Ketogenic dietary therapy for other conditions

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Ketogenic therapy has been successfully used to treat intractable epilepsy for many years and more recently there is increasing interest in its use as a therapy for neurological cancers. A growing body of scientific research suggests this type of diet may also have potential as a treatment for a wider range of disorders which are discussed in this insight.

The primary metabolic changes induced by ketogenic therapy are enhancement of mitochondrial function and reduced use of glucose as a metabolic substrate. This may convey neuroprotective benefits and provide efficient energy sources in neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease and Amyotrophic lateral sclerosis which are associated with mitochondrial dysfunction and metabolic abnormalities (1,2,3). There is also interest in the influence of ketogenic therapy on the normal aging process in the brain (4).

A particular metabolic abnormality in Alzheimer's disease is the formation of extracellular plaques containing amyloid protein. A ketogenic diet protected against the effects of amyloid deposition in mice (5,6) and calorie restriction may also have benefits via the regulation of a family of proteins called sirtuins which are involved in mediating the anti-aging process (1,7). The pre-clinical stage of Alzheimer's disease is associated with a reduction in brain glucose metabolism (8) which may be a contributory risk factor in development of disease as well as a result of the disease process. As the uptake of brain ketones remains normal these may have therapeutic benefits in early stages of the disease by compensating for the deficiency in glucose metabolism (8,9). The level of ketosis needed is likely to be lower than that in epilepsy and on-going research is examining how this might be achieved by a high fat diet, medium chain triglyceride (MCT) supplements or use of ketone esters. In a randomized, double blind study of 152 patients with mild to moderate Alzheimers disease, the group treated with MCT ketogenic compound showed significant improvement in cognitive function compared with controls (10) although the benefit of the diet was only seen in patients lacking a particular genotype (APOε4 – a risk factor for the disease). Cognition-enhancing benefits of MCT may be unrelated to ketone production; treatment with C8 and C10 medium chain fatty acids improved cognitive performance of aged rats but did not increase their brain ketone levels (11). The increased essential fatty acid intake provided by a high fat diet may also improve cognitive dysfunction (12).

Parkinson's disease is characterised by the progressive death of brain dopaminergic neurons caused by mitochondrial dysfunction. Ketones could provide a fuel source for these at-risk neurons and the ketone-induced enhancement of mitochondrial function may protect cells against insults that demand a high energy supply (1). Animal studies suggest the ketogenic diet may protect against dopaminergic neurodegeneration and improve motor function (13, 14) with glutathione playing an important role (15). A feasibility study on use of the ketogenic diet in 7 patients with Parkinson's disease reported a decrease in the average disease rating score in the 5 patients who completed the trial (16).

Amyotrophic lateral sclerosis is a progressive motor neuron disease that leads to weakness and loss of skeletal muscle. There are no published results from clinical studies but animal studies indicate that a ketogenic diet may help slow the progressive loss of neurons by increasing mitochondrial function and ATP production (17,18), although a high calorie diet per se may also prolong survival in this group (19). There is clearly future potential for using ketogenic therapy within the management of neurodegenerative and neuromuscular disorders but further studies are needed before it can be incorporated into clinical practice in order to clarify who would benefit from this type of treatment and how best it should be implemented.

There is some evidence from animal studies suggesting that ketogenic therapy may have a role in protecting the brain from trauma and ischaemia (1,2); again further studies are needed. One small study which treated autistic children with an intermittently-applied modified MCT diet has suggested that ketogenic therapy may be of benefit in this group (20). However the study has potential limitations (1,2), and further work is needed before any recommendations can be made. Other reports have suggested a modified Atkins style ketogenic diet could be used to treat headache (21) and narcolepsy (22). Further research is again necessary.

