Acetyl-L-Carnitine

Clinical and neurochemical effects of acetyl-L-carnitine in Alzheimer's disease

In a double-blind, placebo study, acetyl-L-carnitine was administered to 7 probable Alzheimer's disease patients who were then compared by clinical and 31P magnetic resonance spectroscopic measures to 5 placebo-treated probable AD patients and 21 age-matched healthy controls over the course of 1 year. Compared to AD patients on placebo, acetyl-L-carnitine-treated patients showed significantly less deterioration in their Mini-Mental Status and Alzheimer's Disease Assessment Scale test scores. Furthermore, the decrease in phosphomonoester levels observed in both the acetyl-L-carnitine and placebo AD groups at entry was normalized in the acetyl-L-carnitine-treated but not in the placebo-treated patients. Similar normalization of high-energy phosphate levels was observed in the acetyl-L-carnitine-treated but not in the placebo-treated patients. This is the first direct in vivo demonstration of a beneficial effect of a drug on both clinical and CNS neurochemical parameters in AD. Pettegrew JW et al. *Neurobiol Aging* 1995 Jan-Feb;16(1):1-4.


In a double-blind, placebo-controlled, parallel-group, randomized clinical trial, we studied the efficacy of long-term (1-year) oral treatment with acetyl-L-carnitine in 130 patients with a clinical diagnosis of Alzheimer's disease. We employed 14 outcome measures to assess functional and cognitive impairment. After 1 year, both the treated and placebo groups worsened, but the treated group showed a slower rate of deterioration in 13 of the 14 outcome measures, reaching statistical significance for the Blessed Dementia Scale, logical intelligence, ideomotor and buccofacial apraxia, and selective attention. Adjusting for initial scores with analysis of covariance, the treated group showed better scores on all outcome measures, reaching statistical significance for the Blessed Dementia Scale, logical intelligence, verbal critical abilities, long-term verbal memory, and selective attention. The analysis for patients with good treatment compliance showed a greater drug benefit than for the overall sample. Reported adverse events were relatively mild, and there was no significant difference between the treated and placebo groups either in incidence or severity. Spagnoli A, Lucca U, Menasce G, Bandera L, Cizza G, Forloni G, Tettamanti M, Frattura L, Tiraboschi P, Comelli M, et al. *Neurology* 1991 Nov;41(11):1726-1732.

Acetyl-L-carnitine in the treatment of mildly demented elderly patients.

It has been hypothesized that acetyl-L-carnitine has a cholinomimetic action. It is for this reason that it has been used in the therapy of Alzheimer's type senile dementia impairment. In the present controlled double-blind study the authors followed two randomized homogeneous groups of both sexes of 30 patients each, aged over 65 years and suffering from mild mental impairment. One group of patients underwent therapy with acetyl-L-carnitine, 2 g/day for three months, while the other group was treated with a placebo. The statistical evaluation of the results was carried-out using non-parametric methods (Friedman-Nemenyi two-way ANOVA). It was possible to affirm that the acetyl-L-carnitine treated patients showed statistically significant improvement in the behavioural scales, in the memory tests, in the attention barrage test and in the Verbal Fluency test. These satisfactory results confirm the therapeutic importance of acetyl-L-carnitine in the treatment of elderly patients with mental impairment, which could be related principally to acetylcholine defects. Passeri M, Cucinotta D, Bonati PA, Iannuccelli M, Parnetti L, Senin U. *Int J Clin Pharmacol Res* 1990;10(1-2):75-79.

Evaluation of the effects of L-acetylcarnitine on senile patients suffering from depression

Twenty-eight patients aged between 70 and 80 years affected by depressive disturbance as defined by DSM III R (cat. 300.40) were subdivided at random into two homogeneous groups of 14 each. One group was treated with 500 mg three times a day of L-acetylcarnitine (LAC) in tablet form, while the other received placebo. Each patient was evaluated by the Hamilton Rating Scale for Depression, the Beck Depression Inventory, the Sandoz Clinical Assessment--Geriatric, and by clinical global impression. This investigation establishes that LAC is effective in counteracting symptoms of depression in the elderly. Relief of depressive symptomatology is expressed by decreased scores in the Hamilton Rating Scale for Depression and Beck Depression Inventory and by beneficial effects with regard to behavioural aspects. Garzya G. *Drugs Exp Clin Res* 1990;16(2):101-6.
L-acetylcarnitine treatment of mental decline in the elderly

