

## The Ketogenic Diet as an Emerging Adjunctive Therapy for Neurological Disorders

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### Abstract

The ketogenic diet (KD), a high-fat, moderate-protein, and low-carbohydrate dietary approach, has emerged as a potential therapeutic intervention for various neurological disorders. By inducing a metabolic state of nutritional ketosis, KD modulates excitatory and inhibitory neurotransmitters, regulates oxidative stress, and influences the gut microbiome. It has demonstrated benefits in conditions such as epilepsy, migraine, autism, multiple sclerosis, and neuro-oncology, as well as psychiatric and metabolic disorders. Preliminary studies suggest that KD may aid in neurological recovery, particularly in spinal cord injuries and traumatic brain injuries, though its long-term safety and efficacy remain uncertain. While KD has the potential to serve as an adjunct therapy, concerns regarding cardiovascular risks, dietary imbalances, and limited long-term applicability necessitate further investigation. Standardization of KD protocols and extensive cohort studies are essential to determine its broader clinical viability in neurology and neurosurgery.

### Keywords

Ketogenic Diet, Nutritional Ketosis, Neurological Disorders, Neuroinflammation, Epilepsy, Spinal Cord Injury, Traumatic Brain Injury, Gut Microbiota, Neuro-oncology, Metabolism, Epigenetics

### Editorial

The ketogenic diet (KD), commonly referred to as the “keto diet,” is increasingly recognized as a potential therapeutic strategy for neurological disorders. This dietary regimen consists

of a high-fat, moderate-protein, and low-carbohydrate composition, inducing a metabolic state known as ‘nutritional ketosis’ [1]. Various formulations of KD exist and can be adapted based on individual requirements. KD has been shown to aid in weight loss, regulate glucose levels, and improve diabetic conditions. As interest in alternative dietary approaches for neurological recovery grows, it is essential to examine KD’s potential role in clinical applications and future research.

KD modulates excitatory and inhibitory neurotransmission, balances oxidative and antioxidative processes, and alters the gut microbiome [1]. It may contribute to neurological recovery by influencing metabolic pathways, inflammatory responses, and pathological gene expression. Notable advantages of KD include its minimal toxicity, affordability, and straightforward implementation. Given the rising prevalence of neurological disorders and the recognized limitations of conventional treatments—such as accessibility, compliance, affordability, and efficacy—alternative therapeutic options warrant exploration.

KD has demonstrated benefits in neurological conditions, including migraine, motor neuron disease, autism, and multiple sclerosis. Additionally, it is used in managing psychiatric and metabolic disorders such as obesity, metabolic syndrome, diabetes mellitus, polycystic ovarian syndrome, and non-alcoholic fatty liver disease. However, some healthcare professionals express concerns about the potential cardiovascular risks associated with excessive saturated fat intake [2]. By enhancing insulin sensitivity and promoting weight loss, KD may reduce neuroinflammation and improve psychiatric well-being. This, in turn, could enhance patient adherence to medical guidance and improve prognosis. Nevertheless, a strict ketogenic regimen that limits fruit and vegetable intake may increase the risk of malignancies and reduce life expectancy [3]. The suitability of KD for individuals with multiple comorbidities remains uncertain. As an adjunct therapy, KD has the potential to reduce medication dependency, particularly benefiting elderly, dependent, and financially disadvantaged patients.

Optimizing neurological recovery in the acute phase is crucial for fostering long-term independence in individuals with spinal cord injuries. Dietary modifications represent a non-invasive approach to neurotrauma recovery. Preliminary results from a study by Demirel et al. indicate that, compared to a standard diet, five weeks of KD led to improvements in upper extremity motor function in patients with acute spinal cord injury [4]. Additionally, a review by Patel et al. examined five dietary patterns and their impact on modifiable risk factors affecting traumatic brain injury outcomes. Diets rich in fiber and nutrients, with limited sugar and saturated fat intake, offer the most significant cardiovascular and central nervous system protection. However, unlike other dietary regimens, long-term KD use beyond six months is not generally advised [5]. Therefore, the role of KD in managing traumatic brain injury and acute spinal trauma recovery remains uncertain due to limited available data.

KD and its variations have shown promise in managing drug-resistant epilepsy, although the precise mechanisms underlying its effects remain unclear. A mini-narrative review suggested that KD influences gut microbiota, leading to a seizure reduction of over 50% in some patients [2]. However, a substantial number of patients did not experience significant improvement despite prolonged adherence to KD. Further long-term studies are necessary to evaluate KD’s sustained impact on epilepsy. The gut-brain axis plays a crucial role in neurological functions, with norepinephrine secretion affecting bowel activity and gut microbiota exerting influences on the central nervous system via the vagus nerve and bioactive compounds, including short-chain fatty acids, tryptophan derivatives, and

secondary bile acids [1]. While the interplay between the brain, gut, and microbiota is intricate, KD's potential benefits in drug-resistant epilepsy remain a promising avenue for research.

Neuro-oncology affects individuals across all age groups, often leading to significant morbidity and mortality. A study by Bello et al. compared KD and standard dietary interventions in tumor-bearing animal models. The findings revealed that KD inhibited pathways mediated by insulin-like growth factor-1 (IGF-1), platelet-derived growth factor (PDGF), and epidermal growth factor receptor (EGFR), which are frequently overexpressed in gliomas [2]. Additionally, KD limits glucose-6-phosphate (G6P) availability, thereby disrupting glycolysis and the pentose phosphate pathway. This, in turn, helps regulate reactive oxygen species (ROS) levels and oxidative stress within cells. The relationship between KD and epigenetic modifications remains an area of ongoing investigation. If confirmed, this link could explain KD's potential ability to influence oncogene and tumor suppressor gene (TSG) expression [2]. As an adjunct to standard therapies, KD could enhance treatment efficacy for brain tumors, particularly glioblastoma, which presents significant treatment challenges. This dietary approach may also provide financial relief to patients, reducing their stress and improving their quality of life. However, further clinical research is needed to establish standardized ketogenic dietary protocols, ensure accessibility for individuals across different financial and healthcare settings, and compare KD with other therapeutic interventions, including surgery, radiology, and pharmacological treatments.

Despite the limitations of conventional neurological and neurosurgical treatments, KD presents a promising adjunctive option. Given the complex pathogenesis of neurological disorders, effective therapies remain limited. The incorporation of KD and its tailored adaptations should be explored based on the specific neurological condition and injury type. Further cohort studies are necessary to assess the safety and efficacy of KD in post-acute neurotrauma recovery. Additionally, investigations into the genetic and epigenetic effects of KD in neuro-oncology are required to enhance our understanding of its molecular and biochemical impact.

### Conclusion

The ketogenic diet presents a promising adjunctive strategy for neurological recovery and disease management. Its metabolic and neuroprotective effects warrant further research to optimize its clinical application. However, concerns regarding long-term adherence, safety, and potential adverse effects highlight the need for well-designed clinical trials to establish evidence-based guidelines for KD in neurological and neuro-oncological care.

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