NUTRITIONAL FACTORS RESPONSIBLE FOR KETOSIS AND FATTY LIVER SYNDROME IN LACTATING DAIRY COWS

Biju Chacko*

Department of Animal Nutrition, College of Veterinary and Animal Sciences,

Pookode, Wayanad, Kerala- 673576

*Corresponding author: bijuchacko@kvasu.ac.in

Recieved: 07-01-2019 Accepted 18-01-2019

ABSTRACT

Metabolic disorders are due to faulty feeding of the animals especially during stress conditions like lactation and parturition. Ketosis and fatty liver syndrome are common metabolic disorder seen in lactating dairy cows, which cause huge economic loss to the farmers. A thorough understanding of the various nutritional factors responsible for this metabolic disorder will help the farmer to adopt the optimum feeding strategy which will in turn help to prevent the incidence, whereby the economic losses can be minimised. A review of the nutritional and physiological changes occurring in the dairy cow during the transition period, underlying mechanisms, associated health problems and prevention strategies are discussed.

Key words: Metabolic disorders, ketosis, fatty liver, transition period, nutritional factors, negative energy balance, non-esterified fatty acids

INTRODUCTION

Over the past several decades dairy cows have undergone intensive genetic selection, which has increased milk yield to a level where the demand for nutrients from the diet and body tissue reserves often results in ill-health and infertility. During the same period systems of dairy production have been significantly developed, with the objective of improving producer profitability as the main driving force. In both extensive and intensive systems, production diseases such as ketosis and fatty liver syndrome are associated with 'imbalances in the 'input' and 'output' of metabolites required for production or deviations in the normal 'throughput' pathways of the body' (Grant and Albright, 1995).

Production diseases of dairy cows are a manifestation of the cow's inability to cope with the metabolic demands of high production, and they continue to be a cause of eco-

nomic loss to the dairy industry and an animal welfare concern (Ingvartsen, 2006). The annual economic losses due to metabolic disorders in cattle in India were Rs. 9.57 crores, in the year 2012-13 (Government of India, 2014).

Nutritional and management spectrum over which lactating dairy cows can maintain metabolite homeostasis is very wide. Therefore, proper nutrition and management of high producing dairy cows becomes increasingly complex and critical.

Transition period of a dairy cow

The transition period for a dairy cow is from three to two weeks prepartum until two to three weeks postpartum (Grummer, 1995). The term transition is to underscore the important physiological, metabolic, and nutritional changes occurring in this time frame (Robinson *et al*., 2006). It constitutes a turning point in the productive cycle of the cow from one lactation to the next. The manner in which these changes occur and how they are managed are of great importance as they are closely linked to lactation performance, clinical and subclinical postpartum diseases, and reproductive performance that can significantly affect profitability (Janovick *et al*., 2011).

Economic losses

Every pound of milk reduced in peak production represents a loss of 200 lbs of milk for the lactation (Ospina *et al*., 2013). It is, therefore, pertinent to elaborate nutritional strategies to facilitate the passage of the cow through this transition phase; while minimising health problems and optimising productivity/ profitability for the remainder of the ensuing lactation.

Transition cow biology

It is a well established fact that dry matter intake (DMI) decreases as calving approaches. Dry matter intake can decrease from 2.0 per cent of body weight (BW) in the first few weeks of the dry period to 1.4 per cent of BW in the 7 to 10 d period before calving (Ingvartsen, 2006). This 30 per cent decrease in DMI appears to occur very rapidly in the transition period. During the third week after calving DMI will increase at the rate of 1.5 to 2.5 kg /week with this increase being more rapid in multiparous cows than primiparous cows (Robinson *et al*., 2006).

The decrease in prepartum DMI has been attributed to the rapid growth of the foetus occupying up abdominal space and displacing rumen volume (Ingvartsen, 2006). However, hormonal and other physiological factors

have also got an impact on this phenomenon. During last week of pregnancy, nutrient demands by the fetal calf and placenta are at their greatest, yet DMI may be decreased by 10 to 30 per cent compared with the early dry period (Schirmann *et al*., 2013).

Physiological changes

A number of profound physiologic changes occur in the transition cow that modifies her metabolism drastically. The rapidly increasing demands of the fetus and the development of the mammary glands, including the initiation of synthesis of milk components, are causing these changes (Ingvartsen, 2006).

The concentration of plasma insulin continually declines in the transition period until calving and that of somatotropin increases rapidly between the end of gestation and the initiation of lactation. Concentration of plasma progesterone, which is high in gestation, rapidly falls at calving and there is a transitory elevation in estrogens and glucocorticoids in the periparturient period (Grummer, 1995). These hormonal changes not only contribute to the decline in DMI, but also coordinate the metabolic changes that favor, if not force, the mobilisation of body fat reserves from adipocytes (Contreras and Sordillo, 2011). Esposito *et al*. (2014) observed that mobilisation of lipids, is associated with an increase in concentration of plasma non-esterified fatty acids (NEFA), which rise gradually in the prepartum transition period, but rapidly in the last three days of gestation.

