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Response to dietary-induced energy restriction in dairy sheep divergently selected for resistance or susceptibility to mastitis

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ABSTRACT

Dairy ruminants experiencing a severe postpartum negative energy balance (NEB) are considered to be more susceptible to mastitis. Although the genetic variability of mastitis resistance is well established, the biological basis of the link between energy metabolism and resistance is mostly unknown. The aim of this study was to characterize the effect of NEB on metabolism and immune response according to the genetic background for mastitis resistance or susceptibility. Forty-eight ewes from high and low somatic cell score (SCS) genetic lines were allocated to 2 homogeneous subgroups 2 wk after lambing: one group (NEB) received an energy-restricted diet to cover 60% of their energy requirements, and the other group received a control (positive energy balance: PEB) diet. Both diets met the protein requirements. After 10 d on either the NEB or PEB diet, all ewes were injected with a Pam3CSK4/MDP solution in one half-udder to induce an inflammatory response. The ewes were monitored for milk production, somatic cell count (SCC), body weight (BW), body condition score (BCS), and blood metabolites. Differential milk cell counts were determined by flow cytometry. Plasma concentrations of glucose, insulin, nonesterified fatty acids (NEFA), β-hydroxybutyrate (BHB), and triiodothyronine were determined. Energy restriction resulted in an increased fat:protein ratio in milk and decreased milk yield, BW, and BCS. The NEB ewes had significantly higher NEFA and BHB and lower plasma glucose concentrations than PEB ewes, reflecting a mobilization of body reserves and ketone body synthesis. High-SCS ewes had a higher SCS than low-SCS throughout the experiment, except after the inflammatory challenge, which resulted in similar SCS in all 4 groups. A noteworthy interaction between genetic background and diet was evidenced on metabolic parameters and BW. Indeed, high-SCS ewes subjected to NEB showed greater decrease in BW and increased NEFA and BHB concentrations compared with low-SCS ewes. Thus, NEB in early lactation led to extensive mobilization of body reserves and intense ketone body synthesis in mastitis-susceptible sheep. These results reinforce the hypothesis of a genetic association between mastitis susceptibility and energy metabolism and open the way to further studies on the biological basis for this association.
Key words: mastitis susceptibility, negative energy balance, dairy ruminant

INTRODUCTION

Mastitis is considered the most frequent and costly disease of dairy cattle (Barkema et al., 2009) and sheep (Bergonier et al., 2003), which makes it one of the major concerns in dairy production. The highly successful selection for milk production achieved over recent decades has led to a poorer mastitis resistance (Heringstad et al., 2005). Thus, genetic improvement might be a useful option for diminishing mastitis frequency. In this context, we developed a divergent breeding protocol in Lacaune dairy sheep based on extreme values of log-transformed SCC (Rupp et al., 2009). Measurements of the frequency and duration of bacteria in milk (Rupp et al., 2009) showed that low-SCS and high-SCS ewes have lower and higher rate of IMI in natural conditions, respectively. Additionally, bacteriological titer after experimental challenge (Bonnefont et al., 2011) in the 2 genetic lines (high vs. low SCS) demonstrated that bacterial clearance is more efficient in low-SCS ewes than in the high-SCS ewes. Accordingly, low-SCS and high-SCS ewes were further defined as high- and low-resistant sheep.

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Increased susceptibility to mastitis during the peripartum period has been widely documented, as reviewed by Mallard et al. (1998). The potential role of a functional link between the immune and endocrine systems during the peripartum period has been mentioned. Dairy cattle experiencing a severe negative energy balance (**NEB**) are considered to be more susceptible to mastitis (Suriyasathaporn et al., 2000; Goff, 2006). Some degree of NEB can be expected during the periparturient period due to the increased energy required to support lactation coupled with a reduced feed intake (Drackley, 1999), especially in high milk-producing animals. The severity and duration of NEB associated with early lactation lead to extensive mobilization of FA from the adipose tissue and result in higher blood nonesterified fatty acids (**NEFA**) or BHB concentrations, or both (Dann et al., 2006).

Several studies have reported an impairment of immune functions in response to increased concentrations of FA and ketone bodies in vitro. The phagocytic and bactericidal capacities of polymorphonuclear neutrophils (PMNL) in vitro are impaired by ketone body concentrations similar to those observed around parturition (Suriyasathaporn et al., 1999). Moreover, Scalia et al. (2006) showed that high concentrations of NEFA reduced bovine PMN viability in vitro. However, the mechanisms behind the relationship between energy balance and immune function in vivo remain unclear.

Although large-scale studies demonstrated an association between NEFA and BHB and the risk of mastitis during early lactation (Jánosi et al., 2003; Nyman et al., 2008), no firm conclusions could be drawn from studies based on diet-induced NEB models. For instance, Moyes et al. (2009) fed mid lactation cows with either 60% of their maintenance requirements or ad libitum. Diet had no effect on the chemotaxis of blood neutrophils and only a slight effect on phagocytosis capability.

Several studies have reported positive genetic associations between mastitis and ketosis (Heringstad et al., 2005; Zwald et al., 2004). Moreover, Koeck et al. (2014) recently showed that a lower BHB during the early stages of lactation was genetically associated with less frequent clinical ketosis (genetic correlation = 0.48) and lower SCC (Pearson correlations with EBV = 0.11). Altogether, these studies support a biological and genetic association between mastitis and metabolic diseases in early lactation. However, to our knowledge, the direct relationship between early lactation NEB and genetic predisposition to mastitis has never been investigated in vivo. Hence, our model of divergent genetic lines provides a unique opportunity to examine the response of ewes with contrasting genetic backgrounds in mastitis susceptibility to metabolic stress. Our objective was therefore to determine the consequences of experimentally induced NEB during early lactation on production traits and metabolic response in 2 divergent genetic lines, respectively selected for either enhanced or reduced resistance to mastitis.

MATERIALS AND METHODS

The experiment was carried out following the procedures approved by the Ethics Committee on Animal Experimentation of Toulouse (France), Agreement 01557/01.

Animals

Forty-eight primiparous Lacaune ewes bred at the INRA experimental facility of La Fage (UE321, Roquefort, France) were used for the study. They were enrolled 5 wk before their first lambing until 1 mo after lambing. They belonged to the 2 genetic lines, high and low SCS, divergently selected as described in Rupp et al. (2009). Briefly, the ewes were obtained by one-generation divergent selection of French Lacaune dairy ewes based on dams and progeny-tested rams selected for extreme breeding values for log-transformed SCC. Previous studies had shown that low-SCS ewes are characterized by higher mastitis resistance than high-SCS ewes (Rupp et al., 2009). Ewes in both genetic lines (high vs. low SCS) were housed together in the same facility and managed identically. After lambing, the ewes were left with their lamb for 24 h to allow colostrum consumption. After 24 h, the lambs were removed and fed a milk replacer. The ewes were then machine-milked together, in no predefined milking order, twice a day (0800 and 1700 h) and had free access to water. The bedding before lambing was straw and wood shavings thereafter.

Experimental Design and Diets

A preliminary phase was instigated 5 wk before lambing to adapt the ewes to the diet and individual feeding system. This system was electronically controlled to allow access of each animal to its correct place and to measure the refused feed. As shown in Figure 1, the experiment per se consisted of 4 phases: a postlambing adjustment period, an energy restriction period, an inflammatory challenge period, and a postrestriction period. Phase 1 consisted of a 2-wk period of adjustment after lambing during which individual measurements were taken to calculate the amount of feed to be offered thereafter and to constitute the experimental groups. These groups were based on the genetic line (high-SCS or low-SCS) and diet, namely NEB ewes,