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Short communication: The association of adiponectin and leptin concentrations with prepartum dietary energy supply, parity, body condition, and postpartum hyperketonemia in transition dairy cows

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ABSTRACT

Adipokines—hormones produced by adipose tissue—have important regulatory functions, and their concentrations can change around the time of calving when energy balance rapidly decreases. Hence, energy balance may be an important factor in determining the circulating concentrations of adipokines, particularly adiponectin and leptin. The objective of our study was to investigate the association between the level of energy fed to prepartum Holstein cows and circulating concentrations of adiponectin and leptin before and after calving. Holstein dairy cows entering second or greater lactation were fed either a controlled-energy diet formulated to supply approximately 100% of energy requirements (n = 28) or a high-energy diet formulated to supply approximately 150% of energy requirements throughout the entire dry period (n = 28). Serum samples were analyzed for adiponectin and leptin concentrations at 56, 28, 10, and 1 d prepartum as well as on d 1, 10, 21, and 42 postpartum using ELISA. Parity was dichotomized into cows entering second versus higher parity. Average peripartum body condition score (BCS) was computed from weekly measurements and dichotomized into animals with an average BCS of ≤3.25 and >3.25. In addition, cows were classified according to the occurrence of hyperketonemia (β-hydroxybutyrate concentrations ≥1.2 mmol/L at any time between 3 and 21 d in milk). Data were analyzed using repeated measures ANOVA. Serum leptin but not adiponectin concentrations were associated with prepartum feeding level such that leptin concentrations increased transiently during the dry period in cows overfed energy, but concentrations were not different postpartum. Cows entering second parity had higher adiponectin and lower leptin concentrations compared with cows in higher parities. Cows that developed hyperketonemia postpartum had consistently lower adiponectin concentrations during the study period. Cows with average BCS >3.25 had higher leptin concentrations during the dry period only, but adiponectin concentrations were not associated with BCS. In conclusion, prepartum energy level had only transient effects on leptin concentrations and did not lead to changes in adiponectin concentrations.
Key words: adiponectin, leptin, energy, hyperketonemia, transition

Short Communication

Adipose tissue is an endocrine organ secreting adipokines into circulation that exert different metabolic, reproductive, and immunological effects in dairy cows in an endocrine, autocrine, or paracrine manner (Sauerwein et al., 2014). Adiponectin and leptin are among the most abundant adipokines, and their concentrations change around the time of calving (Chilliard et al., 2005; Giesy et al., 2012). Changes in energy balance due to energy partitioning have been identified as potential key factors in these observed changes of circulating adiponectin (Singh et al., 2014a). Leptin concentration is known to be affected by energy balance in transition dairy cows and is positively correlated with insulin and glucose concentrations (Block et al., 2001, 2003). Recently, De Koster et al. (2017) reported a negative association between adiponectin concentrations and BCS during the dry period. Prepartum energy supply is associated with changes in energy balance and circulating insulin and glucose concentrations (Mann et al., 2016b) as well as degree of adipose tissue breakdown and postpartum hyperketonemia (elevated concentration of BHB concentrations between 3 and 21 d postpartum; Dann et al., 2006; Janovick et al., 2011; Mann et al., 2015). Previously we showed that gene expression of adiponectin was increased at d 10 prepartum in

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subcutaneous adipose tissue of cows overfed energy and with high concentrations of BHB postpartum compared with cows fed a controlled-energy diet and exhibiting low concentrations of BHB (Mann et al., 2016a). The objective of this study was to determine a possible association between the energy level in the dry period and the circulating concentrations of adiponectin and leptin in the transition period of Holstein dairy cows. In addition, we aimed to determine whether parity, BCS, and hyperketonemia, a condition typically associated with excessive negative energy balance postpartum (Baird et al., 1974; Herdt, 2000), were associated with differences in these 2 adipokines.

