Proceedings of the Nutrition Society (2011), **70 (OCE1)**, E28 doi:10.1017/S0029665111000449

Scottish Section Meeting, 5–6 April 2011, 70th Anniversary: Nutrition and health: from conception to adolescence

Impact of route of delivery upon regulators of adipose tissue lipid metabolism in the pig

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Vaginal delivery (VD) is associated with a plethora of physiological adaptations essential for survival of the newborn outside the womb[(1)]. Pre-labour caesarean section (CS) may reduce, or abolish, some of these normal adaptatory responses, leading to an impaired adaptation to extrauterine life. In addition to these short-term effects, CS may promote longer term programming of certain organs and tissues, evidence from Hyde *et al*. have demonstrated that neonatal offspring delivered by VD have hepatic steatosis and alterations in key genes which regulate lipid[(2,3)]. It is unknown whether lipid is stored in the liver in these animals at the expense of normal adipose tissue (AT) storage. The aim of this study was to investigate the impact of CS on regulators of AT lipid metabolism in the neonatal pig.

Sows were randomly allocated to the CS or VD group, routine CS was carried out on day 112 (porcine gestation 114 d), after which sows were humanely euthanised by intravenous injection of sodium pentobarbital. VD sows gave birth normally without intervention. Piglets were dried, given oxygen and vitamin K intramuscularly then provided with 100 ml of milk replacer and *ad libitum* water in separate bowls every 4 h. On day 7 all piglets were euthanised as described above and AT was removed and stored at −80°C until laboratory analysis. Eleven piglets were used in this study, six VD and five delivered by CS. Real-time PCR with optimised porcine primers was used to measure RNA expression of key genes of lipid metabolism and normalised using Genorm (Table 1)[(4)]. AT lipid and protein concentration were assessed by Folch and Bradford assay, respectively. Haematoxylin and eosin staining of 5-μm-thick AT sections were carried out and image analysis conducted to assess average adipocyte diameter. Statistical analysis was carried out using SPSS 17; all results are shown in Table 1.

Table 1. Summary of results VD, vaginal delivery; CS, pre-labour caesarean section; 11βHSD1, 11βhydroxysteroid dehydrogenase type 1; 11βHSD2, 11βhydroxysteroid dehydrogenase type 2; GR, glucocorticoid receptor; LPL, lipoprotein lipase; FABP4, fatty acid binding protein 4; FAS, fatty acid synthase

	VD	CS	*P*
TAG content (mg/g)	30.07±7.02	20.16±7.93	0.20
Protein concentration (mg/g)	277.5±33.3	129.6±20.1	0.03
11βHSD1 ($2^{-\Delta\Delta^{CT}}$)	1.28±0.24	0.67±0.05	0.01
11βHSD2 ($2^{-\Delta\Delta^{CT}}$)	0.14±0.012	0.11±0.01	0.19
GR ($2^{-\Delta\Delta^{CT}}$)	0.67±0.032	0.48±0.05	0.05
LPL ($2^{-\Delta\Delta^{CT}}$)	128.69±46.27	116.79±35.22	1.0
FABP4 ($2^{-\Delta\Delta^{CT}}$)	250.28±77.04	242.37±74.13	0.67
FAS ($2^{-\Delta\Delta^{CT}}$)	34.93±14.53	36.48±7.91	0.39
Average adipocyte diameter (μM)	1303.5±581.88	271.2±113	0.10

Lipid accumulation does not appear to be affected by CS in these enterally fed animals. However, AT development may be impaired, as demonstrated by significantly lower expression of 11βHSD1, GR expression and protein concentration combined with a trend towards reduced adipocyte diameter. These findings suggest a reduced sensitivity to glucocorticoids at an AT level that may have a long-term impact on ability to store and metabolise lipids. Further studies of parenterally fed CS and VD offspring may provide useful additional data.

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