Dynamic Chiropractic

PAIN RELIEF / PREVENTION

Supplements That Treat Neuropathies (Part 2)

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In part 1 of this article, I outlined the key role played by various vitamins in the management of various types of neuropathies. In part 2, I address the important role of other important accessory nutrients that should also be considered in the adjunctive management of various peripheral neuropathies.

Acetyl-L Carnitine (ALC)

Supplementation with acetyl-L carnitine has been shown to increase nerve membrane phospholipid synthesis and synthesis of the neurotransmitter acetylcholine. For muscle contraction to occur, motor nerves must synthesize and release acetylcholine. The binding of acetylcholine to the muscle membrane allows for the initiation of an action potential, which initiates muscle contraction. Human studies using acetyl-L carnitine to treat various neuropathies have used a dosage of 500–1,000 mg, three times daily.

ALC is the ester acetylated form of the amino acid L-carnitine, which transports fatty acids across the mitochondrial membrane to allow beta-oxidation to occur, which generates ATP energy aerobically. As such, the final step in the synthesis of ALC takes place in the mitochondrial matrix by the enzyme acetyl-L-transferase, which uses the substrates carnitine and acetyl-CoA.

As an integral compound in mitochondrial function, ALC is widely distributed throughout tissues, with the highest concentrations found in cardiac and skeletal muscle. The brain also has high levels, and ALC has been shown to influence neurotransmitters, including acetylcholine and dopamine.

ALC may also prevent neural degeneration related to aging in the brain through the preservation of the neurotrophin, nerve growth factor (NGF). These actions of ALC have been known for decades and account for the popular use of ALC as an anti-aging or memory-supportive nutrient.

In the early 1990s, the positive influence on neurotransmitter synthesis was proposed as the mechanism of ALC's anti-nociceptive effect (reducing sensitivity to painful stimuli). More recently, it has been discovered that ALC's anti-nociceptive effects also involve direct actions at the dorsal root ganglia or peripheral axonal synapses. In addition to reducing the perception of pain, there is also evidence suggesting that ALC acts as a neuro-protectant and neuro-regenerative agent. This dual action of both blocking pain perception and protecting the nerve from further damage suggested that ALC would be an ideal candidate to include in the treatment of peripheral neuropathy.

A number of clinical trials have shown positive effects when ALC has been used to treat various forms of peripheral neuropathy. ALC has reduced pain and improved nerve function in clinical trials involving patients suffering from:

- Chemotherapy-induced peripheral neuropathies (CIPN), countering the impact of various

combinations of chemotherapy drugs on nerve damage
- Human immunodeficiency virus (HIV)-associated peripheral neuropathy caused by nucleoside reverse transcriptase inhibitor drugs used in treatment of HIV
- Diabetic peripheral neuropathy
- Compression-induced peripheral neuropathy

In summary, ALC demonstrates multi-modal effects in the treatment of peripheral neuropathies. Some of these mechanisms of action include positive effects on circulating neurotrophins, mitochondrial function (including anti-apoptotic effects), and synaptic transmission, influencing both nerve structure / function and patient perception of neuropathic symptoms.

Clinical trials of several prominent causes of peripheral neuropathy suggest oral doses from 1,000-3,000 mg daily are effective for symptom relief in a majority of patients. Electrophysiological testing and skin biopsies substantiate the regenerative capacity of ALC on nerve innervation. Tolerance to ALC appears to be excellent with mild, infrequent side effects, including insomnia and gastric irritation.[1]

Curcumin

Curcumin is the principal curcuminoid found in the spice turmeric, and has recently been studied for its role in the treatment of various central nervous system disorders. Curcumin demonstrates neuroprotective action in Alzheimer's disease, tardive dyskinesia, major depression, epilepsy, and other related neurodegenerative and neuropsychiatric disorders.

In regard to peripheral neuropathy, curcumin has been shown to possess anti-inflammatory properties , such as its inhibitory effect on the production of inflammatory interleukin-8 (IL-8), interleukin-1β (IL-1β) and TNF-α levels. Animal studies using diabetic peripheral neuropathy models have shown that supplementation with curcumin attenuated many of the peripheral neuropathy symptoms typically associated with diabetic neuropathy.

Some researchers have concluded that curcumin is a novel anti-nociceptive agent and can be used as a therapeutic option in the treatment of neuropathic pain associated with diabetes mellitus. Other experimental studies using curcumin in the treatment of diabetic neuropathy showed that curcumin supplementation also enhanced the glucose-lowering effect of insulin and protects against the onset of diabetic neuropathy.[2]

Gamma Linolenic Acid (GLA)

Studies confirm that the first step in the conversion of the essential fatty acid (EFA) linoleic acid to gamma-linolenic acid (GLA) is impaired in diabetics. This results from a deficit of the enzyme delta-6-desaturase. In more severe cases essential fatty acid metabolism is impaired in two places, which is caused by a production deficit of the delta 5-desaturase enzyme, further down the conversion chain. The result of this broken process is shortage of GLA and its metabolites; prostacyclin and prostaglandins. Diabetic neuropathy is a progressive disease that is strongly associated with chronic deficiency of prostacyclin and prostaglandin-series 1 synthesis. This is central to the pathogenesis of diabetic neuropathy.

