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EFFECTS OF LONG-TERM TREATMENT WITH L-CARNITINE ON THE LIPID PATTERN OF PATIENTS UNDERGOING HAEMODIALYSIS

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Summary

The effect of long-term treatment (28 months) with L-carnitine has been evaluated in 15 of 29 haemodialysis patients already treated in a previous short-term cross-over placebo study.

In all patients (9 of whom did not show improvement in the previous trial) we noted a significant reduction in triglyceride values during the entire observation period with a significant and concomitant increase in HDL-cholesterol. Therefore long-term L-carnitine administration may be useful in the treatment of lipid metabolism disorders in dialysis patients, perhaps adapting the dose and method of administration to individual patient requirement.

Introduction

L-carnitine is a natural substance physiologically present in tissue and biological fluids of many animal species [1]. The presence of adequate carnitine concentrations in the intracellular compartment is essential for normal fatty acids metabolism since L-carnitine is the specific carrier of long-chain fatty acids [2] from the cytoplasm to the mitochondrial matrix where they are oxidized.

During haemodialysis serum L-carnitine falls by approximately 80 per cent and intermittent haemodialysis provokes a dramatic reduction in the muscle pool of the metabolite. Clinical trials of L-carnitine have demonstrated the possibility of considerably increasing serum and muscle concentrations of this metabolite concomitantly with a reduction in the incidence of muscle symptoms (asthenia, cramps) [3,4].

It has been reported that L-carnitine treatment is able to improve hypertriglyceridaemia in haemodialysis patients and to increase HDL-cholesterol values. However, L-carnitine does not have the same effect in all patients, several authors having observed responder and non-responder hypertriglyceridaemic

patients [5,6]. In a previous study we observed that four months of L-carnitine treatment reduces hypertriglyceridaemia in haemodialysis patients with low HDL-cholesterol values (<40mg/100ml) while in patients with high HDL-cholesterol (>40mg/100ml) no effect was seen [6].

This study evaluates the efficacy of long-term L-carnitine treatment (28 months) in some haemodialysis patients with hypertriglyceridaemia already treated in the previous study.

Material and methods

Fifteen hypertriglyceridaemic patients (6 females and 9 males) aged 47±12 years, on thrice-weekly four hour haemodialysis for 56±21 months for chronic uraemia were selected. Nine of these 15 patients were considered as 'non-responder' and six as 'responders' in our previous study [6].

Dialysis was performed with Travenol plate dialysers and a dialysate containing acetate (40mEq/L) and sodium (140mEq/L). The patients had a diet comprising 2400±300 total Cal/day with 1.2g/kg/day of protein and 80~90g/day of lipids.

The patients were treated with L-carnitine (1g ampoules, Sigma-Tay SpA, Pomezia, Rome, Italy), 2g/i.v. at the end of each dialysis for a period of 28 months. Lipid parameters were measured after an overnight fast (before heparin), by the following methods: total triglycerides were determined by a Testomar triglycerides mono kit (Behring Institute), but subtracting free-glycerol from total glycerol using the method described by Eggstein and Kuhlmann [7]. A Monotest cholesterol kit (Boehringer Mannheim Diagnostica) was used for determining total cholesterol. HDL-cholesterol was assayed using a Test Combination Cholesterol kit (Boehringer Mannheim Diagnostica).

In the present study paired Student's 't' test was used for evaluating the differences found between the last basal (Bas. III) value and the successive controls.

Results

The results of the present study are graphically reported in Figures 1, 2 and 3. On the left side of each graph is summarized the data from our previous study.

During the 28 months of follow-up only slight changes in total cholesterol were observed, even if some variations were statistically significant.

The HDL-cholesterol determinations confirmed our previous study [6]: in the six patients previously classified as 'responders' the HDL-cholesterol increased from 32.17±3.54mg/100ml to values ranging from 39.83±5.49 to 48.17±8.75mg/100ml, and the nine 'non-responder' patients retained values greater than 40mg/100ml during follow-up.

