EFFECTS OF NEGATIVE ENERGY BALANCE ON REPRODUCTION IN DAIRY COWS

RENA TE KNOP, H. CERNESCU
Faculty of Veterinary Medicine Timisoara, Calea Aradului No. 119, 300645, Timisoara, Romania
E-mail: renate.knop@uex-usambt.org

Summary

In many countries the milk production per cow has more than doubled in the last 40 years (OLTENACU, 2007). The increase in production has been accompanied by increasing incidence of health problems, declining ability to reproduce and declining the fertility of modern dairy cows.

High producing dairy cows need to mobilize body reserve to be able to sustain their milk production. In early lactation, until energy intake assures the requirements, dairy cows, especially high producing breeds, enter a state of negative energy balance (NEB), losing high amounts of body condition. The NEB is detectable by measurement of body condition score (BCS), which has been useful in the past and by more sophisticated ways to measure the relationship between adipose tissue and fertility, like metabolic hormones: IGF-I, leptin.

The aim of this study is to summarize the effect of negative energy balance and the risk for reproductive disorders in dairy cows.

Key words: negative energy balance, reproduction, dairy cows.

It is common knowledge that the early lactating cows do not eat as much feed as they do between the second and third months of lactation period, even though the level of milk production may be the same. Feed intake lags behind peak milk production by about two to four weeks. This results in a negative energy balance and, as such, body reserves are mobilized to overcome the energy deficit, which results in some body weight loss. Although it is normal for high-producing cows to lose weight in early lactation, the energy, and especially the protein, available from body stores can supply only a limited amount of the animals needs. As body fat is mobilized to produce more milk, proportionally more energy is available than protein. Therefore, the percent of protein in the ration during early lactation period should be higher in order to maximize the efficiency of energy utilization and to meet the added protein needs.

Because high-producing cows lose body weight in early lactation, a number of studies have attempted to correlate body-weight losses to performance. Both the extent of negative energy balance and the rate of recovery of energy balance appear to be important. In well-fed cows, the negative balances of energy begin to improve at about week four of lactation. Recovery in energy balance from its most negative state may be a signal for initiation of ovarian activity. Thus, negative energy balance may impair fertility by delaying first estrus, limiting the
number of estrus cycles occurring before the preferred breeding period. A number
of studies have indicated that conception is correlated positively with the number of
ovulatory cycles preceding insemination.

First ovulation usually occurs at 17 to 42 days after parturition. It has been
suggested that the greater the level of milk production is, the slower the cow is to
first ovulation. For this reason, many program strategies must be developed so that
high-producing cows to have every opportunity to maximize their production without
compromising on the body needs. (4).

Negative energy balance in dairy cows

Dairy cattle are at increased risk for many diseases and disorders during
early lactation. At this time, usually during the first third of lactation, there is an
increasing milk production, but a lags in feed intake. This combination creates a
negative energy balance (4).

High yielding cows have been selected and bred to produce more milk,
mostly through their ability to mobilize fat and muscle to support milk production in
early lactation. This results in a loss of body condition and is associated with
alterations in blood metabolite and hormone profiles which in turn, influence fertility
(2). In this situation, the cows rely on the mobilization of adipose reserves and they
often lose 60% or more of their body fat in the first weeks after parturition.

PATTON and col. (2006) showed that genetic selection for increased milk
yield has amplified the difference between feed intake potential and milk yield
potential in early lactation, resulting in cows that are genetically predisposed to a
greater risk of NEB.

It has been documented that the severity and duration of NEB are
positively associated with the interval to first postpartum ovulation. In addition, NEB
in early lactation exerts latent negative effects on the quality of oocytes ovulated
80-100 days later, reducing conception rates in the first weeks of the breeding
season. Minimizing the extent and duration of NEB in early lactation is an important
factor for achieving optimum reproductive performance (5).

DE VRIES and VEERKAMP (2000) have shown in their study that a low
nadir of EB is correlated with a delay in the postpartum start of luteal activity. Cows
experiencing stronger negative EB postpartum start lactation with elevated fat
percentages, which decrease to values that are slightly lower than average fat
percentage later in lactation. Therefore, the decrease in fat percentage in the first
weeks postpartum can be used as an indicator of energy deficits during early
lactation and of EB-related problems of a cow, such as delayed resumption of
ovarian activity (6).

Management of prepartum period is also very important to control because
high body condition score (BCS) at calving leads to a greater loss after calving and
thus a lower postpartum BCS. This excessively rapid mobilization of fat early in the
postpartum period is a major risk factor for prolonged anovulatory periods. The
delay to the beginning of energy balance recovery after parturition is positively correlated with the delay from parturition to first ovulation (2).

**Metabolic and endocrine changes in the periparturient cow**

The major adaptive changes occur around the time of parturition. The late dry period coincides with the last phase of fetal growth when nutrient requirements for gravid uterus increase.