In addition to consequences on the nerve cell membrane, the very low levels of prostacyclin/prostaglandins among diabetics also results in the membranes of red blood corpuscles of

diabetics becoming brittle and unable to be deformed. The consequence is that the oxygen-carrying corpuscles are less able to squeeze into the small capillary vessels, including those of the endoneurium. As such, nerve cells become hypoxic, which further contributes to the pathology in diabetic neuropathy.

A 1990 study showed that endoneural capillary density increased by 22 percent with supplementation of a high GLA-yielding essential fatty acid supplement. Results were enhanced with concomitant supplementation with vitamin C.[3]

Human studies have confirmed that GLA supplementation can be an effective agent in the adjunctive treatment of distal diabetic polyneuropathy. In a double-blind study involving 22 patients, the treatment group received either 360 mg gamma-linolenic acid for six months. Compared to the placebo group, patients supplemented with gamma-linolenic acid showed statistically significant improvement in neuropathy symptom scores, median nerve motor conduction velocity and compound muscle action potential amplitude, peroneal nerve motor conduction velocity and compound muscle action potential amplitude, median and sural sensory nerve action and potential amplitude, and ankle heat threshold, and cold threshold values.[4]

Other human trials have shown similar results. For example, a double-blind study followed 111 people with diabetes for one year. Results showed an improvement in subjective symptoms of peripheral neuropathy, such as pain and numbness, as well as objective signs of nerve injury. People with good blood sugar control improved the most.[5]

Other experimental studies have shown that GLA supplementation can protect nerves from diabetes-induced injury.[6-7] The therapeutic dosage to consider is 330-440 mg per day. Essential oils with high GLA concentrations include borage seed oil (22 percent), black currant oil (22 percent) and evening primrose oil (9 percent).

As omega-3 fatty acids have also been shown to reduce inflammation and improve the lipid profile in diabetic patients, according to human clinical studies,[8] some experts suggest an essential fatty acid supplement best suited for diabetics should include a combination of fish, flaxseed and borage seed oils. If each 1,200 capsule contains 400 mg of each of these oils, then a daily dosage of 4-6 capsules would be an appropriate therapeutic dosage for the diabetic patient.

Coenzyme Q_{10}

In experimental studies involving diabetic rats, supplementation with coenzyme Q_{10} restored conduction velocities to that of healthy control rats, which had slowed down as a result of their diabetic state. The authors state, "In addition to its effects on mitochondrial alterations (increasing ATP energy production), these positive effects of CoQ_{10} on diabetic neuropathy can be attributed to its antioxidant activity."

CoQ_{10} protects mitochondria in an important antioxidant role, enabling mitochondrial DNA to repair damage and increase ATP energy required to reverse various aspects of the pathology found in neuropathies.[9] The dosage consideration would range from 100–200 mg.

Supplement Protocol for Patients With Neuropathy

Based on the data presented in part 1 and part 2 of this article series, the following represents a comprehensive clinical approach to supplementation of the patient with peripheral neuropathy from various causes:

1. High-potency multivitamin containing a daily dosage of vitamin C (1,000 mg), vitamin E (400 IU), a B-50 complex, vitamin D (1,000 IU) and a complete A–to-zinc formula)
2. Essential fatty acid supplement (1,200 mg capsule containing 400 mg each of borage seed oil, flaxseed oil and fish oil) – 4-6 capsules per day
3. Alpha-lipoic acid: 600 mg/day, increasing to 1,800 mg if necessary in divided doses
4. Curcumin: 500 mg, 3-4 times daily)
5. Benfotiamine: 150-300 mg, 2 times daily
6. Additional vitamin E: 1,000-1,600 IU per day
7. Pantothenic acid: 100–500 mg/day
8. Vitamin B12: 500 mcg, three times daily
9. Acetyl–L carnitine: 500 mg, three times daily
10. Coenzyme Q_{10}: 100 mg/day

It is important not to overwhelm the patient with an extensive and costly supplement program if possible. As such, as a rule of thumb you may wish to use recommendations #1–4 above as your foundation program for all neuropathy patients. In more extensive cases, such as severe CIPN, hereditary neuropathies (Charcot-Marie-Tooth disease, etc.) and advanced diabetic polyneuropathies, the addition of some or all of recommendations #5-10 above should be considered.

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