Part of the increase in NEFA is obligatory and is under hormonal control while another portion is the result of an energy deficit (negative energy balance or NEB). The magnitude of the NEB prepartum, therefore, appears to be a variable that can be mitigated through nutritional management (Contreras and Sordillo, 2011). Additionally, the NEB and resulting increase in plasma NEFA, if sufficiently high, contributes to the development of fatty liver; which itself is a contributing factor to other health problems in the postpartum period (Esposito *et al*., 2014).

Rumen function

During the dry period, cows generally consume a diet that is principally composed of forages and, by consequence, is more fibrous than the type of diet offered in lactation (Kertz *et al.*, 1991). This nuance affects rumen function in 2 ways. First, the rumen flora is adapted to a diet that is low in non-fiber carbohydrates (NFC) during the dry period, allowing for a large population of cellulolytic bacteria and a low population of amylolytic bacteria. As the amylolytic bacteria also generate lactic acid, their decrease is accompa-

nied by a decrease in the bacteria that utilize lactic acid (Schirmann *et al*., 2013).

If the ration is changed abruptly at calving the capacity of the rumen flora to metabolise lactate, the principal acid responsible for acute rumen acidosis, is at a minimum at the initiation of lactation. The lactate producing bacteria increase in numbers rapidly as the amount of NFC in the diet increases, but the lactate-utilising bacteria adapt more slowly (3 to 4 wk). Therefore, the risk of lactate accumulation in the rumen is high with abrupt changes from high to low fiber diets (Schirmann *et al*., 2013).

Further, as DMI increases, rate of passage from the rumen increases as well. After calving, when DMI is relatively low, rate of passage is slow; allowing for greater extent of fermentation and acid accumulation in the rumen (Maynard *et al*., 1985; McDonald *et al*., 1995).

If dietary NFC increases abruptly at calving, with high levels of fermentable carbohydrates, the amount of VFA produced far exceeds the capacity of the rumen to absorb them leading to elevated concentrations of VFA in the rumen. This situation leads to the phenomenon known as subacute rumen acidosis (SARA) and contributes to reduced DMI and feed digestibility as well as laminitis in the early postpartum period (Krause and Oetzel, 2006).

Health problems associated with the transition period

The conditions described above favor the occurrence of health problems during the transition period. According to Mulligan and Doherty (2008), the principal metabolic disorders related to energy metabolism are ketosis, fatty liver, subacute and acute ruminal acidosis

Nutritional considerations

The transition period is marked by major hormonal changes, as described earlier. While these hormones are causing a reduction in DMI there is an increase in nutrient requirements by the cow to support fetal growth, mammogenesis, and lactogenesis. This increase in nutrient demand is partially met by the DMI and partially by the mobilisation of body tissues (Contreras and Sordillo, 2011). Although the hormonal milieu will drive a certain amount of body mobilisation, excessive body catabolism is undesirable for health, reproduction, and milk production (Esposito *et al*., 2014). It is, therefore, essential to pay particularly close attention to the formulation of rations in this transition period, both pre- and post-partum.

Requirements and the negative energy balance (NEB)

The energetic demands of gestating cows reach 1.3 to 1.5 times the maintenance requirements by the end of gestation. The growth of fetal tissues follows an exponential curve beginning in the third trimester of pregnancy (Ingvartsen, 2006). The fetal, placental, and mammogenesis requirements for nutrients during the third trimester of pregnancy will added on to the requirements (Esposito *et al*., 2014).

During both the prepartum and postpartum transition period, cows require more energy than they are able to consume resulting in NEB and the concomitant loss of body weight to supply the necessary energy, is inevitable, even in healthy cows (Maynard *et al*., 1985). The NEB and body weight loss begins in the prepartum transition period, but the NEB is greatest in the first week postpartum (Kertz *et al.,* 1991). However, there is considerable variation in the magnitude of the NEB after calving depending upon body condition score at calving, the severity of the depression in DMI, the quality of the ration, and season (Esposito *et al*., 2014).

A severe NEB in the transition period can aid in the development of metabolic diseases, prolong the interval between calving and first ovulation and decrease fertility (Robinson *et al*. 2006). The first ovulation in cows occurs 10 days after the nadir in NEB (Janovick *et al*., 2011). Energy during the transition period; therefore, has a major impact on cow performance and longevity. Severe NEB can lead to fatty livers and compromised liver function as liver is a very vital organ essential in all metabolic functions including detoxification, as observed by Esposito *et al*. (2014).

Regulation of energy metabolism and glucose homeostasis

Glucose is a substance that plays a fundamental role in all living beings. In the last week of foetal development, the foetus uses an estimated 46 per cent of maternal glucose taken up by the uterus. Additionally, a cow producing 30 kg of milk/d uses at least 2 kg of blood glucose to synthesise lactose for milk (Ingvartsen, 2006). The end of pregnancy and the beginning of lactation; therefore, represent a time when there is a massive increase in need for glucose. This poses an enormous challenge for the liver that has to synthesise all of this glucose from propionate and amino acids as well as a challenge for other tissues and organs that have to adapt to a reduction of glucose availability. Glucose is an equally important energy source for the ovary and the reduced glucose availability in the beginning

of lactation can negatively impact the re-establishment of ovarian activity after calving (Robinson *et al*., 2006)..

