneous regions. Energy balance is expressed by the blood molecule β-Hydroxybutyric acid (BHBA). If the amount of non-esterified fatty acids entering the liver exceeds the capacity for fatty acid oxidation, ketone bodies increase. Blood analysis should be performed in the second week of lactation and 5 hours after feeding to assess BHBA levels in the blood. The BHBA blood threshold is 1.2 to 1.4 mmol/L. There is a strong link between milk yield and energy status. When there is an energy deficiency, microbial protein synthesis and the number of amino acids in mammary tissue decrease, lowering the level of milk protein. A milk protein content of less than 2.7% relates to a negative energy value. Blood analysis should be used to determine milk protein concentration between weeks 1 and 12 of lactation, and 5 hours after feeding. Milk fat levels increase but milk protein levels decrease during lactation due to a negative energy balance. A high fat/protein ratio at the start of lactation suggests a negative energy balance. If the fat/protein ratio exceeds 1.4, it indicates that fat is being mobilized in the adipose tissue and that the animal is in a negative energy state. Milk acetone levels are commonly used to diagnose subclinical ketosis. If the milk acetone concentration exceeds 0.7 mmol/L, the animal may be in ketosis. It is important to focus on the number of samples that surpass the threshold values rather than the average value when interpreting metabolic indicator data. If more than 10% of the cows in the herd surpass the BHBA threshold, this is a strong indication of a negative energy balance in the herd (Serbester et al., 2012).

Holtenius and Holtenius (1996) classified ketosis as type I and type II. Type I ketosis usually develops a few weeks after parturition, when milk supply and mammary gland glucose demands are high. However, it is not generally associated with high hepatic fat concentrations. Type II occurs at or around parturition and is typically linked with fatty liver. Type II ketosis is often more difficult to treat than type I (Herdt, 2000; NASEM, 2021). This classification method indicates two major causes of ketosis. The risk factors and causes of type II ketosis are similar to those of fatty liver. Type I cows had lower blood glucose and insulin concentrations, as well as higher ketone concentrations compared to healthy cows. Low insulin increases fatty acid oxidation, likely by reducing hepatocyte malonyl-CoA levels and decreasing the sensitivity of carnitine palmitoyl-transferase 1 to malonyl-CoA. (Emery et al., 1992; NASEM, 2021). Carnitine palmitoyltransferase 1 is responsible for the transport of fatty acids from the cytosol to the mitochondria for oxidation, and it is highly active in type I ketosis. Thus, this suggests that type I ketosis is caused by an insufficient supply of gluconeogenic precursors. Low dry matter intake could be the cause of limited substrate supply. Studies reveal that increasing dietary starch postpartum lowers blood BHBA while increasing glucose (Rabelo et al., 2005; McCarthy et al., 2015; NASEM, 2021). Propylene glycol administered as a drip or bolus can lower blood BHBA levels (Nielsen and Ingvartsen, 2004).

Fatty liver

Ketone bodies are produced when excess NEFA enters the liver. Subclinical ketosis may occur because not all NEFA can be completely oxidized. Negative energy balance leads to ketosis. When the body's energy reserves are mobilized, the concentrations of NEFA and ketone bodies (acetoacetate, BHBA, and acetone) increase. Increased NEFA concentration contributes to ketosis (Weber et al., 2013).

Fat accumulates in the liver when fatty acid intake exceeds the liver's ability to oxidize or eliminate fatty acids, which occurs when blood concentrations of stored fatty acids increase (Bobe et al., 2004; Grummer, 2008). Ketosis almost always develops when cows have moderate (5 to 10% of liver wet weight raised as triacylglycerides) to severe (more than 10% increased as triacylglycerides) fatty liver. Plasma NEFA concentrations in healthy cows are low (less than 0.2 mEq/L) until a few days before parturition, increases to as high as 0.8 mEq/L during parturition, remain high for several days, and then gradually fall (Bertics et al., 1992; NASEM, 2021). Cows with a higher risk of postpartum metabolic disorders often have plasma NEFA concentrations higher than 0.5 mEq/L prepartum and higher than 1.0 mEq/L postpartum (LeBlanc et al., 2005; NASEM, 2021).

