The role of linoleic acid in placental inflammatory response and fatty acid metabolism

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Long chain polyunsaturated fatty acids (LCPUFA) are essential for the rapid cellular growth and development of the foetus. LCPUFA are transported within a cell *via* fatty acid-transporters (FATP) and fatty-acid binding proteins (FABP). During pregnancy, the mother must transport LCPUFA to the foetus *via* the placenta; however, the specific placental proteins responsible for this transport are unknown. In modern diets, LCPUFA are increasing in abundance, and in non-pregnant rodents, excessive consumption of LCPUFA such as linoleic acid (LA) has been shown to increase inflammation. Placental inflammation is associated with pregnancy complications mediated by obesity and gestational diabetes mellitus (GDM). Currently, there is a paucity of research exploring the effects of the excessive consumption of LA during pregnancy on the developing foetus and the placenta. We hypothesized that exposure to high LA concentrations may increase inflammatory proteins in the placenta and affect cellular viability. Further, we hypothesize that specific FATP and FABP will be altered in response to elevated LA concentrations.

Human placental trophoblast cells (Swan 71 cell line) were treated with various physiologically relevant concentrations of LA (100, 200, 400, 500 or 1000 μM) for 24 hours. Cell viability was assessed by the 3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide (MTT) assay. The cell growth rate was monitored using the Juli Br live cell analyser (NanoEntek Systems). Mitochondrial respiration was measured using an oxygraph 2k (OROBOROS Instruments) in cells treated with LA. Gene expressions of inflammatory markers and fatty acid transport proteins were evaluated by quantitative PCR.

Cell viability was significantly decreased after treatment with LA for 24 hours compared to normal control and vehicle control. This was significant at all doses with modest decreases in viability at the lower doses (~20% for 100, 200, 400 μM) and more severe decreases at high concentrations (34% decrease at 500 μM and 56% decrease at 1000 μM). Mitochondrial respiration was significantly decreased by 2.6 and 3.5 fold in the cells treated with 400 and 500 μM LA respectively. LA significantly decreased IL-6 mRNA expression at doses greater than 200 μM in a dose dependant manner. IL-8 mRNA expression was increased by LA at 400 μM only. A higher concentration of LA (500 μM) significantly upregulated FATP4 and FABP5, whilst FABP3 was significantly decreased by the treatment of LA at all concentrations.

This study demonstrated that high LA alters placental cell viability, mitochondrial respiration, inflammatory responses and fatty acid transporters, which may lead to altered placental and foetal growth. Thus, these data may have implications for women that consume high levels of LA during pregnancy.