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Energy Metabolism in Diabetic Peripheral Neuropathy: Implications for Human Nutrition and Dietetics

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Abstract

Diabetes mellitus is a well-known lifestyle-associated metabolic disorder leading to microvascular and macrovascular complications as a consequence of insulin resistance and chronic hyperglycemia. Diabetic peripheral neuropathy (DPN) is the leading microvascular complication of DM, with disabling neuropathic pain, sensory/motor deficits and associated psychosocial disturbances.This short communication was aimed at exploring the role of energy metabolism in the pathogenesis, diagnosis and therapy for DPN and found evidence for altered lipid metabolism, with persistent anerobic glycolysis in peripheral nerves of DPN and efficacy of alpha-lipoic acid supplementation in DPN.

Keywords: Metabolic neuropathy; Nutritional Endocrinology; Energy metabolism; Diet Neurology.

Diabetes mellitus is a well-known lifestyle-associated metabolic disorder leading to microvascular and macrovascular complications as a consequence of insulin resistance and chronic hyperglycemia. Diabetic peripheral neuropathy (DPN) is the leading microvascular complication of DM, with disabling neuropathic pain, sensory/motor deficits and associated psychosocial disturbances.

Pathogenetically, Vincent *et al*[1] presented evidence that both chronic and acute hyperglycemia cause oxidative stress in the peripheral nervous system that can promote the development of diabetic neuropathy. They said, "proteins that are damaged by oxidative stress have decreased biological activity leading to loss of energy metabolism, cell signaling, transport, and, ultimately, to cell death."

Diagnostically, Low *et al*[2] examined the effect of ischemia on nerve conduction in experimental diabetic neuropathy (EDN) and related electrophysiological changes to nerve adenosine triphosphate (ATP), creatine phosphate (CP), and lactate under anoxic conditions and their findings suggested that the maintenance of nerve transmission in anoxic-ischemic states depended upon anaerobic metabolism and that resistance to ischemic conduction block (RICB) in EDN was due to anaerobic glycolysis maintained for a longer time than normal nerves.

Pande *et al*[3] examined changes in global gene expression in DPN and identified pathways that included lipid metabolism, carbohydrate metabolism, energy metabolism, and peroxisome proliferator-activated receptor signaling, apoptosis, and axon guidance, and the gene expression changes were consistent with structural changes of axonal degeneration.

Suzuki *et al*[4] studied 36 Type II (non-insulin-dependent) diabetic patients without occlusive arterial diseases in the lower extremities and 12 age-matched and sex-matched non-diabetic subjects to clarify the association between diabetic polyneuropathy and foot ulcers using 1H-and 31P-magnetic resonance spectroscopy and imaging, and

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their findings indicated that motor nerve dysfunction in diabetic patients was closely associated with impaired energy metabolism, fatty infiltration and increased intracellular p^H of plantar muscles and high frequency of foot ulcers.

Thurston *et al*[5] found increases in the nerve content of glucose, sorbitol, and fructose in alloxan-induced diabetic rats and proposed five major hypotheses to explain the pathogenesis of diabetic neuropathy: 1) hypoxia/ischemia, 2) hyperglycemic pseudohypoxia, 3) myo-inositol deficiency, 4) fructose and polyol accumulation and osmotic disequilibrium, and 5) nonenzymatic glycation of macromolecules by fructose and glucose.

Therapeutically, Kishiet *et al*[6] evaluated the effect of Alpha-lipoic acid on glucose uptake, nerve energy metabolism, the polyol pathway, and protein kinase C (PKC) activity in experimental diabetic neuropathy (EDN) induced by streptozotocin. Alpha-lipoic acid supplementation reversed the deficits in EDN, increasing endoneurial glucose, fructose, and sorbitol levels while myo-inositol was significantly reduced.

Stevens *et al*[7] reported the selective effects of administration of the antioxidant DL-alpha-lipoic acid (ALA) to streptozotocin-injected diabetic rats as follows: "ALA improved digital sensory but not sciatic-tibial motor NCV, corrected endoneurial nutritive but not composite nerve blood flow (NBF), increased the mitochondrial oxidative state without correcting nerve energy depletion, and enhanced the accumulation of polyol pathway intermediates without worsening myo-inositol or taurine depletion."

References

1. Vincent AM, Russell JW, Low P, Feldman EL. Oxidative stress in the pathogenesis of diabetic neuropathy. *Endocr Rev.* 2004; 25(4): 612-28.
2. Low PA, Ward K, Schmelzer JD, Brimijoin S. Ischemic conduction failure and energy metabolism in experimental diabetic neuropathy. *Am J Physiol.* 1985; 248(4 Pt 1): E457-62.
3. Pande M, Hur J, Hong Y, Backus C, Hayes JM, Oh SS *et al.* Transcriptional profiling of diabetic neuropathy in the BKS db/db mouse: a model of type 2 diabetes. *Diabetes.* 2011; 60(7): 1981-9.
4. Suzuki E, Kashiwagi A, Hidaka H, Maegawa H, Nishio Y, Kojima H *et al.* 1H- and 31P-magnetic resonance spectroscopy and imaging as a new diagnostic tool to evaluate neuropathic foot ulcers in Type II diabetic patients. *Diabetologia.* 2000; 43(2): 165-72.
5. Thurston JH, McDougal DB Jr, Hauhart RE, Schulz DW. Effects of acute, subacute, and chronic diabetes on carbohydrate and energy metabolism in rat sciatic nerve. Relation to mechanisms of peripheral neuropathy. *Diabetes.* 1995; 44(2): 190-5.
6. Kishi Y, Schmelzer JD, Yao JK, Zollman PJ, Nickander KK, Tritschler HJ *et al.* Alpha-lipoic acid: effect on glucose uptake, sorbitol pathway, and energy metabolism in experimental diabetic neuropathy. *Diabetes.* 1999; 48(10): 2045-51.
7. Stevens MJ, Obrosova I, Cao X, Van Huysen C, Greene DA. Effects of DL-alpha-lipoic acid on peripheral nerve conduction, blood flow, energy metabolism, and oxidative stress in experimental diabetic neuropathy. *Diabetes.* 2000; 49(6): 1006-15.