J. Dairy Sci. 99:1–21
http://dx.doi.org/10.3168/jds.2015-9694

Associations between the degree of early lactation inflammation and performance, metabolism, and immune function in dairy cows

M. M. McCarthy,* T. Yasui,* M. J. B. Felippe,† and T. R. Overton*[1]
*Department of Animal Science, and
†Department of Clinical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853

ABSTRACT

The objective of the current study was to determine associations between the severity of systemic inflammation during the early postpartum period and performance, energy metabolism, and immune function in dairy cows. Cows were assigned to categorical quartiles (Q; Q1 = 0.18–0.59, Q2 = 0.60–1.14, Q3 = 1.15–2.05, and Q4 = 2.06–2.50 g of haptoglobin/L) based on the highest plasma haptoglobin (Hp) concentration measured during wk 1 postpartum. Although cows were assigned to different categories of inflammation during the postpartum period, we detected a quadratic relationship of inflammation on prepartum dry matter intake (DMI) and body weight (BW) such that cows in Q2 had lower prepartum DMI and cows in Q2 and Q3 had lower prepartum BW compared with cows in the other quartiles. We also detected a quadratic association of inflammation with postpartum DMI and BW such that cows in Q2 and Q3 also had generally lower postpartum DMI and BW compared with cows in Q1. There was a tendency for a Q × time interaction for milk yield and Q × time interactions for 3.5% fat-corrected milk and energy-corrected milk yields; quadratic relationships suggested decreased milk yield for Q2 and Q3 cows. We also found Q × parity and Q × time interactions for plasma glucose and insulin concentrations, suggesting alterations with differing degrees of inflammation. There was also a Q × time interaction for plasma nonesterified fatty acids concentration. In addition, alterations in liver triglyceride and glycogen contents for cows with inflammation as well as alterations in [1-^{14}C]propionate oxidation in vitro were observed. Although we observed limited effects of inflammation on neutrophil and monocyte phagocytosis at d 7 postpartum, inflammation appeared to alter neutrophil and monocyte oxidative burst. Overall, cows with any degree of elevated haptoglobin in the first week after calving had alterations in both pre- and postpartum intake and postpartum metabolism.
Key words: early lactation, haptoglobin, energy metabolism, immune function

INTRODUCTION

During the immediate postpartum period, systemic inflammation can be identified by a marked increase in plasma acute phase protein concentrations (Bionaz et al., 2007; LeBlanc, 2012). Inflammation can develop upon pathogen recognition, as well as in response to trauma or stress, and is an essential component of the initial immune response for recruitment of immune cells to the affected tissues. Cytokines that are produced by immune cells [especially proinflammatory tumor necrosis factor-α (**TNF-α**) and IL-6] induce the production and release of acute phase proteins (e.g., haptoglobin, **Hp**) from the liver. Haptoglobin has been used as a marker of systemic inflammation in transition dairy cows, as it is elevated during the immediate postpartum period (Huzzey et al., 2009, 2011; Galvão et al., 2010). Elevated postpartum Hp has been associated with the occurrence of metritis (Huzzey et al., 2009; Galvão et al., 2010), greater risk for developing a metabolic disorder within 30 d postpartum (Huzzey et al., 2011), and decreased milk production (Huzzey et al., 2012).

In human patients with severe sepsis or major trauma, resting energy expenditure increases to 40% above normal and continues to be elevated for 3 wk after the onset of illness (Plank and Hill, 2000). These data suggest that an immune disturbance increases the energy maintenance requirement. Negative energy balance (**NEB**) has been negatively correlated with both energy status (Galvão et al., 2010) and neutrophil function (Hammon et al., 2006). Together these data suggest that insufficient energy availability impairs the ability of the animal to mount a sufficient immune response. However, the energetic cost of immune activation in dairy cows has not been well-studied, and further investigation is warranted.

