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Response of plasma glucose, insulin, and nonesterified fatty acids to intravenous glucose tolerance tests in dairy cows during a 670-day lactation

L. C. Marett,*[1] M. J. Auldist,* P. J. Moate,* W. J. Wales,* K. L. Macmillan,† F. R. Dunshea,‡ and B. J. Leury‡
*Agriculture Research Division, Department of Environment and Primary Industries, Ellinbank, Victoria 3821, Australia
†Faculty of Veterinary Science, The University of Melbourne, Werribee, Victoria 3030, Australia
‡Melbourne School of Land and Environment, The University of Melbourne, Parkville, Victoria 3010, Australia

ABSTRACT

This experiment investigated the metabolic response of dairy cows undergoing an extended lactation to a frequently sampled intravenous glucose tolerance test. The experiment used 12 multiparous Holstein cows that calved in late winter in a seasonally calving pasture-based system and were managed for a 670-d lactation by delaying rebreeding. In each of four 5-wk experimental periods commencing at approximately 73, 217, 422, and 520 (±9.1) days in milk (DIM), cows were offered a diet of perennial ryegrass (73 and 422 DIM) or pasture hay and silage (217 and 520 DIM) supplemented with 1 kg of DM grain (control; CON) or 6 kg of DM grain (GRN) as a ration. Daily energy intake was approximately 160 and 215 MJ of metabolizable energy/cow for the CON and GRN treatments, respectively. At all other times, cows were managed as a single herd and grazed pasture supplemented with grain to an estimated minimum daily total intake of 180 MJ of metabolizable energy/cow. Cows were fitted with an indwelling jugular catheter during the final week of each experimental period. The standard intravenous glucose tolerance test using 0.3 g of glucose per kilogram of body weight was performed on each cow at approximately 100, 250, 460, and 560 DIM. Plasma concentrations of glucose, insulin, and nonesterified fatty acids (NEFA) responses were measured. Milk yield, milk solids yield, body weight, and basal plasma glucose were greater in the GRN compared with the CON treatment. The area under the plasma response curve relative to baseline (AUC) for glucose, insulin, and NEFA and their apparent fractional clearance rates indicated varied whole body responsiveness to insulin in terms of glucose metabolism throughout the 670-d lactation. The glucose AUC 0 to 20 min postinfusion was increased at 560 DIM, indicating reduced utilization of glucose by the mammary gland at this stage of lactation. The NEFA clearance rate, 6 to 30 min postinfusion, was greater at 460 and 560 DIM. These data indicated an increase in lipogenic activity or a decrease in lipolysis as lactation progressed, suggestive of an overall increase in responsiveness to insulin in terms of whole body lipid metabolism as lactation progressed. These observations are consistent with decreased priority of lactation beyond 300 DIM. Cows in the GRN treatment had decreased whole body responsiveness to hyperglycemia compared with CON cows in terms of glucose clearance and AUC for the glucose response. Variation in the response curves of plasma glucose, NEFA, and insulin was predominantly a result of stage of lactation and not diet. This may be due to changes in mammary gland uptake of glucose that is independent of insulin and the responsiveness of peripheral tissues to the actions of insulin at different stages of the lactation that are independent of diet.
Key words: extended lactation, glucose tolerance, insulin sensitivity, fatty acid metabolism

INTRODUCTION

Dairy farm systems that incorporate extended lactations up to 670 d alleviate the need for cows to conceive during peak production. Such systems can allow farmers to take advantage of the reduced risk of metabolic disorders, lowered costs associated with reproduction, and milk price incentives during winter (Borman et al., 2004), yet with minimal loss in annualized milk solids production (Auldist et al., 2007; Kolver et al., 2007). Previous experiments have shown marked variation in the milk production capacity of Holstein cows undergoing extended lactations in pasture-based dairying systems (Auldist et al., 2007; Grainger et al., 2009; Kay et al., 2009). It is known that genotype interacts with diet (Kolver et al., 2007; Sorensen et al., 2008; Grainger et al., 2009) in terms of extended lactation capacity in grazing systems. However, less is known about the physiological regulation of nutrient partitioning during extended lactations.