References:

1. Barañano KW, Hartman AL (2008) The ketogenic diet: uses in epilepsy and other neurologic illnesses. Curr Treat Options Neurol. 10(6):410-9.
2. Stafstrom CE, Rho JM (2012) The Ketogenic Diet as a Treatment Paradigm for Diverse Neurological Disorders. Front Pharmacol. 3:59.
3. Paoli A, Bianco A, Damiani E, Bosco G (2014) Ketogenic Diet in Neuromuscular and Neurodegenerative Diseases. Biomed Res Int. 2014: 474296.
4. Balietti M, Casoli T, Di Stefano G, Giorgetti B, Aicardi G, Fattoretti P (2010) Ketogenic diets: an historical antiepileptic therapy with promising potentialities for the aging brain. Ageing Res Rev. 9(3):273-9.
5. Van der Auwera I, Wera S, Van Leuven F, Henderson ST (2005) A ketogenic diet reduces amyloid beta 40 and 42 in a mouse model of Alzheimer's disease. Nutr Metab (Lond) 2:28.
6. Kashiwaya Y, Bergman C, Lee J, et al (2013) A ketone ester diet exhibits anxiolytic and cognition-sparing properties, and lessens amyloid and tau pathologies in a mouse model of Alzheimer's disease. Neurobiology of Aging. 34(6):1530–9.
7. Qin W, Yang T, Ho L, et al (2006) Neuronal SIRT1 activation as a novel mechanism underlying the prevention of Alzheimer disease amyloid neuropathology by calorie restriction. J Biol Chem. 281(31):21745-54..
8. Hertz L, Chen Y, Waagepetersen HS (2015) Effects of ketone bodies in Alzheimer's disease in relation to neural hypometabolism, β-amyloid toxicity, and astrocyte function. J Neurochem. 134(1):7-20
9. Cunnane SC, Courchesne-Loyer A, St-Pierre V, et al (2016) Can ketones compensate for deteriorating brain glucose uptake during aging? Implications for the risk and treatment of Alzheimer's disease. Ann. N.Y. Acad. Sci. 1367:12-20.
10. Henderson ST, Vogel JL, Barr LJ, Garvin F, Jones JJ, Costantini LC (2009) Study of the ketogenic agent AC-1202 in mild to moderate Alzheimer's disease: a randomized, double-blind, placebo-controlled, multicenter trial. Nutr Metab (Lond) 6:31.
11. Wang D, Mitchell ES (2016) Cognition and Synaptic-Plasticity Related Changes in Aged Rats Supplemented with 8- and 10-Carbon Medium Chain Triglycerides. PLoS One. 11(8): e0160159.
12. Kotani S, Sakaguchi E, Warashina S, et al (2006) Dietary supplementation of arachidonic and docosahexaenoic acids improves cognitive dysfunction. Neurosci Res. 56(2):159-64.
13. Tieu K, Perier C, Caspersen C, et al (2003) D-beta-hydroxybutyrate rescues mitochondrial respiration and mitigates features of Parkinson disease. J Clin Invest. 112(6):892-901.
14. Shaafi S, Najmi S, Aliasgharpour H, et al (2016) The efficacy of the ketogenic diet on motor functions in Parkinson's disease: A rat model. Iran J Neurol. 15(2):63-9.
15. Cheng B, Yang X, An L, Gao B, Liu X, Liu S (2009) Ketogenic diet protects dopaminergic neurons against 6-OHDA neurotoxicity via up-regulating glutathione in a rat model of Parkinson's disease. Brain Res. 1286:25-31.

16. Vanitallie TB, Nonas C, Di Rocco A, Boyar K, Hyams K, Heymsfield SB (2005) Treatment of Parkinson disease with diet-induced hyperketonemia: a feasibility study. Neurology 64(4):728-30.
17. Zhao Z, Lange DJ, Voustianiouk A, et al (2006) A ketogenic diet as a potential novel therapeutic intervention in amyotrophic lateral sclerosis. BMC Neurosci. 3;7:29.
18. Siva N (2006) Can ketogenic diet slow progression of ALS? Lancet Neurol. 5(6):476.
19. Paganoni S, Wills AM. (2013) High-fat and ketogenic diets in amyotrophic lateral sclerosis. J Child Neurol. 28(8):989-92
20. Evangeliou A, Vlachonikolis I, Mihailidou H, et al (2003) Application of a ketogenic diet in children with autistic behavior: pilot study. J Child Neurol. 18(2):113-8.
21. Kossoff EH, Huffman J, Turner Z, Gladstein J (2010) Use of the modified Atkins diet for adolescents with chronic daily headache. Cephalalgia. 30(8):1014-6.
22. Husain AM, Yancy WS Jr, Carwile ST, Miller PP, Westman EC (2004) Diet therapy for narcolepsy. Neurology 62(12):2300-2.

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