Differential metabolic effects of medium-chain triglycerides and omega-3 fatty acids in benign and malignant prostate cells – evidence for a ketogenic diet as adjuvant therapy for prostate cancer

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INTRODUCTION & OBJECTIVES: One of the most prominent metabolic alterations of malignant cells is their increased glucose consumption and lactic acid production also under aerobic conditions (Warburg effect). Therefore, glucose restriction by administration of a ketogenic diet containing low carbohydrates supplemented with high fat could be used as a potential Achilles Heel for the treatment of cancer. In this study, a ketogenic diet supplemented with medium chain triglycerides (MCTs) and omega-3 fatty acids that might selectively impair the energy metabolism of prostate carcinoma cells (PCa) compared to benign cells is investigated. MCTs are dietary fatty acids that are easier soluble and compatible and, in addition, are considered to induce high levels of ketone bodies in the liver.

MATERIAL & METHODS: The effects of MCT oil consisting of MCTs and omega-3 fatty acids, as well as MCTs and omega-3 fatty acids alone, respectively, have been investigated in primary (stromal cells PM147), benign (EP156T, RWPE1) and prostate cancer cell lines (LNCaP, LNCaPabl, PC-3). Cell viability and cell counts were assessed by means of a colorimetric WST-1 assay 72 hours after MCT treatment and cell counting using a Neubauer chamber after 14 days (6 treatments), respectively. Glucose consumption and lactate production were measured using enzymatical assays based on the conversion of a colorimetric dye. Starvation of cells was performed in DMEM under reduced glucose and serum conditions for 72 hours following MCT treatment.

RESULTS: First results showed that under normal glycolytic conditions (1g/L glucose) benign and primary prostate cells significantly increased in cell viability while the carcinoma cell lines slightly decreased after 72 hours treatment with MCTs (25-400 µM). Similar effects were seen on cell number after long-term treatment over 14 days. The strongest effect was obtained after treatment with omega-3 fatty acids. Moreover, glucose consumption and lactic acid production was reduced in benign cells upon MCT treatment, estimating that these cells are able to use fatty acids as energy source, while such an effect could not be seen in cancerous cells. Additionaly, when cells were starved by step-wise glucose-withdrawal (0-0.12-0.25-0.5g/L), cell death was induced in all cancer cells and was not altered by supplementation with MCTs. These effects will be further investigated in benign cell lines.

CONCLUSIONS: This first evidence support the theory that cancerous cells are incapable of compensating for glucose restriction by metabolising fatty acids in vitro, showing a potential disadvantage of PCa cells compared to benign cells. Future experiments will specifically evaluate changes in glucose and fatty acid metabolic marker in response to a MCT-based ketogenic diet. Moreover, co-cultures with liver cells (HepG2) will be established to investigate into the effects of an MCT diet-induced ketone body production on benign and malignant prostate cells.