Within a few days before calving, a further dramatic rise in the demand for glucose, amino acids and fatty acids for milk synthesis occurs as lactation becomes established. Nonesterified fatty acids (NEFA) released from lipid stores are taken up by the liver, where they may be oxidized to carbon dioxide to provide energy, or partially oxidized to produce ketone bodies or acetate. These are transported for use elsewhere in the body. Alternatively NEFAs may be esterified to triacylglycerols (TAGs) which accumulate in the liver, peaking in concentration at 7-13 days after calving, then declining gradually.

Beta-hydroxybutyrate (BHB) is the predominant form of ketone body in blood and its concentration is an index of fatty acid oxidation. At least 50% of all dairy cows are thought to go through a temporary period of subclinical ketosis in the first month of lactation. This adaptive strategy is for maintaining blood glucose; despite the large increase in demand, circulating concentrations of glucose generally only show a brief fall for around 1-2 weeks at calving.

Blood urea level often fluctuates around calving, influenced by a variety of factors. Glucose availability may be supplemented by increased catabolism of amino acids stored in skeletal muscle and other tissue proteins, thus increasing urea production.

Many metabolic hormones and their receptors also alter in concentration over this critical peripartum period. In particular, interdependent changes occur in the GH-insulin-IGF-I-glucose signaling pathway. IGF-I is believed to be the main mediator of GH (growth hormone) on milk production, regulating milk synthesis by the mammary gland. Most IGF-I in the circulation is released from the liver in response to growth hormone (GH) coupling to GH receptors, with systemic IGF-I negatively feeding back to the pituitary to regulate GH release. During NEB, however, the GH-IGF axis uncouples due to a down-regulation in liver GH-R, associated with a reduction in IGF-I and elevated GH concentrations. This, coupled with the low prevailing insulin, provides an endocrine environment which promotes the direct action of GH on lipolysis and gluconeogenesis in early lactation. At the same time, the indirect actions of GH on growth, which are supported by IGF-I in peripheral tissues, are attenuated. This uncoupling means that the relationship between IGF-I concentrations and yield is initially negative in early lactation, whereas later in lactation, an increase in liver GH-R restores the positive relationship between GH and milk production (2).
Changes in blood metabolites associated with lipid mobilization may affect oocyte quality directly, or indirectly, via alterations in the follicular environment as presented in Fig. 1 (2). Profound changes in the liver lead to reductions in the concentration of GH receptor, IGF-I, several of IGF binding proteins and the acid labile subunit whilst IGFBP-2 is increased. This results in a marked decline in the circulating concentration and half-life of IGF-I which can also impair follicular maturation and steroidogenesis. The uterine repair mechanisms, after calving, are so delayed although it remains uncertain how this effect is mediated.

Leptin is another metabolic hormone of interest in relation to EB as its circulating concentrations is strongly correlated to BCS and falls in late pregnancy (2).

**Leptin related to reproduction**

Leptin is a cytokine-hormone secreted mainly by adipose tissue that has been proposed to act as a direct metabolic signal to the sites in central nervous system that control pulsatile LH release. It seems very likely that leptin accompanies IGF-I in the control of the resumption of ovulation.

Kadokawa and Martin (2) made a study on the relationship between plasma leptin concentrations and the timing of the first ovulation postpartum in Holstein dairy cows. Leptin concentrations declined after parturition and, after reaching nadir, it increased and became stable near the first time of first ovulation. The delay to first ovulation was correlated with the interval from parturition to the leptin nadir, suggesting that a delay in the recovery of leptin secretion increases the delay to the first ovulation.
Other studies found that leptin levels are low during the early postpartum period, when LH pulses are likely to be inhibited because GnRH neuronal activity is suppressed by various neurotransmitters, such as opioids. The decline in leptin production is likely to be due in part to the negative energy.

These observations suggest that there should be a direct relationship between pulsatile LH release and leptin concentrations in dairy cows during the postpartum period before the first ovulation.

The authors, Kadokawa and Martin (2), have tested this hypothesis, and found that LH pulse frequency was positively correlated with energy balance and the plasma concentrations of leptin, and also that LH pulse amplitude was correlated only with leptin values. Between leptin production and the reproductive axis seems to be a strong physiological link, thus, the most obvious possibility is that leptin is being involved in the control of pulsatile LH secretion as a major factor in the ovulatory process (2).

Leptin concentrations remain low postpartum even when the EB status has improved. Like this, leptin can influence voluntary feed intake and may also contribute to the peripheral insulin resistance which occurs in peripartum ruminants (2).

In ruminants, circulating leptin concentrations are positively correlated with body fatness, but this relationship only explains about 10-30% of variation in plasma leptin concentration. This means that other factors must be playing more important roles. Kadokawa and Martin (2) consider that among those factors is also the feed intake. In their study they observed postprandial increases in leptin concentration; glucose did not affect leptin secretion from ruminant adipocytes, but it is possible that there are indirect effects induced by glucose infusion or by volatile fatty acids (VFA), which may stimulate the leptin secretion.

Therefore, leptin secretion is regulated in the short, mid- and long term by feed intake, nutrients and hormones by feeding level, energy balance, physiological stage, body fatness and the reflection of the nutritional history of the animals.

In conclusion, in the aim to apply a new method of measuring the NEB, other than BCS, we should focus our attention on the adipose tissue cells, the adipocytes and the role of the hormone that they produce, leptin. This hormone affects pulsatile LH release and, in dairy cows it seems to be linked to the first postpartum ovulation.

