J. Dairy Sci. 100:1–17
https://doi.org/10.3168/jds.2016-11790

Far-off and close-up dry matter intake modulate indicators of immunometabolic adaptations to lactation in subcutaneous adipose tissue of pasture-based transition dairy cows

M. Vailati-Riboni,* G. Farina,*† F. Batistel,* A. Heiser,‡ M. D. Mitchell,§ M. A. Crookenden,# C. G. Walker,# J. K. Kay,‖ S. Meier,‖ J. R. Roche,‖ and J. J. Loor*[1]
*Department of Animal Sciences and Division of Nutritional Sciences, University of Illinois, Urbana 61801
†Dipartimento di Patologia Animale, Igiene e Sanità Pubblica Veterinaria, Università di Milano, Milan, Italy 20122
‡AgResearch, Hopkirk Research Institute, Grasslands Research Centre, Palmerston North, New Zealand 4442
§University of Queensland, Centre for Clinical Research, Royal Brisbane and Women's Hospital Campus, Herston, Queensland, Australia 4029
#DairyNZ Limited, c/o University of Auckland, 3A Symonds St., Auckland, New Zealand 1010
‖DairyNZ Limited, Private Bag 3221, Hamilton, New Zealand 3240

ABSTRACT

The common practice of increasing dietary energy density during the close-up dry period (last ~3 wk prepartum) has been recently associated with a higher incidence of metabolic disorders after calving. Despite these reports, over-feeding of metabolizable energy (ME) during the far-off, nonlactating period is a common management policy aimed at achieving optimum calving body condition score (BCS) in pasture-based systems, as cows are generally thinner than total mixed ration cows at the end of lactation. Our hypothesis was that both far-off and close-up overfeeding influence the peripartum adipose tissue changes associated with energy balance and inflammatory state. Sixty mid-lactation, grazing dairy cows of mixed age and breed were randomly allocated to 1 of 2 groups that were managed through late lactation to achieve a low and high BCS (approximately 4.25 and 5.0 on a 10-point scale) at dry-off. The low BCS cows were then overfed ME to ensure that they achieved the same BCS as the higher BCS group by calving. Within each rate of BCS gain treatment, cows were offered 65, 90, or 120% of their pre-calving ME requirements for 3 wk pre-calving in a 2 × 3 factorial arrangement of treatments (i.e., 10 cows/treatment). Subcutaneous adipose tissue was collected via biopsy at −1, 1, and 4 wk relative to parturition. Quantitative PCR was used to measure mRNA and microRNA expression of targets related to adipogenesis and inflammation. Cows overfed in the far-off period had increased expression of miR-143 and miR-378 prepartum (−1 wk) indicating greater adipogenesis, consistent with their rapid gain in BCS following dry-off. Furthermore, the lower postpartum expression of *IL6*, *TNF*, *TLR4*, *TLR9*, and miR-145, and a higher abundance of miR-99a indicated lower body fat mobilization in early lactation in the same group. In the close-up period, feeding either 65 or 120% of ME requirements caused changes in *FASN*, *IL1B*, *IL6R*, *TLR9*, and the microRNA miR-143, miR-155, and miR-378. Their respective expression patterns indicate a tentative negative-feedback mechanism in metabolically compromised, feed-restricted cows, and a possible immune-related stimulation of lipolysis in apparently static adipocytes in overfed cows. Data from cows fed 90% of ME requirements indicate the existence of a balance between lipolytic (inflammatory-related) and anti-lipolytic signals, to prime the mobilization machinery in light of imminent lactation. Overall, results indicate that far-off dry cow nutrition influences peripartum adipose tissue metabolism, with neither strategy negatively affecting the physiological adaptation to lactation. Furthermore, to ensure a favorable transition, cows should be subjected to a small feed restriction in the close-up period, irrespective of far-off nutritional management.
Key words: nutrition, transition period, inflammation, metabolism

INTRODUCTION

The BCS of a dairy cow is an assessment of the amount of body fat that it possesses. It is an important factor in dairy cattle management (Roche et al., 2009), due to its association with production and reproduction parameters and the chances for a successful lactation (Waltner et al., 1993; Roche et al., 2005; Pires et al., 2013; Randall et al., 2015). The progression of BCS in a TMR-based system during the lactation cycle (e.g., intercalving) is inversely related to the lactation curve

Received July 27, 2016.
Accepted November 13, 2016.
[1]Corresponding author: jloor@illinois.edu

(i.e., it declines to a nadir 40 to 100 d after calving as milk production peaks, before increasing again as milk production declines; Roche et al., 2009). However, in seasonal spring-calving cows grazing fresh pasture, a second period of loss in mid-lactation (Roche et al., 2007) leads to thinner cows at the end of lactation, compared with counterparts fed a TMR (Roche et al., 2007).