Triglycerides in the six 'responders' at the beginning of the study (Bas. III) were 409±49mg/100ml and during the following 28 months, always showed values significantly lower although they had considerable fluctuation. These patients reached the values of the prior study (about 150mg/100ml) only at the sixteenth month of L-carnitine treatment, while in the other controls the values ranged between 205±28 and 300±68mg/100ml.

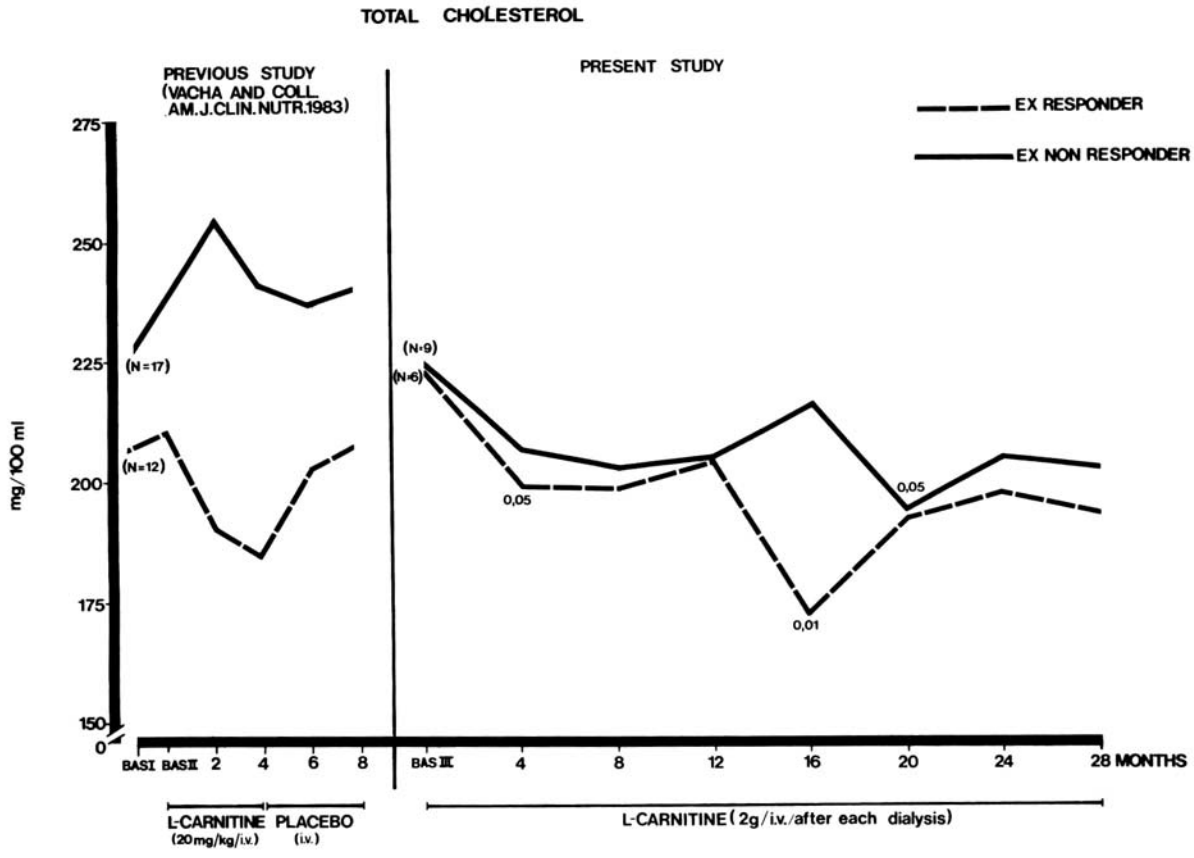

Figure 1. Total cholesterol during the previous study [6] and during the 28 months of the present study

