Domestic Animal Endocrinology 47 (2014) 35–46

Contents lists available at ScienceDirect

Domestic Animal Endocrinology

journal homepage: www.domesticanimalendo.com

Lactation driven dynamics of adiponectin supply from different fat depots to circulation in cows

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ARTICLE INFO

Article history:
Received 2 October 2013
Received in revised form 11 December 2013
Accepted 12 December 2013

Keywords:
Adipose tissue depots
Adiponectin
Dairy cow
Lactation

ABSTRACT

Adipose tissue (AT) depots are heterogeneous in terms of morphology and adipocyte metabolism. Adiponectin, one of the most abundant adipokines, is known for its insulin sensitizing effects and its role in glucose and lipid metabolism. Little is known about the presence of adiponectin protein in visceral (vc) and subcutaneous (sc) AT depots. We assessed serum adiponectin and adiponectin protein concentrations and the molecular weight forms in vc (mesenterial, omental, and retroperitoneal) and sc (sternum, tail-head, and withers) AT of primiparous dairy cows during early lactation. Primiparous German Holstein cows (n = 25) were divided into a control (CON) and a conjugated linoleic acid (CLA) group. From day 1 of lactation until slaughter, CLA cows were fed 100 g of a CLA supplement/d (approximately 6% of *cis*-9, *trans*-11 and *trans*-10, *cis*-12 isomers each), whereas the CON cows received 100 g of a fatty acid mixture/d instead of CLA. Blood samples from all animals were collected from 3 wk before calving until slaughter on day 1 (n = 5, CON cows), 42 (n = 5 each of CON and CLA cows), and 105 (n = 5 each of CON and CLA cows) of lactation when samples from different AT depots were obtained. Adiponectin was measured in serum and tissue by ELISA. In all AT depots adiponectin concentrations were lowest on day 1 than on day 42 and day 105, and circulating adiponectin reached a nadir around parturition. Retroperitoneal AT had the lowest adiponectin concentrations; however, when taking total depot mass into consideration, the portion of circulating adiponectin was higher in vc than sc AT. Serum adiponectin was positively correlated with adiponectin protein concentrations but not with the mRNA abundance in all fat depots. The CLA supplementation did not affect adiponectin concentrations in AT depots. Furthermore, inverse associations between circulating adiponectin and measures of body condition (empty body weight, back fat thickness, and vc AT mass) were observed. In all AT depots at each time, adiponectin was present as high (approximately 300 kDa) and medium (approximately 150 kDa) molecular weight complexes similar to that of the blood serum. These data suggest differential contribution of AT depots to circulating adiponectin.

1. Introduction

Adipose tissue (AT) is considered as an active endocrine organ synthesizing and secreting a series of bioactive molecules collectively termed as adipokines. Adiponectin (AdipoQ), one of the most abundant circulating adipokines,

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http://dx.doi.org/10.1016/j.domaniend.2013.12.001

is primarily expressed by adipocytes and exerts mainly insulin sensitizing effects [1]. Synthesized as a 30-kDa monomer, AdipoQ is assembled to various oligomeric forms via disulfide bonds through an amino-terminal cysteine and may occur in circulation as low molecular weight (trimer), medium molecular weight (MMW; hexamer), and high molecular weight (HMW; congregated multimers) oligomers [2]. Among all molecular weight isoforms, the HMW isoform is considered as the most biologically active, being associated with improving insulin sensitivity (IS) [3] and activation of adenosine monophosphate-activated protein kinase in muscle [2]. Regulation of adiponectin isoform secretion is regulated at the level of AT [3], and the spontaneous interconversion of hexamers (MMW) and HMW do not occur in circulation [4]. Besides its role in regulation of glucose and lipid metabolism, proapoptotic and antiapoptotic functions of AdipoQ have also been reported (reviewed by Sun and Chen [5]). Therefore, AdipoQ might affect the rate of apoptosis also in AT through autocrine or paracrine mechanisms.

