The ketogenic diet for the treatment of glioma: Insights from genetic profiling.

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Abstract

Seizures, particularly first onset seizures in adults, are a diagnostic hallmark of brain tumors (Giglio and Villano, 2010). Unfortunately, malignant brain tumors are almost uniformly fatal due, in part, to the limitations of available therapies. Improvement in the survival of brain cancer patients requires the design of new therapeutic modalities including those that enhance currently available therapies. One potential strategy is to exploit differences in metabolic regulation between normal cells and tumor cells through dietary approaches. Previous studies have shown that a high-fat, low-carbohydrate ketogenic diet (KD) extends survival in animal models of glioma; however, the mechanism for this effect is not entirely known. We examined the effects of an experimental KD on a mouse model of glioma, and compared patterns of gene expression in tumors versus contralateral non-tumor containing brain from animals fed either a KD or a standard diet. We found that the KD reduced reactive oxygen species (ROS) production in tumor cells. Gene expression profiling demonstrated that the KD induces an overall reversion to expression patterns seen in non-tumor specimens, and a number of genes involved in modulating ROS levels and oxidative stress were altered in tumor cells. In addition, there was reduced expression of genes involved in signal transduction from growth factors known to be involved in glioma growth. These results suggest that the anti-tumor effect of the KD is multifactorial, and elucidation of genes whose expression is altered will help identify mechanisms through which ketones inhibit tumor growth, reduce seizure activity and provide neuroprotection.

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