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Antepartal insulin-like growth factor 1 and insulin-like growth factor binding protein 2 concentrations are indicative of ketosis in dairy cows

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ABSTRACT

A study involving a small number of cows found that the concentrations of insulin-like growth hormone 1 (IGF1) may be a useful predictor of metabolic disease. Further, IGF1 may provide also a pathophysiological link to metabolic diseases such as ketosis. The objective of the current study was to test whether the low antepartal total IGF1 or IGF1 binding protein (IGFBP) concentrations might predict ketosis under field conditions. Clinical examinations and blood sampling were performed antepartum (262–270 d after artificial insemination) on 377 pluriparous pregnant Holstein Friesian cows. The presence of postpartum diseases were recorded (ketosis, fatty liver, displacement of the abomasum, hypocalcemia, mastitis, retention of fetal membranes, and clinical metritis or endometritis), and the concentrations of IGF1, IGFBP2, IGFBP3, and nonesterified fatty acids were measured. Cows with postpartum clinical ketosis had lower IGF1 concentrations antepartum than healthy cows. The sensitivity of antepartal IGF1 as a marker for postpartum ketosis was 0.87, and the specificity was 0.43; a positive predictive value of 0.91 and a negative predictive value of 0.35 were calculated. The cows with ketosis and retained fetal membranes had lower IGFBP2 concentrations compared with the healthy cows. It can be speculated that lower IGF1 production in the liver during late pregnancy may increase growth hormone secretions and lipolysis, thereby increasing the risk of ketosis. Lower IGFBP2 concentrations may reflect the suppression of IGFBP2 levels through higher growth hormone secretion. In conclusion, compared with nonesterified fatty acids as a predictive parameter, IGF1 and IGFBP2 may represent earlier biomarkers of inadequate metabolic adaptation to the high energy demand required postpartum.

Key words: dairy cow, transition period, insulin-like growth factor 1, insulin-like growth factor binding protein 2, ketosis

INTRODUCTION

The growth hormone (**GH**)-IGF axis is an important endocrine control center for metabolic adaptation in dairy cows. Studies have indicated that IGF1 may be useful as a predictive marker for postpartum (**pp**) production diseases (Piechotta et al., 2012) or for successful early ovulation pp (Kawashima et al., 2007). Moreover, from in vitro studies, IGF1 is known to be an important signal for gluconeogenesis (Wang et al., 2012). Therefore, a physiological association between IGF1 and particularly metabolic diseases, such as ketosis, is likely, but the exact mechanisms between the somatotropic axis and the pathogenesis of ketosis are not well studied. Studies have attempted to influence the GH-IGF1 axis by administering bST antepartum (**ap**). Although ap bST administration did not affect the incidence of hyperketonemia, DMI, or clinical ketosis (Gohary et al., 2014), a clear association between low IGF1 concentrations and metabolic production diseases was evident (Piechotta et al., 2012). Cows that were classified based on low versus high IGF1 levels revealed no differences in the hepatic GH receptor mRNA expression (Piechotta et al., 2013, 2014), which might explain why bST administration did not have an effect on the incidence of ketosis. However, from these studies, it was not clear which factors might be responsible for the association between low total IGF1 levels and the incidence of metabolic diseases. Moreover, the number of cattle used in the study was low, and only IGF1 was measured (Piechotta et al., 2012). However, IGF1 is bound to 6 different high-affinity IGF binding proteins (**IGFBP**) that determine the half-life of IGF1 and its delivery through the endothelium to the target cells. The IGFBP concentration might be one factor for different total IGF1 concentrations. Therefore, the concentrations of the 2 most abundant IGFBP (IGFBP2

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and IGFBP3) were determined in the present study with a greater number of animals under field conditions to clarify whether ap total IGF1 or IGFBP concentrations might predict the risk of ketosis or other pp production diseases.

