QUANTITATIVE ASSESSMENT OF CARNITINE LOSS DURING HAEMODIALYSIS AND HAEMOFILTRATION

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Summary

Carnitine concentrations were measured in plasma, haemofiltrate, dialysate and urine of patients on regular dialysis treatment and in normal controls. Patients on haemofiltration and on haemodialysis exhibited moderately decreased plasma values, whereas in eight patients on CAPD mean values did not differ from controls. Carnitine loss into the haemofiltrate was significantly lower than urinary carnitine excretion in normal subjects. Major disturbances of intestinal carnitine absorption in patients on regular dialysis treatment were not observed. It is concluded that patients on regular dialysis are in a state of moderate carnitine deficiency and that therapeutically induced carnitine losses or grossly impaired intestinal absorption are not major factors in the development of carnitine deficiency in these patients.

Introduction

Carnitine plays an important role in lipid catabolism. It is necessary to transport long chain fatty acids across the inner mitochondrial membrane. Carnitine deficiency has been claimed to be responsible for the myopathy and cardiomyopathy observed in dialysis patients and low carnitine values have been reported in plasma [1, 2] and muscle tissue [3] of dialysis patients. Loss of carnitine during dialysis treatment is regarded as a major cause of carnitine deficiency.

The present investigation quantitatively assesses carnitine loss during dialysis and haemofiltration and compares it to urinary carnitine excretion in healthy subjects. Furthermore we studied intestinal carnitine absorption in patients on regular dialysis and in normal controls.

Material and methods

Carnitine concentrations in plasma, dialysate, haemofiltrate and urine were measured by a radioenzymatic assay according to McGarry and Foster [4].

Plasma carnitine was determined in 43 healthy subjects, 39 patients on chronic haemodialysis or haemofiltration and in eight patients on CAPD. In nine patients on chronic haemofiltration and in eight patients on CAPD carnitine concentrations were determined in the haemofiltrate and the dialysate, respectively. Urinary carnitine excretion was determined in 27 subjects with normal renal function.

In four normal volunteers and in four patients on regular dialysis intestinal absorption of L-carnitine was determined by following carnitine plasma concentrations for 24 hours after the ingestion of 3gm of L-carnitine (Sigma-Tau, Rome, Italy).

Values are given as means ± SE. Urinary carnitine excretion and carnitine loss by dialysis were calculated per week. Student's t-test was used for statistical analysis.

Results

Plasma carnitine concentrations in the group of patients on chronic haemodialysis or haemofiltration were significantly lower than in normal controls (39.9 ± 2.7 μmol/L versus 49.0 ± 2.0μmol/L; $p < 0.001$). Haemodialysis and haemofiltration treatment led to a further significant decrease (33.1 ± 3.5μmol/L; $p < 0.001$). Plasma concentrations in eight patients on CAPD (40.0 ± 16.2μmol/L) were not significantly different from control values ($p < 0.1$).

Urinary carnitine excretion in 27 patients with normal renal function amounted to 1534 ± 133μmol/week. This was significantly more ($p < 0.001$) than the loss of carnitine into the haemofiltrate of nine patients which amounted to 795 ± 84μmol/week. Carnitine loss into the dialysate in eight patients on CAPD (1905 ± 711μmol/week) was not significantly different from urinary carnitine losses in subjects with normal renal function ($p < 0.2$).

Figure 1 shows plasma carnitine concentrations after oral ingestion of 3gm of L-carnitine. The mean increases in plasma carnitine are comparable in patients on regular dialysis treatment and in healthy controls, although carnitine absorption seems to be somewhat delayed in dialysis patients. During the late period of this study, however, dialysis patients exhibit even higher plasma carnitine concentrations than normal subjects. This is probably a consequence of the lack of urinary excretion in these patients.

Discussion

Our results show decreased values of free carnitine in patients on chronic haemodialysis and haemofiltration, confirming previous studies [1, 2]. Thus, a moderate degree of carnitine deficiency may exist in these patients. Böhmer [3] suggested that therapeutically induced carnitine losses by dialysis treatment were responsible for this deficiency. Our results, however, demonstrate that the amount of carnitine loss into the haemofiltrate is low compared with urinary carnitine losses in healthy subjects. In our opinion this excludes dialysis induced losses as a major factor in carnitine deficiency of patients on regular dialysis treatment. Interestingly, plasma carnitine concentrations in CAPD patients were not significantly decreased, although carnitine loss into the dialysate was substantial. This group of patients,