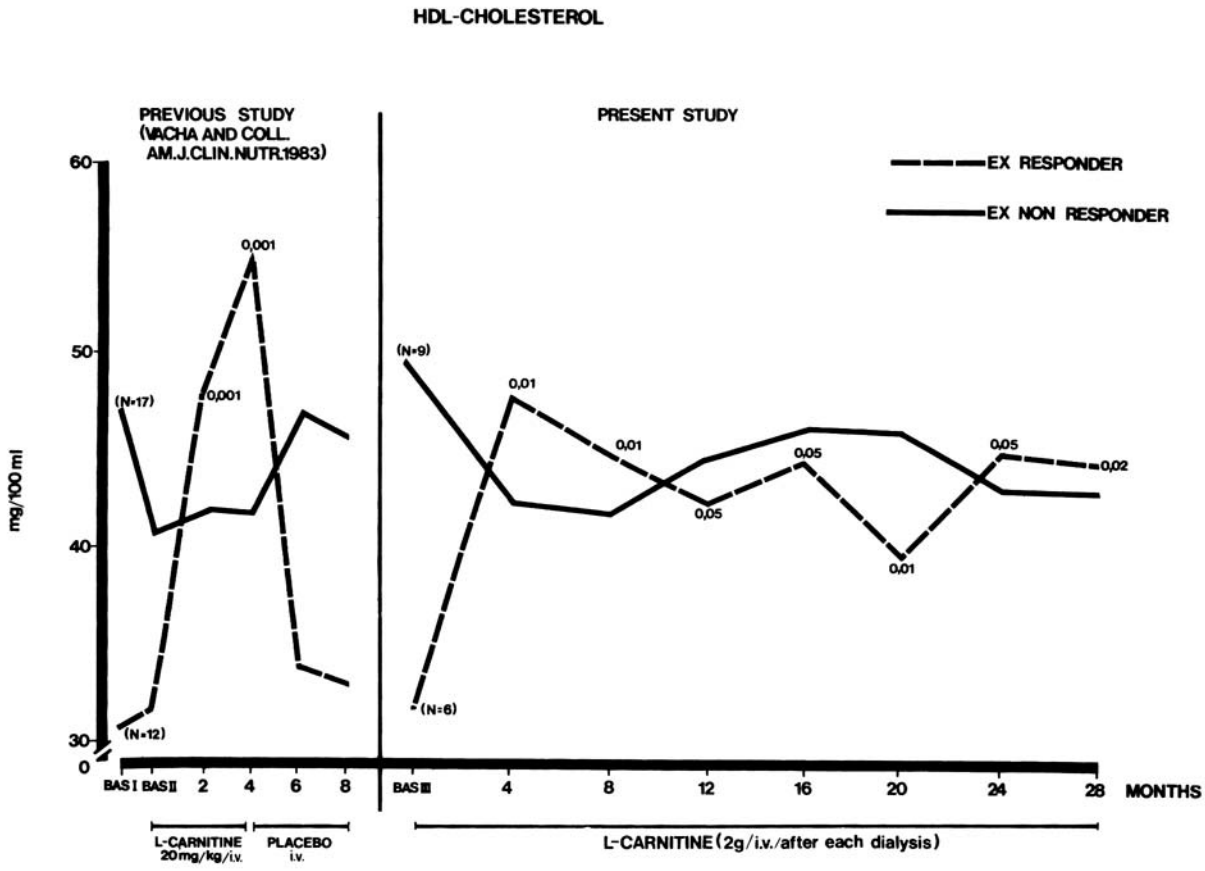

Figure 2. HDL-cholesterol during the previous study [6] and during the 28 months of the present study