MATERIALS AND METHODS

Animals

In one large-scale dairy farm (~1,300 cows) in eastern Germany (Göritz), 377 pluriparous Holstein Friesian cows in late pregnancy [second to fourth lactation; 305-d milk yield = 11,200 ± 97 kg (mean ± SEM)] were examined and blood samples were obtained. The experimental procedure was approved by the German legislation responsible for animal welfare [Landesamt für Umwelt, Gesundheit und Verbraucherschutz, Abteilung Verbraucherschutz in Frankfurt (Oder); 23–2347-A19–3-2010]. The cows were housed during all seasons in a freestall barn with rubber mats and were fed automatically by a band-conveyor system twice daily with a TMR depending on the lactation period (Tables 1 and 2). The cows were provided with a mineral supply (Deutsche Vilomix Tierernährung GmbH, Neuenkirchen-Vörden, Germany) and they had free access to water. The cows were kept in groups depending on the lactation interval [early (50 d pp), mid, late, and dried-off]. The cows were dried-off approximately 6 wk before the expected calving date. Approximately 10 d before calving, the cows were placed in a freestall barn with straw bedding in which the cows were monitored for signs of birth every 2 h by the farm staff. The cows were milked 3 times daily, and the milk yields were recorded once a month by the routine control office (Landeskontrollverband Brandenburg, Brandenburg, Germany).

Monitoring of Health Status and Blood Sampling

The cows were monitored daily by the farm staff via observing the feed intake ap and pp and recording milk yield, milk character, and the udder after calving. If the cows showed a reduction in either feed intake or milk yield, a farm veterinarian was summoned and the cows were diagnosed and treated. Moreover, the cows were examined clinically by a study veterinarian once ap between 262 and 270 d after AI and 2 times pp at 3 (16–21 d pp) and 4 wk (22–28 d pp) after calving. At each examination, behavior, posture, body temperature, and BCS were recorded (Edmonson et al., 1989). Additionally, the milk yield during the previous lactation was documented. A gynecological examination was performed to assess the occurrence of metritis or endometritis in accordance with Sheldon et al. (2008). After each examination, a blood sample was obtained from a coccygeal vessel directly into tubes with EDTA and without any anticoagulants to acquire serum (Sarstedt, Nümbrecht, Germany). The EDTA containing the samples was kept on ice, whereas the serum samples were kept until clotting at ~20°C. After centrifugation (2,000 × *g*, 15 min, 4°C; Hettich EBA 20, Boston, MA), which occurred within 2 h after sampling, the samples were kept at –20°C until further analyses. Moreover, if a decrease in the milk yield or feed intake of the cows was detected by the farm stuff, the farm veterinarian conducted a clinical examination and recorded the diagnosis according to the stated definitions provided herein. The day of AI and the

Table 1. Ingredients of the TMR fed with regard to the different lactation periods

	Dry-off ration		Fresh cow ration
Item (kg of DM)	wk 6–2 antepartum	wk 2–0 antepartum	>d 1 postpartum
Grass silage	10.4	2.4	5.2
Corn silage	1.3	6.6	8.1
Sugar beet pulp	—	—	3.6
Rye straw	0.3	—	-
Wheat	0.4	—	0.6
Straw	2.4	—	0.5
Glycerin[1]	—	—	0.2
Corn	—	—	2.3
Urea[2]	—	—	0.03
Feed-fat[2]	1.7	—	0.4
Soy pellet[3]	—	—	1.7
Rape expellers[3]	—	—	1.2
Cattle salt[4]	0.03	0.03	0.03
Rumen-protected protein[1]	—	—	1.9
Propylene-glycol[1]	0.2	—	0.2
Sugar beet chips	0.32	—	—
Flavorful acid salt[4]	0.5	—	—

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[4]Blattin Mineralfutterwerk Seitschen GmbH &Co KG, Göda, Germany.

Table 2. Chemical composition of the TMR fed with regard to the different lactation periods

	Dry-off ration		Fresh cow ration
Item	wk 6–2 antepartum	wk 2–0 antepartum	>d 1 postpartum
NE_L (MJ/kg of DM)	5.53	6.39	7.54
Crude ash (g/kg of DM)	93	63	53
Crude fat (g/kg of DM)	36	29	52
CP (g/kg of DM)	134	142	170
Crude fiber (g/kg of DM)	267	193	157