Introduction

Dairy cattle are at an increased risk for many diseases and disorders during early lactation (10). At this time, there is increasing milk production, but a lag in feed intake. This combination creates a negative energy balance. The animal attempts to supply the needs for milk production by drawing on body fat reserves. This release of free fatty acids results in the production of the major ketone bodies, acetone, acetoacetate and beta-hydroxybutyrate (BHB) (11). These compounds are important as a source of energy when carbohydrate levels are reduced (2). However, the accumulation of these compounds can lead to ketosis (2). Ketosis has been shown to significantly reduce milk yield in dairy herds (12,13). There can be an average loss of production of 25% or 353.4kg per lactation (10,13) with clinical ketosis. Even with subclinical ketosis, there is a loss of 1-1.5kg/day of milk production (2). Clinical ketosis typically occurs within the first six to eight weeks post calving, and results in rapid loss of condition, decreased milk production, and hard dry feces (10). In addition, the milk fat yield of ketotic cows is increased due to the availability of beta-hydroxybutyric acid (BHB) and fatty acids. Occasionally, cows with clinical ketosis will show nervous signs, such as licking and blindness (11).

Diagnosis

Subclinical ketosis is a disorder that is associated with increased levels of circulating ketone bodies without the signs that accompany the clinical form (2). Subclinical ketosis is identified by the concentrations of ketone bodies that are present in the serum, milk and urine (2). There have been many thresholds that have been used to distinguish between clinical and subclinical ketosis (15, 16, 17). However, BHB levels between 1000 μmol/L and 1400 μmol/L have been reported as thresholds that can be used for subclinical ketosis (2). There are a number of cowside tests that have been evaluated for the detection of ketone levels in serum, milk or urine (15,17,18). Most of these tests lack sensitivity as compared to serum BHB, which remains the gold standard for studying ketosis. Cows are at risk for subclinical ketosis within the first two months postpartum (2). The reported prevalence of subclinical ketosis ranges from 7%-34% (2). In the first 65 days of lactation the prevalence ranges from 12.1% to 14.1% (3,19). It has been observed in previous studies that the occurrence of displaced abomasum (DA) is closely correlated to ketosis (20,21,22). Cows with BHB levels at or above 1400 μmol/L, which is in the range for subclinical ketosis, were three times more likely to develop a displaced abomasum (23).

Marked decrease in DMI immediately before calving is extremely important in the development of excessive negative energy balance (2). Monitoring changes in DMI in the immediate prepartum period can be accomplished in an intensive research situation. However, these data are extremely difficult to collect in commercial dairy herds. It is felt that the circulating levels of
non-esterified fatty acids (NEFA) is a valid measure of energy metabolism, especially in the immediate prepartum transition period of the dairy cow. The measurement of NEFA currently involves a laboratory test procedure to determine levels in serum or plasma. However, a rapid detection system has been developed that will identify cows starting into marked negative energy balance. It is distinctly possible that these cows could respond to therapy that would resolve the metabolic problem and avert losses from periparturient disease, reduced reproductive performance, and poor passive transfer of colostral immunity.

Prepartum, blood NEFA concentration may be used to detect cows at risk for problems with severe NEB. Serum NEFA greater than 0.4 mEq/L NEFA has been proposed to identify excessive prepartum NEB. Measuring NEFA has traditionally involved submission of serum to a diagnostic laboratory. The DVM NEFA test (Veterinary Diagnostics. Newburg, Wisconsin, USA) is a new, rapid, spectrophotometry method to determine NEFA concentration in serum through light absorbance. The objective of this study was to determine the test characteristics of the DVM NEFA test and its usefulness as a method of identifying problems with NEB in prepartum dairy cows. Primaparous and multiparous animals were enrolled between 7 and 4 days prior to their expected calving date. Blood was collected by coccygeal venapuncture and serum harvested. Cows were re-sampled twice weekly until calving. In addition, each cow was sampled in Week 1 and Week 2 postpartum for BHB and other indicators of metabolism. NEFA concentration was measured using the DVM NEFA test. An aliquot of each serum sample was submitted to the Animal Health Laboratory (AHL) at the University of Guelph for analysis by a Hitachi 911 automated analyzer (Roche, Laval, Quebec). The AHL NEFA concentration was considered the gold standard for this evaluation. A total of 491 samples from 256 cows from eight farms in the Guelph, Ontario area were utilized in this study. The Pearson correlation coefficient between the DVM NEFA and the AHL NEFA determination was 0.75. Using 350 samples drawn within 14 days prepartum, and NEFA > 0.4 mEq/L from the AHL test as the gold standard, the sensitivity and specificity of the DVM NEFA test were 84% and 96%, respectively. It is noteworthy that changing the NEFA cut-off level to > 0.5 mEq/L resulted in a similar sensitivity and specificity of 85% and 97%, respectively. There was a significant association between prepartum DVM NEF A and postpartum BHB in the first week after calving (n=280) (P<0.01 for Corrected Yates). The odds ratio was 2.33, meaning that cows detected with high prepartum DVM NEFA values are 2.3 times more likely to have subclinical ketosis (BHB > 1400) in the first week after calving. Furthermore, the association between prepartum DVM NEFA and postpartum BHB for both Week 1 and Week 2 postpartum were also statistically significant (P<0.02 for Pearson's Chi Square and the Corrected Yates). In this case, the odds ratio indicates that cows with detected high DVM NEFA prepartum were 2.0 times more likely to have subclinical ketosis (BHB > 1400) in both of the first two weeks after calving. It was concluded that the DVM NEFA test characteristics were satisfactory for detection of cows with elevated prepartum NEFA, and useful for prediction of cows with increased risk of postpartum subclinical ketosis.

