The Effect of Chronic High Dose Vitamin a Supplementation on Lipid Metabolism in Adipose Tissue (P02-013-19)

Kieran Finney,[1] Anthony Oxley,[1] Catherine Winder,[2] Andrew Southam,[3] Andris Jankevics,[3] Gavin Lloyd,[3] Tim Giles,[4] Neil Foster,[4] Warwick Dunn,[5] and Georg Lietz[1]

[1]Human Nutrition Research Centre - Institute of Cellular Medicine, Newcastle University; [2]Phenome Centre Birmingham; [3]University of Birmingham; [4]School of Veterinary Medicine and Science, University of Nottingham; and [5]Phenome Centre-University of Birmingham

Objectives: The objective of this study was to assess the impact of high-dose vitamin A (VA) on lipid metabolism. Previously, VA has been shown to enhance fat mobilisation, leading to a reduction in body fat. We hypothesise that hypervitaminosis A will increase expression of genes associated with lipid catabolism.

Methods: To induce chronic hypervitaminosis A, two groups of pigs ($n = 8$) were fed a commercial diet. The treatment group was additionally dosed, daily, with an oral supplement of retinyl propionate of 10,000 µg/KgBW for 17 weeks. To assess the impact of VA on lipid metabolism, a microarray analysis was performed to identify gene expression in adipose tissue. Differentially expressed transcripts and pathways were identified using Genespring and mapped to human orthologues for Ingenuity Pathway Analysis (IPA); gene fold changes were confirmed using qRT-PCR. Additionally, an untargeted UPLC-MS lipidomic analysis was carried out in serum samples to identify changes in lipd classes and their metabolites.

Results: In dosed animals, significant increases in plasma retinol (0.66 μmol/L) and liver retinyl ester concentrations (11.98 μmol/g both $P < 0.001$), as well as an increase in serum NEFA of 92.84 μmol/L ($P = 0.001$) were observed. Gene expression fold changes in subcutaneous adipose tissue were related to mitochondrial dysfunction and lipid metabolism, including increased expression of MT-CYTB (↑4.78x, $P < 0.05$) and ATP5A1 (↑3.13x, $P < 0.05$). Metabolomics confirmed changes in lipids and their metabolites relevant to adipose tissue in blood ($P = 0.05$), namely a decrease in triacylglyceride concentration and increases in acyl carnitine and cardiolipin concentrations.

Conclusions: An integrated pathway is suggested to explain the role of vitamin A in leading to increased lipolysis, β-oxidation and oxidative phosphorylation, but when in excess, markers of mitochondrial dysfunction were observed.

Funding Sources: Funded by the Bill and Melinda Gates foundation.