The uptake of NEFA by the liver is proportional to NEFA concentrations in the blood (Emery et al., 1992) and NEFA taken up by the liver can be esterified or oxidized (Drackley, 1999). Triglycerides, the primary result of esterification, can be absorbed or retained as part of very low density lipoprotein. Compared to other species, ruminants absorb triglycerides at a very slow pace (Kleppe et al., 1988; Pullen et al., 1990). As a result, fatty acid esterification and triglyceride buildup occur in the liver when it takes up excessive levels of hepatic NEFA.

Negative energy balance

When milk production begins, the cow's energy need increases by around threefold compared to the period before parturition (Van Dorland et al., 2009). As milk production begins, glucose and metabolic energy needs increase two to threefold by the 21st day postpartum, compared to the 21st day prepartum (Drackley et al., 2001).

More than fifty percent of cows are thought to have at least one subclinical illness throughout the transition phase (Overton and Waldron, 2004). The negative energy picture is shaped by the imbalance between stagnant dry matter consumption during the transition period and increased energy demand during lactation.

The relationship between energy expended through milk production during lactation, the mobilization of body fat, and energy intake from feed defines the condition known as ketosis (Collard et al., 2000; Mulligan et al., 2006). The transition period for high-yielding dairy cattle is extremely challenging. During this time, the animal frequently enters a negative energy state. A cow with a negative energy balance requires more energy than it can receive from feed (De vries et al., 1999). Dry matter consumption during this time is most likely determined by NEFA oxidation in the liver (Allen et al., 2009).

Microorganisms in the rumen produce the volatile fatty acids butyric acid, propionic acid, and acetic acid. The liver uses acetic acid as a source of acetyl coenzyme A to make ATP. The rumen absorbs butyric acid, which is then transformed into ketone bodies (BHBA). The liver uses propionic acid in the process of gluconeogenesis (Reynolds et al., 1988).

During the far off dry period, 4 to 6 weeks before parturition, insulin level was found to be consistent with liver lipid concentrations in cows fed a high energy diet compared to those on a restricted diet. However, because it was higher, this level was found to be inconsistent with the NEFA and BHBA levels (Dann et al., 2006). Compared to cows fed a high energy intensive diet, more significant and relevant results were found in dry matter consumption and energy balance in cows fed a restricted diet throughout the far off dry period. It was reported that during the far-off dry period, cows fed a restricted energy diet eliminated negative energy balance and achieved a balanced energy state more quickly than those fed an intensive diet. Additionally, it was noted that cows overfed during the far-off dry period following parturition showed signs of health issues (Dann et al., 2006, Kelley, 2014). Cows tend to consume more feed during the dry period to gain fat, which provides energy after parturition.

Cows that are in negative energy balance which can happen when their dry matter intake decreases during the prepartum phase and almost always happens during the first few weeks of lactation have higher plasma NEFA levels because their energy needs are high and their intake is low, which causes their body reserves to be mobilized. Most cows in the early stages of lactation have some degree of hepatic fat accumulation since NEFA levels are elevated in most of them during the peripartum period (Jorritsma et al., 2001; Bobe et al., 2004; NASEM, 2021).

Ketosis, also known as hyperketonaemia, occurs when an excess of long chain fatty acids is oxidized by B -oxidation. Cows with a severe negative energy balance after calving release an excessive amount of long-chain fatty acids. Ketone bodies (B-hydroxybutyric acid and acetoacetate) are the byproducts of B-oxidation, and when they accumulate in the blood, clinical symptoms can appear. When plasma insulin levels are low and glucagon levels are high, fatty acid release from adipose tissue and subsequent B-oxidation are triggered (Holtenius and Holtenius, 1996; NASEM, 2021).

Conclusion

The transition period includes the three weeks preceding parturition and the three weeks following parturition. Almost all high-milk-yielding cows

experience a negative energy balance throughout the transition period. This negative energy balance results from an increased need for energy following parturition, which is caused by a decrease in dry matter intake and the onset of milk secretion. In a negative energy balance, the cow mobilizes body fat to meet its NEFA (Non-Esterified Fatty Acids) requirements. The cow with a negative energy balance attempts to correct the imbalance by boosting NEFA and BHBA (Beta Hydroxy Butyric Acid) levels. Because the cow is in negative energy balance during ketosis, ration energy cannot be used to make up the difference. Thus, conducting a ration study during ketosis might not yield useful results.

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