

Supplements That Help Treat Neuropathies: Part 1

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Practitioners who routinely treat neuro-musculo-skeletal disorders and pain syndromes commonly encounter patients presenting with various types of neuropathies, such as diabetic neuropathy, compression and entrapment neuropathy, chemotherapy-induced neuropathy, post-traumatic neuropathy, inherited neuropathy (e.g. Charcot-Marie-Tooth), neuritis, and on occasion, neuropathy due to vitamin B12 or niacin deficiency, or vitamin B6 or niacin toxicity. Excluding vitamin B12 or niacin deficiency and/or vitamin B6 or niacin toxicity in which the management is very straight forward, emerging evidence suggests that targeted nutritional supplements can help reverse many types of neuropathies, and should be included in the comprehensive treatment plan for these patients.

Energy Production in Nerves Relies Heavily on Pyruvate Dehydrogenase and Its 5 Coenzymes

The additional energy required by nerve cells to repair internal nerve damage is highly dependent upon the ability of nerve cells to convert pyruvate to acetyl-coA within the mitochondria of the cell. Unlike many peripheral cells, nerve cells are almost exclusively dependent upon glucose for energy (although they can switch to ketones to a large degree in a low blood sugar or uncontrolled diabetic state). Within nerve cells, glucose first undergoes glycolysis to form pyruvate (generating a minimal amount of ATP energy for nerve cell function and repair). In turn, pyruvate passes from the cytosol into the mitochondria where it is converted to acetyl-coA by the enzyme pyruvate dehydrogenase (PD). This is an important step as acetyl-CoA then reacts with oxaloacetate to form citrate, enabling the Krebs cycle to generate a significant amount of ATP energy via oxidative phosphorylation. What often gets overlooked is the fact that pyruvate dehydrogenase (PD) requires the presence of five coenzymes in order to catalyze this vital reaction in nerve energy production. The five coenzymes required by PD include four B-vitamins and alpha lipoic acid:

- Vitamin B1 (thiamine) - in the form of thiamine diphosphate or TDP – previously known as TPP
- Vitamin B2 (riboflavin) – in the form of FAD (flavin adenine dinucleotide)
- Vitamin B3 (niacin) – in the form of NAD (nicotinamide adenine dinucleotide)
- Pantothenic Acid – in the form of coenzyme A (CoA)
- Alpha Lipoic Acid (1).

In addition to their role as coenzymes for PD, alpha lipoic acid is also known to protect the mitochondria of cells from free radical damage (oxidative stress) and reduce inflammation as a secondary function of this involvement. Halting mitochondrial damage enables mitochondrial DNA to repair mitochondrial damage, which ultimately improves ATP synthesis required for nerve repair mechanisms to be effective in reversing any pathology (2,3,4). Vitamin B1 (TDP) is also required to form other intermediates in the energy producing Krebs cycle. Some thiamine is also converted to thiamine triphosphate (ThP), whereby its main role is to facilitate normal nerve transmission within nerve cells, in a non-coenzyme role (5). Riboflavin (as FAD/FADH) is also

involved in energy production, transferring electrons within the oxidative phosphorylation system of mitochondria (6). Pantothenic acid (as CoA) is also required for the synthesis of certain Krebs cycle intermediates, the synthesis of myelin and the synthesis of acetylcholine – an important neurotransmitter synthesizer, which is secreted by motor nerves to initiate muscle contraction (7).

Based on these known biochemical and physiological functions, various researchers have tested super-physiological doses of these nutrients in the treatment of various forms of neuropathies. In many instances, positive results have been documented. The intent of these supplementation methods was to help optimize the function of PD, increase Krebs cycle intermediates, reduce oxidative stress and inflammation within nerve cells, optimize mitochondrial ATP production for nerve function and repair, and to support myelin synthesis and regeneration.

Thiamine Supplementation and Neuropathy

The most impressive studies using thiamine supplementation have used a fat-soluble form of thiamine known as Benfotiamine. Benfotiamine is absorbed up to 3.6 times greater than vitamin B1, and is associated with a 120-fold greater increase in levels of metabolically active TDP. Its lipid solubility enables it to penetrate nerve membranes more efficiently than thiamine triphosphate (ThP). Experimentally, it has also been shown to reduce activation of inflammatory cytokines and transcription factors, including Nuclear Factor kappa-beta (NF-kb). A number of impressive studies have shown that Benfotiamine supplementation can reduce peripheral neuropathy symptoms and increase nerve conduction. Most of these studies involved diabetic neuropathy. The most common daily dosage was 150-300 mg, twice daily (8,9,10)

Pantothenic Acid and Neuropathy

Clinical studies using pantothenic supplementation in certain types of neuropathy have also shown promising results. The common daily dosage was 100-500 mg per day (11).

Alpha Lipoic Acid and Neuropathy

Alpha lipoic acid supplementation has been an approved treatment for diabetic neuropathy in Germany since 1959. It has been shown to help repair nerve damage and supports nerve function as outlined above. The typical daily dosage is 600 mg, 1-3 times daily. Start with a dosage of 600 mg per day then increase dosage slowly over the next two weeks if necessary (2,3,4).

Other Vitamins Shown To Reverse or Prevent Neuropathies in High-Risk Individuals

Vitamin B12

Vitamin B12 is well known for its role in myelin synthesis and repair. Vitamin B12 is a coenzyme for methylmalonyl CoA mutase (MUT) required in myelin synthesis. Vitamin B12 converts methylmalonyl CoA to succinyl Co A. Excessive methylmalonyl CoA prevents normal fatty acid synthesis, required to form the myelin sheath around the nerve cells. As such, some impressive research shows that vitamin B12 supplementation has been helpful in treating certain neuropathies and improving some of the symptoms of multiple sclerosis (a demyelinating

disease). The typical daily dosage is 500 mcg, 3-4 times per day daily, usually administered along with a B-50 Complex supplement (12,13,14,15,16).

Vitamin E

Some small trials have shown that vitamin E supplementation was able to attenuate or prevent peripheral neuropathy caused by chemotherapy drugs (six courses of cumulative cisplatin, paclitaxel, or their combination), when given prophylactically during chemotherapy and 3 months after its cessation (17). It is known that vitamin E deficiency causes neuropathy and that vitamin E protects nerve cell membranes and mitochondria from oxidative damage (18).

Chemotherapy-induced peripheral neuropathy (CIPN) is a major side effect of many commonly used chemotherapeutic agents, including platinum drugs, taxanes, epothilones and vinca alkaloids, and also newer agents such as bortezomib and lenolidamide. Vinca alkaloids, cisplatin, and taxanes are the drugs that commonly cause chemotherapy-induced peripheral neuropathy, with incidences of CIPN from these agents ranging from 30% to 40% (18,19). Some evidence strongly suggests that intravenous calcium and magnesium therapy can attenuate the development of oxaliplatin-induced CIPN, without reducing treatment response. Some studies show that vitamin E may also attenuate the development of CIPN. Other natural agents that look promising in preliminary studies, but need substantiation, include glutamine, glutathione, N-acetylcysteine – all of which increase intracellular stores of the antioxidant and detoxification tripeptide known as glutathione.

The daily dosage of vitamin E used in these studies was 400-600 IU per day (20,21).

In part 2 of this article I will outline the research pertaining to the use of other important supplements (curcumin, L-carnitine, CoQ10, essential fatty acids) shown to be useful in treating peripheral neuropathies from various causes. Part 2 also includes a summary of all information presented with a suggested supplement protocol for patients to follow.

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