A detailed description of enrollment, treatment diets, and sampling procedures for the animals included in this study was published previously (Mann et al., 2015). Briefly, cows were randomly assigned to receive either a TMR formulated to supply approximately 100% of predicted energy requirements during the dry period (~57 d; **CE**; n = 28) or a TMR that was formulated to supply approximately 150% of predicted energy requirements (**HE**; n = 28). All animals were fed the same postpartum ration, and all diets were fed to allow a minimum of 5% of refusals. Cows were housed in tiestalls with feed bins. Serum samples were collected before morning feeding, aliquotted as previously described (Mann et al., 2015), and stored at −80°C until analysis. To address the study objectives, serum samples were selected for the following time points: enrollment (~56 d before calving); 28, 10, and 1 d prepartum; and 1, 10, 21, and 42 d postpartum.

Leptin concentrations were measured using a competitive ELISA (Sauerwein et al., 2004). Adiponectin concentrations were measured with a bovine-specific indirect competitive ELISA as described previously (Mielenz et al., 2013) with modifications according to Kesser et al. (2015). The analytic sensitivity for leptin and adiponectin was 0.6 and 0.03 ng/mL, respectively. The inter- and mean intra-assay coefficient of variation were 9.9 and 3.6% for leptin and 9.1 and 5.5% for adiponectin, respectively.

Body condition score was determined weekly by 1 of 2 trained investigators on a scale of 1 to 5 in 0.25-unit increments (Edmonson et al., 1989). Average BCS during the study period was calculated from weekly scores. Information on average weekly DMI and ultrasonographically assessed backfat thickness (**BFT**) at 6 time points of all cows was available (Mann et al., 2015, 2016a). Cows were classified as hyperketonemia positive (**HYK**) or negative (non-HYK) based on the presence or absence of at least 1 episode of whole-blood BHB ≥1.2 mmol/L between 3 and 21 DIM when cows were sampled 3 times per week before the morning feeding.

For descriptive statistical analysis, the difference of average BCS between the 2 treatment groups was calculated using a 2-way ANOVA controlling for the effect of parity. Data collected over time were analyzed using repeated measures ANOVA with the MIXED procedure in SAS (version 9.4; SAS Institute, Cary, NC). For both adiponectin and leptin the fixed effects included time, treatment group, average BCS, and parity in all models. In addition, the interaction of treatment group and time for the treatment group model, as well as the interaction between parity and time for the parity model, were included. Hyperketonemia status and the interaction of HYK with time were included only in the model describing its association with adipokines. To determine the association between body condition and adipokines, a separate model for each adipokine was built where the average BCS in the study period was dichotomized into 2 groups: ≤3.25 and >3.25. The model included the fixed effect of BCS group, the interaction of BCS group and time, and the fixed effect of treatment group, time, and parity. The time variable was specified in all models as the repeated effect, and cow nested in treatment group was included as the subject effect. Covariance structures tested allowed for uneven spacing of samples over time and included unstructured, spatial power law, Gaussian, and spherical. The covariance structure resulting in the lowest Akaike information criterion was chosen for final analysis. Outlier diagnostics were performed after each model fit using the influence statement in the MIXED procedure of SAS for each animal. Animals were removed from the analysis following a predefined cutoff of Cook's D ≥0.5. Residuals were evaluated for homoscedasticity and normality to satisfy model assumptions. Results are presented as mean or geometric mean and 95% confidence interval unless otherwise specified.

Spearman rank correlation was computed for adiponectin and leptin with BFT, BCS, and average weekly DMI (CORR procedure, SAS version 9.4) at 4 time points throughout the study: 28 and 10 d before calving as well as 4 and 21 d postpartum. None of the animals was classified as an outlier in any of the models, and all observations were retained in the final analysis. Parity distribution resulted in 35 animals entering second parity, whereas 21 animals entered third or higher parity. Nineteen animals (33.9%) were classified as HYK, whereas 37 animals (66.1%) were classified as non-HYK. Detailed information about energy balance and DMI was described previously (Mann et al., 2015). All energy balance predictions were estimated using CNCPS software (version 6.1; Cornell University, Ithaca, NY). Briefly, average (SD) energy balance in group HE was 169 (15), 156 (22), and 122% (18) of predicted