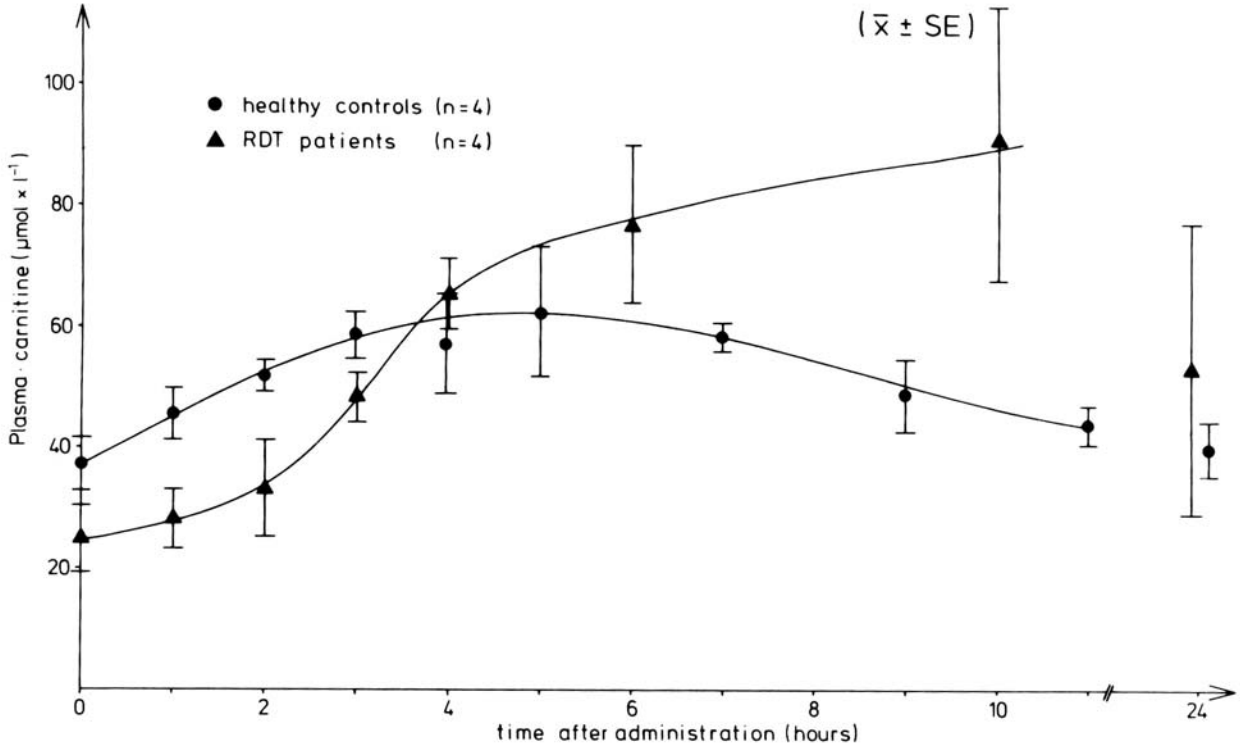

Figure 1. Plasma carnitine concentrations in patients on regular dialysis treatment and in healthy controls after oral administration of 3gm (18.5mmol) of L-carnitine

however, was on dialysis treatment for a rather short period as compared with the patients on haemodialysis or haemofiltration, and carnitine deficiency may not have had time to develop.

Since therapeutically induced carnitine losses seem to play a minor role in dialysis patients, other factors may be involved. As demonstrated in Figure 1 major disturbances in the intestinal absorption of L-carnitine do not seem to be present. However, inadequate nutrition, which is frequently seen in dialysis patients, may also contribute to carnitine deficiency.

Since endogenous carnitine synthesis is the most important factor in carnitine supply, the most plausible explanation for a carnitine deficiency in dialysis patients seems to be impaired endogenous carnitine synthesis during prolonged uraemia. This is also suggested by studies of Carter and Frenkel [5] who demonstrated that butyrobetaine, a precursor of carnitine, is predominantly synthesised by the kidneys. Thus, destruction of structural and metabolic integrity of the kidney in chronic renal failure may lead to decreased endogenous carnitine synthesis and ultimately to carnitine deficiency.

To summarise, our results show a moderate degree of carnitine deficiency in patients on regular dialysis treatment and a normal intestinal absorption of L-carnitine. From our results it is also apparent that dialysis losses of carnitine are not a major factor in the development of carnitine deficiency in these patients.

References

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