To avoid the detrimental physiological and metabolic effects of calving with a low BCS (Pires et al., 2013; Akbar et al., 2015), cows in pasture-based systems have to consume ME in excess of requirements during the far-off nonlactating period (>4 wk before calving) to achieve optimal calving BCS targets (Roche et al., 2009). However, Dann et al. (2006), working with TMR-fed cows, provided evidence that overfeeding in the far-off period might increase the risk of metabolic dysfunction during early lactation.

To further complicate peripartal nutritional management, cows are historically allowed ad libitum access to energy-dense feeds during the weeks before calving (Boutflour, 1928; i.e., during the so-called close-up dry period), thereby ensuring that cows do not lose condition pre-calving. Recent studies from different research groups have demonstrated, however, that this practice can lead to undesired outcomes including detrimental metabolic shifts such as increased postpartum blood FA concentration (Rukkwamsuk et al., 1999; Holtenius et al., 2003; Janovick et al., 2011; Ji et al., 2014; Khan et al., 2014) and poorer postpartum health indices (Dann et al., 2006; Soliman et al., 2007; Graugnard et al., 2013; Shahzad et al., 2014).

Adipose tissue plays an important role in the cow's adaptation to lactation and its metabolism is directly linked and responsive to DMI (McNamara, 1991, 1997). Furthermore, data from nonruminants underscore that it plays an active role in its self-regulation [e.g., through the production of adipokines (Adamczak and Wiecek, 2013; McGown et al., 2014; Musi and Guardado-Mendoza, 2014)]. Among its self-regulating features, adipose has the ability to generate a local inflammatory response, also (in human and mice models) through the recruitment and regulation of the innate immune system (Grant and Dixit, 2015), leading scientists to hypothesize a homeorhetic role of inflammation as a physiological adaptation to lactation (Mukesh et al., 2009; Farney et al., 2013; Vailati Riboni et al., 2015; Vailati Riboni et al., 2016).

A recent study (Arner and Kulyte, 2015) investigated the involvement of microRNA (**miRNA**) in fat cell formation (adipogenesis) and regulation of metabolic and endocrine functions; the results demonstrated how adipocyte metabolic pathways are not only controlled by the well-established changes in mRNA expression, but also that miRNA signaling through complex networks involving transcription factors plays an important role in the control of inflammation. Furthermore, miRNA expression patterns in humans have also been associated with levels of inflammatory molecules (e.g., cytokines) and the degree of immune cell infiltration (Kloting et al., 2009).

We previously demonstrated that prepartum BCS and level of nutrition in grazing cows can affect adipose tissue adaptation to lactation through complex immunometabolic pathways (Vailati-Riboni et al., 2016). Overfeeding optimally conditioned cows during close-up primed adipose tissue for accretion of lipid and caused a robust localized inflammatory response, which upon parturition may increase the probability for metabolic disorders. We hypothesized that far-off overfeeding could impair the adipose tissue adaptation to lactation, with further detrimental effects, or mitigation of these, when combined with close-up overfeeding, or feed-restriction, respectively. In the present study, gene and miRNA expression profiling was used to further understand the adipose responses to the physiological changes induced by the high metabolic demands of early lactation, and their interaction with far-off and close-up nutritional strategies.

MATERIALS AND METHODS

Animal Management

Complete details of the experimental design are reported elsewhere (Roche et al., 2016). Briefly, a group of 150 mid-lactation dairy cows (that passed a veterinary clinical examination, which included a full pathology health panel) of mixed age and breed (Holstein-Friesian, Jersey, Holstein-Friesian × Jersey) were allocated randomly to one of 2 treatment groups (75 cows per group) 18 wk before planned start of calving, and managed through late lactation to achieve a high and low BCS (approximately 4.75 and 4.25, on a 10-point scale, where 1 is emaciated and 10 is obese; Roche et al., 2004). Consequently, to reach optimal calving BCS (5.00, Roche et al., 2004), the high BCS group had <0.25 BCS units to gain during the 5-wk far-off period (**SlowBCS** gain), whereas the low BCS cows were overfed to ensure a gain of 0.75 to 1.0 BCS units in the same period (**FastBCS** gain). From approximately 3 wk before calving, cows within each BCS gain group were randomly assigned in a 2 × 3 factorial arrangement of treatments to 1 of 3 feeding level categories: 65, 90, and 120% of estimated ME requirements (**Feed65**, **Feed90**, and **Feed120**, respectively). Although cow allocation to treatment was random, groups were assessed to ensure they were balanced for