

Alpha-Lipoic Acid for Treatment of Diabetic Peripheral Neuropathy

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This series is coordinated by John E. Delzell Jr., MD, MSPH, Assistant Medical Editor.

Clinical Question

Does alpha-lipoic acid (ALA) improve diabetic peripheral neuropathy?

Evidence-Based Answer

Intravenous (IV) ALA can improve neuropathy symptoms when administered for three weeks, but symptom improvement with oral ALA is not clinically significant. (Strength of Recommendation: B, based on two meta-analyses of randomized controlled trials [RCTs].) There is no evidence evaluating long-term treatment.

Hyperglycemia can increase production of free oxygen radicals. Increased levels of free radicals have been associated with diabetic complications. Antioxidants such as ALA could theoretically be effective in treating diabetic peripheral neuropathy. A meta-analysis of four RCTs (N = 653) evaluated the effectiveness of ALA vs. placebo to reduce symptoms of preexisting diabetic peripheral neuropathy.¹ Most of the participants had type 2 diabetes mellitus and were 18 to 74 years of age. Diabetic neuropathy was assessed using the total symptom score (range from 0 [asymptomatic] to 14.6 [constant and severe pain, burning, paresthesia, and numbness]). A 30% change (or at least 2 points for patients with a baseline score of at least 4) was considered clinically relevant. Compared with placebo, IV ALA (600 mg per day for three weeks) decreased symptoms of neuropathy (two RCTs, N = 448; standardized mean difference [SMD] = -2.8; 95% confidence interval [CI], -4.2 to -1.5). Oral ALA (600 mg or more per day for three to five weeks) led to minimal improvement in neuropathy symptoms compared with placebo, but did not meet the criteria for

clinical significance (two RCTs, N = 205; SMD = -1.8; 95% CI, -2.5 to -1.1). It is unclear why IV therapy was more effective than oral therapy.

A 2012 meta-analysis of 15 RCTs (N = 1,058) evaluated IV ALA (300 to 600 mg) compared with control vitamins that were given for 14 to 28 days.² The participants had diabetic peripheral neuropathy, and their average age was 57 years. The type of diabetes was not specified. Nine trials (N = 651) evaluated effectiveness, defined as an improvement in symptoms, tendon reflexes, and nerve conduction velocities. IV therapy demonstrated greater effectiveness compared with placebo (odds ratio = 4.0; 95% CI, 2.7 to 5.9), although the scales for symptom and tendon reflex improvement were not defined. Nerve conduction velocities increased significantly in the treatment groups. The studies included in this meta-analysis were lower in quality (sample size was small, and randomization, allocation concealment, and withdrawals were not reported).

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Author disclosure: No relevant financial affiliations.

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