Adipocytes are always sensing energy status and they control leptin secretion dynamically, so blood leptin concentration can change acutely, even when there is no detectable change in BCS.

Leptin secretion seems to be determined by the secretory activity of each adipocyte as well as the total mass of adipocytes in the body of the animal. Kadokawa and Martin (2), consider that the strong relationship between BCS, leptin concentration and reproductive function in dairy cows suggests that the interval of the recovery from prepartum and postpartum damages, the need for high milk yields at the last lactation causing the dry-off stress and the subsequent troubles should be reconsidered. Also, the authors consider that the current drive to reduce...
calving interval should be re-assessed, because milk yields during the early stages of lactation are economically very important but high yields seem to cause several metabolic and reproductive disorders in modern dairy cows (2).

Dietary energy source and reproduction

The products of metabolism supply intermediate signals, which may have an effect on energy balance (EB), health and reproduction in dairy cows in early lactation. Carbohydrates and protein in the diet provide substrates for rumen fermentation, which results in the production of volatile fatty acids (VFA). The main VFA produced are acetate, propionate and butyrate. Acetate and butyrate split into fragments containing two carbon atoms (C2) and are considered lipogenic nutrients. Propionate is a fragment containing three carbon atoms (C3) and is considered a glucogenic nutrient. Dietary ingredients that are resistant to rumen degradation can be digested and absorbed in the intestine and provide either lipogenic or glucogenic nutrients. Dairy cows with metabolic and reproductive disorders in early lactation may suffer from an imbalance in availability of C2 and C3 compounds induced by NEB. Lipogenic nutrients are expected to increase the C2-C3 compound ratio, while glucogenic nutrients decrease the C2-C3 compound ratio.

A.T.M. van Kneegsel et al. (3) made a summary of three recent studies, with the objective to see the effect of dietary energy source on the EB and the risk for metabolic and reproductive disorders in dairy cows, in the period of early lactation. The study showed that multiparous cows fed the glucogenic diet tended to have less days postpartum to the rise of P4 (progesterone concentration in ng/ml milk) than cows fed the mixed diet or lipogenic diet. Mean P4 during the first luteal phase tended to be greater for multiparous cows fed the mixed diet or lipogenic diet compared with the glucogenic diet. In conclusion, glucogenic diets fed during the transition period and early lactation decreased milk fat and milk energy output and tended to stimulate the partitioning of energy to body reserves and improve the EB in early lactation compared with lipogenic diets. As indicated by lower plasma BHBA, NEFA and liver TAG concentration, multiparous cows fed a mainly glucogenic diet seemed to have a decreased risk for metabolic disorders, like ketosis and fatty liver. Multiparous cows fed a glucogenic diet tended to have fewer days to first postpartum ovulation (3).

Conclusions

There is clear evidence that a period of severe NEB around calving adversely affects the future fertility of the cow, in some cases resulting in an animal which fails to conceive at all and must therefore be culled. Many factors influence the extent of the EB deficit. In cows calving for the first time, the age, state of maturity and BCS before calving are all important. In mature cows with a higher
potential for milk production, an adequate BCS at the start of the service period is essential and this is affected by the genetic potential of the cow to mobilize tissue to achieve a high peak yield in early lactation. Once the cow has entered a state of severe NEB, this is very difficult to rectify by remedial veterinary management during the lactation and the process of recovery may take many weeks.

The nutritional management of the cow in the prepartum period is therefore absolutely crucial to prevent metabolic diseases and a difficult calving. Recent suggestions that current feeding practices for dry cows may promote deposition of fat in the liver and viscera, thus predisposing the animal to later health problems, make this issue worth revisiting in an attempt to improve fertility. It is also more difficult to manage high genetic merit animals appropriately. Consideration therefore needs to be given on an individual farm basis as to the optimum genotype to select for that environment, to provide animals in the herd which can achieve reasonable yields whilst maintaining health and fertility.

A period of severe NEB may affect fertility through a variety of mechanisms. NEB reduces the ability of the uterus to recover after calving and may result in persistent inflammatory mediated damage. The metabolic changes associated with tissue mobilization can probably cause damage to oocytes either directly or via alterations of the follicular environment. Adaptive alterations in the GH-IGF axis reduce the bioavailability of circulating IGF-I. This is likely to be a key mediator of EB status on reproductive function, delaying the time to first ovulation and reducing conception rates, possibly through actions on the oviductal and uterine environments. Elevated urea concentrations at the start of the service period are also associated with reduced fertility, but it remains uncertain if this is a direct effect or another symptom of the poor EB status (2).

In ruminants, circulating leptin concentrations are positively correlated with body fatness, feed intake, nutrients and hormones (especially glucose and insulin), LH pulse. In short, this hormone is responsible for the linkage between nutritional status and reproductive function (2).

The general thinking has been that calving interval must be short because short intervals are more profitable. However, if we consider that main product from dairy cows is milk and that a short calving interval is very difficult without reproductive problems, and then a longer calving interval might be more sensible and also more profitable (2).

References

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