Abstract

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Alpha-lipoic acid in the treatment of diabetic polyneuropathy in Germany: current evidence from clinical trials.

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BACKGROUND: Diabetic neuropathy represents a major health problem, as it is responsible for substantial morbidity, increased mortality, and impaired quality of life. Near-normoglycaemia is now generally accepted as the primary approach to prevention of diabetic neuropathy, but is not achievable in a considerable number of patients. In the past two decades several medical treatments that exert their effects despite hyperglycaemia have been derived from the experimental pathogenetic concepts of diabetic neuropathy. Such compounds have been designed to improve or slow the progression of the neuropathic process and are being evaluated in clinical trials, but with the exception of alpha-lipoic acid (thioctic acid) which is available in Germany, none of these drugs is currently available in clinical practice.

OBJECTIVE AND METHODS: Here we review the current evidence from the clinical trials that assessed the therapeutic efficacy and safety of thioctic acid in diabetic polyneuropathy. Thus far, 15 clinical trials have been completed using different study designs, durations of treatment, doses, sample sizes, and patient populations. Within this variety of clinical trials, those with beneficial effects of thioctic acid on either neuropathic symptoms and deficits due to polyneuropathy or reduced heart rate variability resulting from cardiac autonomic neuropathy used doses of at least 600 mg per day.

RESULTS: The following conclusions can be drawn from the recent controlled clinical trials. 1.) Short-term treatment for 3 weeks using 600 mg of thioctic acid i.v. per day appears to reduce the chief symptoms of diabetic polyneuropathy. A 3-week pilot study of 1800 mg per day given orally indicates that the therapeutic effect may be independent of the route of administration, but this needs to be confirmed in a larger sample size. 2.) The effect on symptoms is accompanied by an improvement of neuropathic deficits. 3.) Oral treatment for 4-7 months tends to reduce neuropathic deficits and improves cardiac autonomic neuropathy. 4.) Preliminary data over 2 years indicate possible long-term improvement in motor and sensory nerve conduction in the lower limbs. 5.) Clinical and postmarketing surveillance studies have revealed a highly favourable safety profile of the drug.

CONCLUSIONS: Based on these findings, a pivotal long-term multicenter trial of oral treatment with thioctic acid (NATHAN I Study) is being conducted in North America and Europe aimed at slowing the progression of diabetic polyneuropathy using a clinically meaningful and reliable primary outcome measure that combines clinical and neurophysiological assessment.