The AT from different anatomic locations differs in fatty acid metabolism [6]. Visceral (vc) AT mass is more strongly correlated with IS [7], increased risk of developing diabetes type 2, and atherosclerosis [8] than subcutaneous (sc) AT. Regardless of weight-loss interventions such as caloric restriction, pharmacologic therapy, or exercise, individuals preferentially lose vc AT mass [9], thus suggesting that vc adipocytes have a higher lipolytic capacity. Moreover, in rodents and humans, removal of sc fat did not improve IS, supporting the hypothesis that vc AT may be metabolically more active [10,11]. Site-dependent differences in the functional activities of vc (retroperitoneal AT) and sc AT depots have also been shown for dairy cows [12,13]. When studying the role of AT in processes of homeorhetic regulation in which metabolism of all body tissues is dynamically adapted to support a physiological state, such as pregnancy or lactation, the anatomic location of AT requires careful consideration. Most mammals undergo a period of negative energy balance during early lactation; however, in dairy cows selected for high milk yields both the extent and the duration of negative energy balance exceed the ones in other mammalian species [14–16]. In early lactation, the priority of the mammary gland for glucose uptake is accomplished by insulin-independent glucose transporters in the mammary gland together with a decrease of IS in other peripheral tissues [17]. Concomitant with the peripartal decrease in IS, the circulating AdipoQ concentrations were recently found to decline with the use of semiquantitative Western immunoblot methods [18,19]. Recent human studies suggest that by 24 h after delivery HMW and MMW isoforms decline, which correspond with approximately an 80% reduction of serum AdipoQ concentrations [20].

On the basis of the heterogeneity of the metabolic activity in different AT depots and the relationship of AdipoQ with IS and lipolysis, we hypothesized that the expression of the AdipoQ protein in sc and vc AT depots will change during early lactation. Dietary supplementation with conjugated linoleic acids (CLAs) affect lipid metabolism and is known to cause decline in milk fat content in dairy cows [21,22]. Therefore, we aimed to assess the AdipoQ protein concentrations and the distribution of its different isomeric forms (low molecular weight, MMW, and HMW) in 3 different sc and 3 different vc AT depots at 3 time points during the first 105 d of lactation in primiparous dairy cows with or without CLA supplementation. By assuming that not only the AdipoQ protein expression by each individual AT will change but also the mass of the individual depot, we took the respective fat masses into consideration to estimate the portion of circulating AdipoQ present in different fat depots. In addition, we tested for correlations between AT AdipoQ, serum AdipoQ, adipocyte size, adipocyte apoptotic rate, several blood metabolites, and hormones, including a surrogate marker of IS (Revised Quantitative Insulin Sensitivity Check Index [RQUICKI]) and variables that characterize body fat such as body condition score (BCS), back fat thickness (BFT), live weight, and empty body weight (EBW).

2. Materials and methods

2.1. Experimental animals and treatments

In compliance with the European Union Guidelines about the protection of experimental animals and with approval by the Lower Saxony State Office for Consumer Protection and Food Safety, Oldenburg, Germany (file number 33.11.42502-04-071/07), the present experiment was conducted at the experimental station of the Institute of Animal Nutrition, Friedrich-Loeffler-Institute, Braunschweig, Germany. The experimental design is described in detail elsewhere [23]. In brief, primiparous lactating German Holstein-Friesian cows (n = 25) with an average age at parturition of 23 ± 0.2 mo were included in the study 3 wk before the expected date of calving and were slaughtered on day 1, 42, and 105 of lactation. For this purpose, the animals were kept in a free-stall barn, with free access to water. Before parturition, all cows received a similar diet that consisted of 60% corn silage and 40% grass silage on a dry matter (DM) basis (6.7 MJ of NE_L/kg DM) ad libitum and 2 kg of concentrate/d (6.7 MJ of NE_L/kg DM). During lactation, the partial mixed ration (PMR) fed comprised 38% corn silage, 25% grass silage (DM basis, 7.5 MJ of NE_L/kg DM) and 37% PMR-concentrate (13.5 MJ of NE_L/kg DM). In addition, each animal was provided with concentrate by a computerized concentrate feeding station (3.5 kg/d on a DM basis). Feed ingredients of the concentrates are presented in Table 1.

Beginning at the day of calving, the animals were randomly assigned to receive either a supplement that contained CLA (100 g/d Lutrell Pure; BASF SE, Ludwigshafen, Germany; group CLA, n = 10) or a control (CON) fat supplement in which CLA was replaced by stearic acid (Silafat; BASF SE; 100 g/d; group CON, n = 15) until experimental slaughter. The supplements were provided with the concentrate; the CLA group consumed 6.0 g/d of the *trans*-10, *cis*-12 CLA isomer and 5.7 g/d of the *cis*-9, *trans*-11 CLA isomer (calculated on the basis of the analyzed proportion in concentrates) [23]. Five animals of the CON group were slaughtered on day 1, and thereafter 5 animals of both groups were slaughtered each at day 42 and day 105 of lactation.