A single-blind clinical trial was carried out on 481 subjects enrolled in 44 geriatric and neurologic units following a strict selection criteria: age, Mini Mental State Examination (MMSE) Global Deterioration Scale and Geriatric Depression Scale (GDS). After the initial screening and enrollment, the trial was run for 150 days in four phases: phase T0 (placebo treatment for 30 days), phases T1 and T2 (L-acetylcarnitine (LAC) 1500 mg/day for 90 days), phase T3 (further 30 days of placebo treatment). Drug efficacy was evaluated according to changes occurring from the beginning to the end of the tests which evaluate either whole and specific cognitive performances, or emotional-affective and relational behaviour. The outcome of phase T3 enabled the authors to estimate the possible favourable effects persisting after termination of L-acetylcarnitine therapy. The cognitive sphere evaluated by MMSE showed a significant increase in the total score at the end of LAC treatment (p < 0.0001). The Randt Memory Test also revealed that LAC treatment improved the items tested: the total score and the memory index increased significantly and the favourable effect persisted after LAC was discontinued. The emotional-affective area showed a significant improvement in the total score of the GDS after LAC therapy, and the positive results were confirmed by the Hamilton Rating Scale (p < 0.0001). The behavioura-relational aspects evaluated by the Family Stress Scale showed a significant decrease in the total score after treatment (p < 0.0004); the same trend was observed in the scores for instability and negative feeling. No significant adverse drug reaction occurred during the trial. In conclusion, the statistical analysis of the data from this single-blind, multicentre trial of mild mental impairment in the elderly showed a significant improvement of several performances during and after LAC treatment. Other reports indicate that this drug may be effective in the treatment of dementia. Salvioli G, Neri M. Drugs Exp Clin Res 1994;20(4):169-76.

Effect of acetyl-L-carnitine on geriatric patients suffering from dysthymic disorders.

Sixty senile subjects (60-80 years old) with dysthymic disturbances as defined by DSM III (Cat. 390.40) were randomized into two homogeneous groups, one of which was given acetyl-L-carnitine (3 g/day per os) while the other received a placebo. After a washout phase of one week, each patient was evaluated by scoring on the Hamilton Rating Scale for Depression and the Beck Depression Inventory, as well as the Sandoz Clinical Assessment-Geriatric. These tests were administered at the beginning of the trial, prior to drug administration, and repeated during the treatment phase after 30 and 60 days. The results showed that treatment with acetyl-L-carnitine induced a significant reduction, as compared to the placebo (p less than 0.002), in the severity of depressive symptoms and also a significant improvement (p less than 0.0027) in the items measuring the quality of life. Bella R; Biondi R; Raffaele R; Pennisi G. Int J Clin Pharmacol Res 10:355-360; 1990.

Neuropsychological changes in demented patients treated with acetyl-L-carnitine

The study was carried out on 24 patients suffering from mild to moderate dementia. The diagnosis of dementia was made according to DMS III criteria. Patients with cerebrovascular pathologies were excluded by using Hachinski Ischaemic Score less than or equal to 4 and computerized tomography parameters. Patients with depression (Hamilton Rating Scale for Depression greater than or equal to 18) were excluded. All the patients, after a wash-out period of two weeks were treated on a simple blind method with acetyl-L-carnitine (No. = 12 patients) and piracetam (12 patients) by intravenous route (two weeks) followed by an oral one for further 10 weeks. A battery of clinical neuropsychological tests was applied to evaluate the cognitive, attentive and behavioural aspects. The results, analysed by non-parametric variance analysis (Friedman Test) show a statistically significant improvement of the behavioural profile, of attention and of psychomotricity in the patients treated with acetyl-L-carnitine. No significant improvement was found in the piracetam group. Sinforiani E. Int J Clin Pharmacol Res 1990;10(1-2):69-74.

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