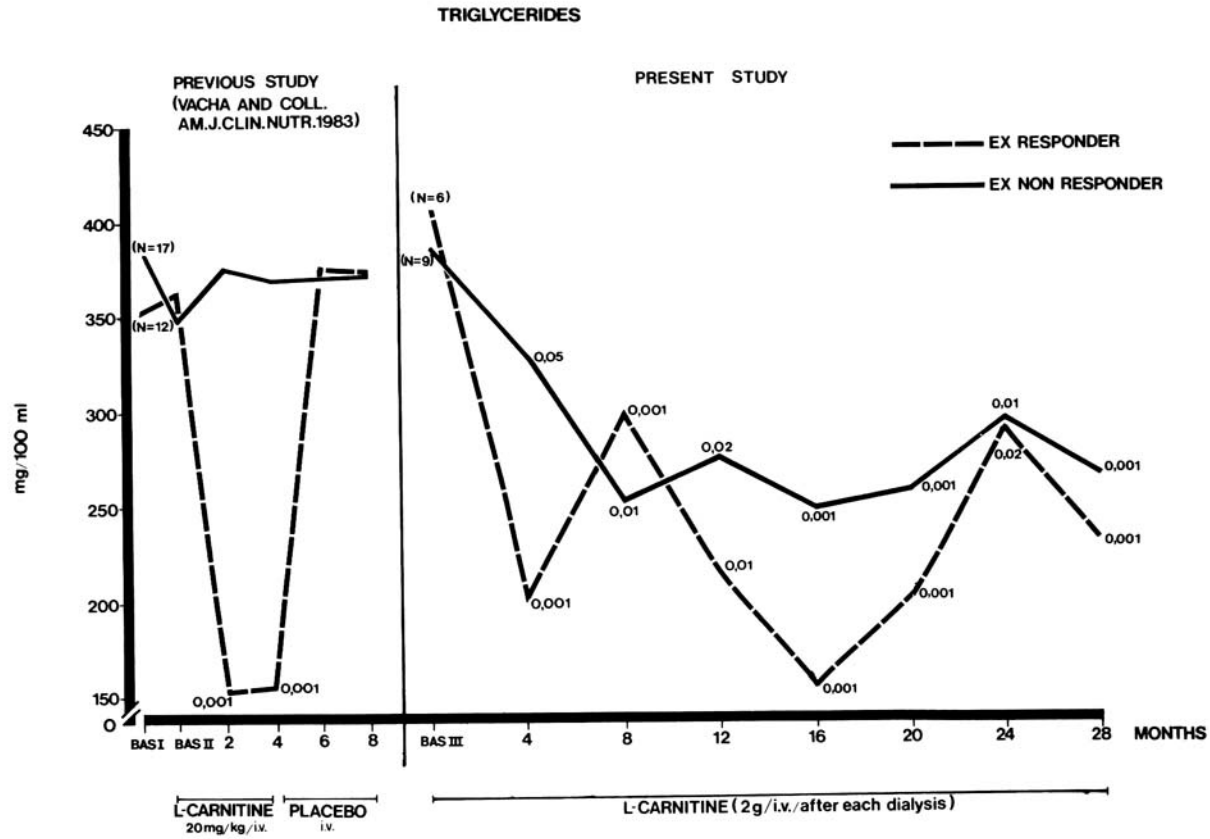

Figure 3. Triglycerides during the previous study [6] and during the 28 months of the present study

The results regarding the nine 'non-responders' have been more surprising. Unexpectedly, during the 28 months of L-carnitine treatment, the triglycerides remained significantly lower in respect to baseline (Bas. III), but without reaching normal values (<170mg/100ml).

Discussion

This study confirms that, in our patients, long-term L-carnitine treatment is able to improve the changes in lipid metabolism in dialysis patients. However, we wish to stress some relevant factors that could limit the statistical inference of these results, i.e. dietary habits, ethnic differences and the actual degree of tissue carnitine deficiency. In the literature [5,6,8,9], contradictory results on the efficacy of carnitine therapy in improving lipid metabolism disturbances in dialysis patients have been reported. It would be too simplistic to explain such differing results with the 'intrinsic quality' of each single study, the variables are undoubtedly numerous and complex.

In a recent study [10] we observed that in five haemodialysis patients treated for 18 months with L-carnitine (2g/i.v./after each dialysis) the muscle acylcarnitine concentration was eight times higher than in the controls. As such tissue accumulation could explain some cases of paradoxical hypertriglyceridaemia, we suggested reducing the quantity of L-carnitine administered in long-term treatment. On the basis of this latter consideration, the interpretation of the results of the present study is not easy. It is interesting to observe that 28 months of L-carnitine treatment (2g/i.v./after each dialysis) produced a significant triglyceride reduction in patients previously considered as 'non-responders' (HDL-cholesterol >40mg/100ml). Consequently we believe that it is important to further examine the role of L-carnitine in haemodialysis, both from a pathophysiological and therapeutic aspect.

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