The concentration of plasma insulin decreases dramatically as calving approaches and remains low in the first week postpartum. The concentration of plasma somatotropin increases dramatically and rapidly postpartum. This decrease in insulin combined with a decrease in sensitivity of adipose tissue to insulin and the increase in somatotropin results in a decrease in the synthesis of triglycerides in adipose and favors their mobilisation. Therefore, there is a resulting increase in plasma NEFA at calving. The somatotropin, in concert with elevated cortisol, stimulates the liver to produce more glucose (Esposito *et al*., 2014).

These coordinated changes in metabolism permit the cow to respond to the accrued nutrient demands for milk synthesis. However, due to many factors, including those previously mentioned, the metabolic processes do not adjust sufficiently and a disequilibrated metabolism leads to many of the typical problems associated with transition cows.

Metabolic problems associated with energy nutrition

The mobilisation of lipids in the beginning of lactation is a normal and required process to help the cow meet her energy demands for lactation. However, when the quantity and/or the speed of mobilisation are exaggerated, the incidence of metabolic problems increase significantly (Contreras and Sordillo, 2011). Suthar *et al.* (2013) reported that it is not uncommon to find a ketotic cow also having problems with fatty liver and displaced abomasum. Ruminal acidosis is also a frequent problem for cows at the beginning of lactation, because of highly fermentable rations and insufficient rumen adaptation (slow passage rates) to these rations, as observed by Esposito *et al*. (2014).

Ketosis and fatty liver syndrome

Fat, or lipid, deposited in adipose tissue is in the form of triglycerides that are mobilised as NEFA plus the glycerol backbone of the triglyceride. The liberated, or mobilised, NEFA have one of the following three desirable fates, as described by Ospina *et al*., (2013):

1. To be utilised by the mammary gland for milk fat synthesis;
2. To be used by peripheral tissues as a source of energy; and
3. To be reesterified by the liver into triglycerides and exported as triglycerides

incorporated into very low density lipoproteins (VLDL).

Complete oxidation of NEFA generates metabolites (acetyl coenzyme A) that can be used to generate energy via the Krebs cycle. However, if the Krebs cycle gets overloaded the acetyl Co A is shunted off to produce ketones (acetoacetic acid, acetone, and β hydroxybutyrate or BHB). Obviously, if ketones reach a high concentration in the blood the cow becomes ketotic (Esposito *et al*., 2014).

The normal concentration of plasma ketones (using BHB as an indicator) is less than 10 mg per dl (Janovick *et al*., 2011). Clinical ketosis is defined as a concentration greater than 35 mg/dl. Concentrations between these 2 values are termed subclinical ketosis. When BHB reaches 1400 µmol/l (14.6 mg/dl) in blood, the incidence of metabolic disorders increases and when the value is above 2000 µmol/l (20.8 mg/dl) milk production begins to suffer (Suthar *et al.,* 2013).

Fatty liver

Esposito *et al*. (2014) opined that when fat mobilisation is high and the liver is reesterifying NEFA into triglyceride it cannot produce VLDL fast enough to export the fat and accumulation begins. This is because the liver has a very limited ability to produce VLDL due to a limited capacity to produce a key component (apoprotein B). Once deposited, the fat accumulated in the liver will remain there until the end of the NEB.

Pronounced accumulation of fat in the liver with liver damage and/or reduced liver function compromises, among other things, glucose synthesis. Most of the glucose that the cow requires is synthesised by gluconeogenesis in the liver from propionic acid, amino acids, and the glycerol liberated from adipose (Ingvartsen, 2006).

Esposito *et al*. (2014) carried out an investigation in transition dairy cows to evaluate the capacity of gluconeogenesis by livers of fat and normal cows at calving and observed that the fat cows had an increase of 446 per cent blood NEFA at three days postpartum compared to their prepartum NEFA concentration, while normal cows exhibited an increase of 123 per cent. Similarly, the concentration of fat in the liver of fat cows had increased by 514 per cent by three days after calving while the normal cows had an increase in liver fat by only 97 per cent. The activity of liver enzymes indicated that gluconeogenic capacity of the fat cows was impaired Esposito *et al*. (2014).

Prevention

Block (2010) observed that weight loss, fat mobilisation, NEB, increase in plasma NEFA and liver fat accumulation are in-

evitable in all high producing dairy cows, immediately after parturition. Therefore, to minimise the predisposition of cows to ketosis and fatty liver, it is necessary to avoid excessive weight loss in the pre and postpartum transition period by minimising the magnitude of the NEB. Every attempt should be made to maximise DMI, increase the energy density of the diets without sacrificing rumen function and maintain body condition scores (BCS) near recommended levels at this critical time, as opined by Esposito *et al*. (2014).

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