Prevention of Negative Energy Balance

Cows that are given monensin in a controlled release capsule have reduced incidence of abomasal displacement, as well as clinical and subclinical ketosis. These effects are associated with the decreased BHB levels and reduced body condition score loss assisted by monensin
administration (31,32,33,34). The results from the cited studies have led to approval of Rumensin® controlled release capsule in Canada, for the prevention of subclinical ketosis and left displaced abomasum (LDA). It has gained widespread use in the dairy industry in Canada.

When treating cows for negative energy balance, it is essential that the need for glucose be met, and that the ketogenic process in the liver are reversed (2,11). Typically, this is achieved with an intravenous, 50% dextrose solution (11). However, the effects of this therapy are short-lived and must be repeated for 2-4 days following initial treatment (11). Therefore, glucocorticoids, propylene glycol or sodium propionate are often administered (10,24). Drenching with propylene glycol has a slight beneficial effect of reducing NEFA and BHB levels (24). Slow release insulin has also been used for therapy of ketosis, and has resulted in increased dry matter intake (DMI) and milk yield (25). In addition, there were reduced liver triglyceride and non-esterified fatty acid levels (25). However, there is evidence that insulin resistance exists in peripheral muscle, adipose and hepatic tissues. Several researchers have found that the addition of more insulin to the system does not help to suppress fatty acid mobilization, increase adipose tissue uptake, or stimulate hepatic glycolysis (26,27,28).

Impact of Negative Energy Balance in Transition Cows

Recent research by the dairy health management group at the University of Guelph has evaluated several metabolic measures immediately before and after calving in 1184 dairy cattle. It was found that cows that developed left displaced abomasum after calving, had significantly elevated blood NEFA levels up to ten days prior to calving (6) (Figure 1). In other recent research, we have identified significant associations between body condition scores, DMI and NEFA during the week before calving, and the levels of BHB after calving (7). Furthermore, it is clear that immediately prepartum, blood NEFA, and to some extent urine BHB, concentrations can be used to detect cows at risk for problems with severe negative energy balance after calving (8).

Research conducted in Europe has shown that subclinical ketosis in prepartum cows has a significant negative impact on the composition of colostrum and the health of newborn calves (9). It is interesting that very little research has been done in this area, even though investigations on the transition period have intensified, and colostrum management programs are known to have a huge influence on calf health. There is a need to combine studies in these areas by following the impact of metabolic changes before calving on colostrum quality and calf health.
immediately before calving is extremely important in the development of excessive negative energy balance (5). Monitoring changes in DMI in the immediate prepartum period can be accomplished in an intensive research situation. However, these data are extremely difficult to collect in commercial dairy herds. It is felt that the circulating levels of non-esterified fatty acids (NEFA) is a valid measure of energy metabolism, especially in the immediate prepartum transition period of the dairy cow. The measurement of NEFA currently involves a laboratory test procedure to determine levels in serum or plasma. However, a rapid detection system can be developed that will identify cows starting into marked negative energy balance, and that these cows will respond to therapy that will resolve the metabolic problem and avert losses from periparturient disease, reduced reproductive performance, and poor passive transfer of colostral immunity.
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