A Supplemented High-Fat Low-Carbohydrate Diet for the Treatment of Glioblastoma.

Martuscello RT, Vedam-Mai V, McCarthy DJ, Schmoll ME, Jundi MA, Louviere CD, Griffith B, Skinner CL, Suslov O, Deleyrolle LP, Reynolds BA.

Abstract

PURPOSE: Dysregulated energetics coupled with uncontrolled proliferation has become a hallmark of cancer, leading to increased interest in metabolic therapies. Glioblastoma (GB) is highly malignant, very metabolically active and typically resistant to current therapies. Dietary treatment options based on glucose deprivation have been explored using a restrictive ketogenic diet (KD), with positive anti-cancer reports. However, negative side effects and a lack of palatability makes the KD difficult to implement in an adult population. Hence, we developed a less stringent, supplemented high-fat low-carbohydrate (sHFLC) diet that mimics the metabolic and anti-tumor effects of the KD, maintains a stable nutritional profile and presents an alternative clinical option for diverse patient populations.

EXPERIMENTAL DESIGN: The dietary paradigm was tested in-vitro and in-vivo, utilizing multiple patient-derived glioma sphere lines. Cellular proliferation, clonogenic frequency and tumor stem cell population effects were determined in-vitro using the neurosphere assay (NSA). Anti-tumor efficacy was tested in-vivo in preclinical xenograft models and mechanistic regulation via the mTOR pathway was explored.

RESULTS: Reducing glucose in-vitro to physiological levels, coupled with ketone supplementation, inhibits proliferation of GB cells and reduces tumor stem cell expansion. In-vivo, while maintaining animal health, the sHFLC diet significantly reduces the growth of tumor cells in a subcutaneous model of tumor progression and increases survival in an orthotopic xenograft model. Dietary-mediated anti-cancer effects correlate with the reduction of mTOR effector expression.

CONCLUSIONS: We demonstrate that the sHFLC diet is a viable treatment alternative to the KD, and should be considered for clinical testing.

Copyright © 2015, American Association for Cancer Research.

PMID: 26631612 [PubMed - as supplied by publisher]