Expression of 11²-HSD1 mRNA in adipose tissue of dairy cows during the periparturient period

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Backgrounds

11-beta-hydroxysteroid-dehydrogenase1 (\textbf{11ßHSD1}):  
- enzyme (reductase)  
- catalyzes the NADPH-dependent reduction of cortisone to cortisol
Backgrounds: HPA axis and tissue metabolism

Activation 11ßHSD1

Clearance ACTH

Immune response

Stress response

Development

Metabolism

Hypothalamus

CRH

Anterior Pituitary

ACTH

Adrenal glands

Cortisol

From Andrew & Homer, 2016. Biochem. Soc. Trans. 44, 645-651
From: Huesler et al. Physiological Reports 1(5):e00101 · October 2013

Tissue metabolism and receptor gating

Anti-inflammatory effects

Pro-inflammatory effects
Glucocorticoid effects in adipose tissue

- Adipogenesis
- Adipocyte metabolism
- Adipokine production
Glucocorticoids in the circulation around calving

Hypothesis and Objectives

Hypothesis: Calving affects $11^{2}$-HSD1 mRNA in adipose tissue

Objectives:
- To assess the mRNA expression of $11^{2}$-HSD1
- To test the effects of different intensities of lipo-mobilization
- To characterize the time course of mRNA abundance during late pregnancy and early lactation
- To compare this time course in subcutaneous versus visceral fat
Experimental design

20 Holstein cows, same diet

High Concentrate diet (HC)
- Concentrate : roughage = 60 : 40
- n = 10
  - n = 5 with niacin*
  - n = 5 without

Low Concentrate diet (LC)
- Concentrate : roughage = 30 : 70
- n = 10
  - n = 5 with niacin*
  - n = 5 without

*24 g/d/cow

Biopsy samples
- Sc fat
- Rp fat

Day 42 ante partum

Day 1 post partum


Day 100 p.p.

All groups on same diet
- Concentrate : roughage = 50 : 50

EAAP Annual Meeting 2016, Belfast, UK
Results

• $11^2$ HSD1 mRNA abundance in rpAT and scAT was not affected by diet
• Longitudinal changes:
$11^2$ HSD1; rpAT (mean ± SE)
Days relative to calving

mRNA abundance (AU)

-42 1 21 100

11βHSD1; scAT (mean±SE)

P < 0.01
**Context setting**

11ßHSD1 mRNA is expressed in bovine adipose tissue (bAT)

Earlier findings in bovine adipose tissue (primiparous cows, comparison of DIM 1, 42 & 105; Friedauer et al., 2015):

- 11ßHSD1 protein (IHC) localized in mature adipocytes
- 11ßHSD1 activity in tissue homogenates: no change with DIM
- Glucocorticoid receptor (IHC) is localized in mature adipocytes
- Mineralocorticoid receptor (IHC) is localized in the stroma vascular fraction and number of positive cells correlated with Pref-1 expression (= preadipocyte marker)

→ Metabolic and anti-inflammatory rather than differentiating effects of cortisol in mature adipocytes
→ potentially paracrine adipogenetic effects of cortisol secreted by mature adipocytes
Conclusions

The patterns observed for 11ßHSD1 mRNA abundance are in support of increased tissue concentrations of cortisol in adipose tissue around calving.

Sustained elevation of 11ßHSD1 mRNA abundance in retroperitoneal vs. subcutaneous adipose tissue on d 21 p.p. may indicate greater generation of cortisol in visceral than in subcutaneous adipose tissue.

Metabolic and anti-inflammatory effects are assumed as main biological consequences.
Thank you
qPCR and analysis of data

Primers: as published by Tetsuka et al. (2010)
Positive Control: liver from slaughterhouse

Reference genes for rpAT:
- LRP10
- EMD
- POLR2A

Reference genes for scAT:
- EIF3K
- LRP10
- MARVELD
- EMD MAR
- Pol2

qbase output: CNRQ = Calibrated Normalized Relative Quantities

Statistical Analyses (SAS): Mixed Procedure, Repeated Measure