

Letters and Replies

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Effect of L-carnitine administration on erythropoietin use in thalassemic minor haemodialysis patients

Sir,

We read with great interest the recent letter by Arduini et al. [1], on the effect of L-carnitine (LC) on erythrocyte survival in haemodialysis patients. In the same issue, there is a paper by Hothi et al. [2] showing that plasma free-carnitine (FC) levels fell from 26.54 ± 2.99 to 15.6 ± 2.34 μmol/l (P < 0.001) in nocturnal haemodialysis (NHD). A similar reduction in plasma acyl-carnitine (AC) levels was observed (from 13.22 ± 1.34 to 6.24 ± 1.20 μmol/l (P < 0.001)). The AC : FC ratio improved from 0.51 ± 0.03 to 0.39 ± 0.03 (P < 0.005) (normal < 0.25). They conclude that NHD is associated with an improvement in AC : FC ratio.

Anaemia is a common finding in patients on chronic haemodialysis (HD), and represents one of the leading causes of increased cardiovascular morbidity and mortality in these patients. While the main defect responsible for anaemia in chronic renal failure patients is inadequate production of erythropoietin, there is evidence that other factors may also be involved. Several studies have shown that LC supplementation may have a beneficial effect on renal anaemia [3].

Arduini et al. [1] report the first randomized controlled trial of the effects of LC on erythrocyte survival in HD patients. Red blood cells (RBC) survival was evaluated by the 51Cr labelling procedure, a gold standard methodology in RBC survival studies [4]. There was a strong trend towards improved RBC survival in the treated group (P = 0.058), and this mechanism might explain in part the reported benefit of LC supplements on anaemia control in HD patients [1].

Several authors suggest various fundamental mechanisms of carnitine deficiency that may contribute to anaemia in patients with chronic uraemia [5–8].

The biophysical properties of the erythrocyte membrane and its cytoskeletal network are fundamental for RBC survival in the blood stream [5]. Indeed, RBCs must survive a variety of chemical and physical insults during their life span, and the loss of their elastic properties may severely compromise tissue oxygenation. Erythrocyte deformability has been found to be impaired in uraemia [5] and to correlate with shortened RBC survival time [9–11]. LC treatment of HD patients seems to alleviate their anaemic condition. Recently, Duranay et al. [12] showed that there was a significant benefit of L-carnitine on C-reactive protein (CRP), transferrin, total protein and albumin levels of haemodialysis patients.

LC treatment of HD patients seems to alleviate their anaemic condition. A recent meta-analysis of the randomized LC trials performed before and after the advent of erythropoietin therapy shows a beneficial effect of LC supplements on anaemia control in maintenance HD patients [1]. This conclusion is consistent with the concept that LC may favourably affect the impaired rheological and metabolic properties of erythrocytes in HD patients.

Both thalassemia and carnitine deficiency represent causes of either anaemia or erythropoietin (EPO) resistance in uraemia, even though the effect of the combined presence of these conditions has never been evaluated [13,14].

We would like to present our prospective study, which involved 12 β-thalassemia minor (β-thal-m) dialysis patients (eight males and four females) previously treated for a 1-year period by administering progressively higher EPO doses in order to reach haemoglobin (Hb) target levels (11–12 g/dl); subsequently, adequate control of anaemia was maintained for a further additional year [14].

We performed a 6 month run-in period in order to verify the stability of Hb levels (coefficient of variation <3%). L-carnitine was then administered at the end of each of the three HD session of the week, at a dose of 2 g/haemodialysis for a 1 year period-time in controls and in β-thal-m dialysis patients. At the end of carntine administration, 6 month follow-up was performed. Patients and controls were comparable at the start of study. In controls and β-thal-m subjects serum iron levels were 78 ± 30 and 89 ± 28 mg/l (P = NS), transferrine saturation 30 ± 4 and 29 ± 5% (NS), ferritine 245 ± 56 and 256 ± 60 mcg/l (P = NS), respectively. PTHs levels were 205 ± 78 in controls and 187 ± 98 pg/ml in β-thal-m (P = NS). serum albumin measured 45 ± 12 and 38 ± 16 mcg/ml, respectively in control and β-thal-m groups (P = NS). Also, groups were similar for age, dialysis age and renal disease (Table 1). Patients did not differ in body weight (60.2 ± 9.9 vs 57.9 ± 14.2 kg), serum albumin levels (3.96 ± 0.08 vs 3.95 ± 0.07 g/dl) and nutrient intake as indicated by protein nitrogen appearance (1.21 ± 0.04 vs 1.19 ± 0.06 g/kg/day). During the study BW, dialysis UF rate, and intradialytic Hb change were stable in the two groups. Controls showed both significant Hb increase and EPO decrease from the third month. β-thal-m patients also demonstrated these changes, but they were registered only after 8 months of carnitine administration. In Thal-m the EPO dose at time zero is 280 UI/kg/dialysis (in controls is 100 UI), and at the peak of the response (at the 12th month) the EPO dose is 170 UI/kg/dialysis (in controls is 60 UI, from third to sixth month); of note, the EPO dose decreases by 39%. Hb levels were unchanged (Figure 1). The study first demonstrates the lowering of EPO need in β-thal-m by a mean of 33% after 1 year carnitine administration, as compared with a 40% reduction that occurred in controls also after 3–6 months. Such a reduction of EPO need was also associated with haemoglobin target.

In summary, carnitine has been shown to be effective in many patients for the adjunctive treatment of anaemia associated with kidney disease [15,16]. Our data suggest that a very long-term carnitine administration would be necessary for uraemic patients on chronic dialysis affected by β-thalassemia with unresponsive anaemia, or requiring large doses of erythropoietin.

Conflict of interest statement. None declared.

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8. Arduini A, Rossi M, Mancinelli G et al. Effect of \(l\)-carnitine and acety-


