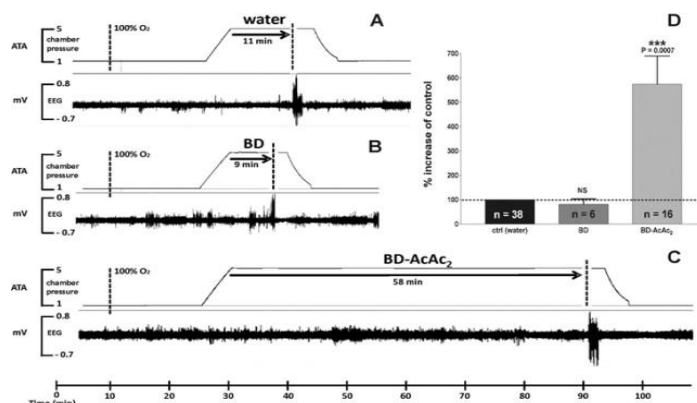


# Therapeutic ketosis and the broad field of applications for the ketogenic diet: Ketone ester applications & clinical updates

Raffaele Pilla, Pharm D

It has been recently shown that nutritional ketosis is effective against seizure disorders and various acute/chronic neurological disorders. Physiologically, glucose is the primary metabolic fuel for cells. However, many neurodegenerative disorders have been associated with impaired glucose transport/metabolism and with mitochondrial dysfunction, such as Alzheimer's/Parkinson's disease, general seizure disorders, and traumatic brain injury. Ketone bodies and tricarboxylic acid cycle intermediates represent alternative fuels for the brain and can bypass the rate-limiting steps associated with impaired neuronal glucose metabolism. Therefore, therapeutic ketosis can be considered as a metabolic therapy by providing alternative energy substrates. It has been estimated that the brain derives over 60% of its total energy from ketones when glucose availability is limited. In fact, after prolonged periods of fasting or ketogenic diet (KD), the body utilizes energy obtained from free fatty acids (FFAs) released from adipose tissue. It has been recently shown that nutritional ketosis is effective against seizure disorders and various acute/chronic neurological disorders. Physiologically, glucose is the primary metabolic fuel for cells. However, many neurodegenerative disorders have been associated with impaired glucose transport/metabolism and with mitochondrial dysfunction, such as Alzheimer's/Parkinson's disease, general seizure disorders, and traumatic brain injury. Ketone bodies and tricarboxylic acid cycle intermediates represent alternative fuels for the brain and can bypass the rate-limiting steps associated with impaired neuronal glucose metabolism. Because the brain is unable to derive significant energy from FFAs, hepatic ketogenesis converts FFAs into ketone bodies-hydroxybutyrate (BHB) and acetoacetate (AcAc)-while a percentage of AcAc spontaneously decarboxylates to acetone. Large quantities of ketone bodies accumulate in the blood through this mechanism. This represents a state of normal physiological ketosis and can be therapeutic. Ketone bodies are transported across the blood-brain barrier by monocarboxylic acid transporters to fuel brain function. Starvation or nutritional ketosis is an essential survival mechanism that ensures metabolic flexibility during prolonged fasting or lack of carbohydrate ingestion. Therapeutic ketosis leads to metabolic adaptations that may improve brain metabolism, restore mitochondrial ATP production, decrease reactive oxygen species production, reduce inflammation, and increase neurotrophic factors' function. It has been shown that KD mimics the effects of fasting and the lack of glucose/insulin signaling, promoting a metabolic shift towards fatty acid utilization. In this work, the author reports a number of successful case reports treated through metabolic ketosis



**Figure 1** (A Figure 1: Ketone Ester significantly increased resistance against Central Nervous System Oxygen Toxicity seizures (D'Agostino D.P. et al., 2013 *Am J Physiol Regul Integr Comp Physiol.* 304(10):R829- 36).

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PhD – St. John of God Hospital – Fatebenefratelli, Benevento, Italy

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Correspondence: Raffaele Pilla, Pharm D, PhD – St. John of God Hospital – Fatebenefratelli, Benevento, Italy

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*PhD – St. John of God Hospital – Fatebenefratelli, Benevento, Italy*

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