Received April 9, 2015.
Accepted August 30, 2015.
[1]Corresponding author: tro2@cornell.edu

Elevated TNF-α has been shown to decrease glucose production (Kettelhut et al., 1987) and decrease fatty acid oxidation (Nachiappan et al., 1994), likely leading to increased triglyceride accumulation in the liver, with further impairment of energy metabolism (Strang et al., 1998). Oral administration of cytokine IFN-α in late gestation resulted in increased plasma BHB concentrations during the first 2 wk after calving (Trevisi et al., 2009), and injections of exogenous TNF-α for 7 d doubled liver triglyceride content in late-lactation dairy cows (Bradford et al., 2009). These data suggest that increased inflammation disrupts normal energy metabolism processes. In addition, delaying the postpartum inflammatory response with salicylate treatment altered the metabolic adaptations of early lactation dairy cows and led to increased glucose utilization by peripheral tissues after salicylate treatment ended (Farney et al., 2013), suggesting that inflammatory pathways are also involved in the homeorhetic adaptation to lactation.

Many of the studies that have utilized early postpartum Hp as a marker of inflammation in early lactation dairy cows have been large field studies with infrequent sampling points (Huzzey et al., 2011) or measured Hp association with specific disease outcomes of interest (Huzzey et al., 2009; Galvão et al., 2010; Yasui et al., 2014). Although excessive inflammation has been shown to be associated with negative downstream consequences, it is unclear how much or what type of inflammation is necessary for postpartum adaptation (Huzzey et al., 2011). This current study further evaluates associations between the severity of systemic inflammation during the early postpartum period and performance, energy metabolism, and immune function.

MATERIALS AND METHODS

Animals and Treatments

All animal procedures were approved by the Cornell University Institutional Animal Care and Use Committee before the onset of the experiment. Data from 70 Holstein cows (primiparous n = 21, multiparous n = 49) from the Cornell University Teaching and Research Center Dairy (Harford, NY) were used for this study. Cows were recruited to address the hypotheses from a separate experiment (McCarthy et al., 2015a,b) that evaluated responses to feeding strategy in the early lactation period (high starch vs. low starch diet during the first 21 d postpartum) and monensin supplementation (0 mg of monensin/d or 400 mg/d of monensin prepartum and 450 mg/d of monensin postpartum; Rumensin; Elanco Animal Health, Greenfield, IN) as the variables of interest; detailed diet descriptions are provided in McCarthy et al. (2015a). Briefly, all cows were fed the same prepartum diet (17.4% starch, 42.9% NDF, 28.2% ADF, 13.0% CP) and either a high starch (26.2% starch, 34.3% NDF, 22.7% ADF, 15.5% CP) or low starch (21.5% starch, 36.9% NDF, 25.2% ADF, 15.4% CP) postpartum diet depending on treatment assignment for the first 21 d of lactation. On d 22 postpartum, all cows were fed the high starch diet until d 63 of lactation. Lactating cows were dried off at least 45 d before expected parturition and moved to the experimental tiestall barn 28 d before expected parturition; data were collected through d 63 of lactation.

Data Collection, Sampling Procedures, and Analytical Methods

All cows were milked 2 times daily for the 9-wk lactation phase of the trial, and daily milk yield was measured electronically. Daily milk yield was the sum of the 2 milkings, and weekly means of daily production were calculated. Weekly milk samples were collected from 2 consecutive milkings obtained over a 24-h period. Individual milk samples were sent to a commercial laboratory for analysis of milk composition (Dairy One, Ithaca, NY) as described by McCarthy et al. (2015a). Weekly yields of milk components were calculated, as well as yields of FCM [3.5% FCM = (0.432 × milk kg) + (16.216 × fat kg)] and ECM [(0.327 × milk kg) + (12.95 × fat kg) + (7.65 × true protein kg)].

Cows were housed in individual tiestalls and fed once daily for ad libitum intake at 0700 h in amounts targeted to provide 2 to 3 kg (wet weight) of refusals. Refusals for each cow were removed daily before feeding, weighed, and recorded. All ingredients were sampled weekly for determination of DM content to adjust ration formulation. Weekly means of daily DMI were calculated before statistical analysis.

All cows were weighed once weekly and BCS were assigned for all cows weekly by 2 scorers using a 5-point system (Wildman et al., 1982), and scores were averaged before statistical analysis. Daily observations and general health records were maintained throughout the study. Prepartum and postpartum energy balance calculations were determined according to NRC (2001) equations as described in McCarthy et al. (2015a).

Plasma Sampling and Analyses

Blood samples were collected via venipuncture of the coccygeal vessels using heparinized Vacutainer tubes (Becton Dickinson, Franklin Lakes, NJ) 1 h before feeding. Blood samples were collected 1×/wk prepartum beginning during the week before commencement