Some of the difference in extended lactation capacity is due to variation in nutrient partitioning (Delany et

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[1]Corresponding author: leah.marett@depi.vic.gov.au

al., 2010; Marett et al., 2011). These studies showed that cows with greater lactation persistency (i.e., beyond 300 d) had higher blood plasma concentrations of growth hormone and NEFA, but lower concentrations of insulin, glucose, and leptin beyond 300 DIM. Cows that were unable to complete a full 670-d lactation gained more BW and BCS than those that were able to continue milking. Dietary restriction under grazing conditions did not decrease the proportion of cows reaching the target 670-d lactation length (Delany et al., 2010; Marett et al., 2011). However, cows fed energy in excess of requirements were less likely to complete the 670-d lactation (Grainger et al., 2009; Delany et al., 2010). Low plasma concentrations of insulin have been reported throughout early lactation compared with the mid and late stages of a traditional lactation (Ronge et al., 1988; Busato et al., 2002; Reist et al., 2002). This occurs because the mammary gland generally does not require insulin to facilitate the movement of glucose across the cell membrane for milk production (Collier et al., 1984), thus low plasma insulin favors the partitioning of nutrients from peripheral tissue deposition. In addition, decreased responsiveness to insulin has been reported just before and after parturition in lactating goats (Debras et al., 1989), sheep (Prior and Christenson, 1978), and cows (Sano et al., 1993; Bell and Bauman, 1997; Vernon and Pond, 1997). These adaptations result in a positive relationship between milk yield and insulin resistance, as demonstrated by low responsiveness of insulin-dependent tissues to the actions of insulin in cows with high milk yield (Cronje, 2000; Chagas et al., 2009).

Some of the variation in nutrient partitioning beyond 300 d of lactation may be due to differences in insulin sensitivity. Patton et al., (2009) reported a greater clearance rate (**CR**) of glucose during an intravenous glucose tolerance test (**IVGTT**) in Holstein-Friesian cows of predominantly New Zealand ancestry compared with North American ancestry in early and midlactation (32 and 127 DIM respectively) and suggested this may be associated with greater tissue accretion in the lower-yielding New Zealand cows. It has been shown that insulin sensitivity during the nonlactating period was not related to feed intake (Schoenberg et al., 2012), but in an experiment by Pires et al. (2007) the infusion of tallow, which resulted in elevated plasma triglyceride concentrations, was associated with decreased sensitivity to insulin. Bergman et al. (1989) showed that lean sheep had greater insulin sensitivity than obese sheep, in addition to lower plasma concentrations of glucose and insulin, highlighting the link between FA metabolism and glucose sensitivity. As milk yield declines and the proportion of nutrients partitioned to body tissue gain increases, insulin sensitivity may be enhanced. Currently no reports exist on insulin sensitivity in relation to glucose or FA metabolism of cows undergoing lactations longer than 300 d.

A better understanding of the metabolic and hormonal regulation of nutrient partitioning is important in developing nutritional strategies for cows managed for extended lactations. In the experiments described here, the frequently sampled IVGTT was employed at several stages of a 670-d lactation to investigate whole body glucose metabolism and insulin sensitivity. The goal of these experiments was to identify sources of variation in metabolic responses to hyperglycemia and a consequent increase in endogenous insulin in cows undergoing an extended lactation. A further goal was to determine whether this variation was affected by cereal grain intake. The hypotheses tested were (1) that the estimated whole body sensitivity, in terms of the insulin, glucose, and FA responses to a glucose load, would increase with increasing DIM, and (2) that the dietary intake of cereal grain would not affect the estimated whole body insulin sensitivity, in terms of insulin, glucose, and FA responses to a glucose load.

MATERIALS AND METHODS

Location

This experiment was conducted at the Department of Environment and Primary Industries' Ellinbank Centre in Victoria, Australia (38°14′S, 145°56′E). All procedures were approved by the Department of Primary Industries Eastern Animal Ethics Committee.

Cows and Management

The experiment used 12 multiparous Holstein-Friesian dairy cows of mixed age that calved in late July (mid-late winter). These cows were a subset of those used in the experiments of Auldist et al. (2011). All cows were managed for an extended lactation by delaying breeding until approximately 450 DIM. This equated to a target lactation length of 670 d. For the majority of the lactation (excluding experimental periods), cows were managed as a single herd and grazed perennial ryegrass (*Lolium perenne* L.) pasture supplemented with cereal grain fed twice daily in the parlor at milking times. When pasture was limiting during the summer and autumn months, pasture hay (approximately 6 kg of DM/cow per day) and pasture silage (approximately 10 kg of DM/cow per day) were also offered to achieve an estimated daily intake of 180 MJ of ME/cow.

During the lactation, 4 experimental periods of 40 d were used, beginning at each of 73, 217, 422, and 520 (±9.1) DIM. During these periods, cows were housed