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Acetyl-L-carnitine for symptomatic diabetic neuropathy

Dear Sir,

Diabetic neuropathy is a progressive disorder that causes functional and structural alterations of peripheral nerves. According to a recent survey in a hospital clinic population in the United Kingdom, the overall prevalence of diabetic peripheral neuropathy may be as high as 28.5% [1]. A beneficial effect of acetyl-L-carnitine (ALC) on nerve function has been demonstrated in animal models of diabetes [2, 3]; moreover, ALC levels are decreased in sciatic nerve from streptozotocin-diabetic rats [4]. ALC is an endogenous substance similar in structure to acetylcarnine and is involved in uptake and oxidation of long-chain fatty acids in mitochondria [5].

We evaluated the therapeutic effectiveness of ALC in 20 (14 female/6 male) diabetic subjects (age 58 ± 3 years, mean ± SD, diabetes duration 18 ± 6 years) with symptomatic peripheral diabetic neuropathy. Diabetic treatment was insulin for 13 patients and oral tablets for the other 7 diabetic subjects. All patients were troubled by symptoms of burning, shooting pain or tingling in the legs. After stopping any previous analgesic or anti-inflammatory drug, they entered a single-blind, randomized, placebo-controlled, cross-over study in which ALC (an intramuscular vial, 500 mg, twice a day), or placebo treatments lasted 15 days and were separated by a 2-week wash-out period. The patients who received ALC on the first occasion took the placebo later and vice versa. The severity of symptoms was assessed by a visual analogue scale graded from 0 to 10 (0 = no symptoms, 10 = very severe) (Table 1). A significant (p < 0.01) amelioration of symptoms occurred when patients took ALC as compared to placebo treatment. Vibration perception threshold (VPT), measured at the great toe and the external malleolus both at the dominant leg, was above the upper limit of normal adjusted for age and did not show any significant change after ALC or placebo.

There are several ways by which ALC may exert beneficial effects on nerve function in diabetic patients. ALC has been shown to acutely increase the plasma concentration of the endogenous opioid peptide beta-endorphin in healthy volunteers (analogic effect) [6]; ALC increases the number of nerve growth factor receptors on the brain and prevents substance P loss in the sciatic nerve and spinal cord of diabetic animals (neurotropic effect) [7]; ALC influences mitochondrial protein synthesis and transport and non-esterified fatty acid oxidation, thereby increasing the oxidative metabolism of neurons (metabolic effect) [5]; finally, ALC enhances the activity of antioxidant factors, such as reduced glutathione, and protects the cells against lipid peroxidation (free radical scavenging effect) [8]. Recent evidence suggests that oxidative injury may be the ultimate factor of aggression to the diabetic nerve [9]. Long-term controlled studies will tell us whether ALC has a role in the treatment of symptomatic diabetic neuropathy.

A. Quatraro, P. Roca, C. Donzella, R. Acampora, R. Marfella, D. Giugliano

References


Antihypertensives retarding progression of diabetic nephropathy

Dear Sir,

With interest I read the study of Elving et al. [1] comparing the effects of atenolol and captopril in retarding progression of diabetic nephropathy. The authors fail to distinguish between results which are identical and those which are not statistically significantly different. For example, baseline values for blood pressure in the captopril-treated group and the atenolol-treated group were described as “identical” despite a 5 mm Hg difference in mean arterial pressure (MAP). In a meta-analysis of observational blood pressure studies involving 420,000 patients, a 5 mm Hg

Table 1. The effect of acetyl-L-carnitine (ALC) in symptomatic peripheral diabetic neuropathy

<table>
<thead>
<tr>
<th>Pain scale</th>
<th>VPT (volts)</th>
<th>Great toe</th>
<th>External malleolus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>7.4 ± 1.1</td>
<td>19 ± 2.4</td>
<td>23 ± 3</td>
</tr>
<tr>
<td>Placebo</td>
<td>7.4 ± 1.3</td>
<td>19 ± 2.2</td>
<td>23.5 ± 2.8</td>
</tr>
<tr>
<td>ALC</td>
<td>3.6 ± 1.7*</td>
<td>18 ± 2.1</td>
<td>23 ± 1.9</td>
</tr>
</tbody>
</table>

VPT, Vibration perception threshold. Great toe and external malleolus both at the dominant leg. *p < 0.01 vs placebo

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Letters to the editor

Yours sincerely,
Dr. K.J.Hardy

References
2. MacMahon S, Peto R, Cutler J et al. (1990) Blood pressure, basis of these data is an overstatement.
3. Collins R, Peto R, MacMahon S et al. (1990) Blood pressure, the risk of a type II error in this study must be high. To con­
4. 100.8 ± 8.5 mm Hg in the captopril- and atenolol-treated pa­

Use of terminology related to fetal insulin secretion

Dear Sir,
I enjoyed reading Hughes’ paper [1] which reports some useful new information relating to insulin secretion by fetal as com­pared to neonatal rat pancreatic islets. My purpose in writing is to suggest a change in perception and terminology in this field. Fetal insulin secretion is variously described as “imma­ture”, “poor”, “abnormal”, “failed” (to release) and to have “impaired coupling”. Similar terms are used in relation to me­tabolism in fetal islets.

There is abundant evidence that insulin production and ac­tion in the fetus is of critical importance for normal fetal growth and development [2]. Thus, fetal insulin secretion must be judged to be entirely normal, mature, appropriate and properly coupled for the roles it fulfils in fetal physiology. My purpose in making what might otherwise be thought to be a rather pedantic point is to suggest that research on fetal insu­lin secretion is in danger of focusing on how “odd” it is rather than on the more interesting questions of how and why it is es­tablished with such a different regulation from that in the adult.

Yours faithfully,
C.N. Hales

References

Response from the authors

Dear Sir,
We thank Dr. Hardy for his comment. We did not perform a power calculation based on blood pressure differences. Our study was designed to examine a possible beneficial effect of ACE-inhibitors, compared to beta-blockers, on the progress­ion of diabetic nephropathy (measured as decline in glomeru­lar filtration rate) independent of blood pressure control. In that regard it was important to attain similar levels of blood pressure during the study in both treatment groups. We cer­tainly feel that we have succeeded in this respect. The mean ± SD of all blood pressure measurements during the 2­year follow-up (17 visits in each patient) was 100.9 ± 6.0 and

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