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Effects of carnitine administration to multiple injury patients receiving total parenteral nutrition

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Abstract. Blood, urine and tissue concentrations of carnitine have been found to be below the normal values in patients receiving total parenteral nutrition (TPN). It might be postulated that the carnitine deficiency is responsible for the metabolic disturbances observed during TPN. To 20 patients (10 male and 10 female) in a state of coma following multiple injuries or brain injury and submitted to a TPN regimen (hypertonic polycarbohydrate, 7% aminoacid solutions on 10% lipid suspensions), we have administered 3–8 g/day of carnitine i.v. as a single bolus each morning. We have found no increase in cholesterol and triglycerides serum levels and a normalization of pyruvate and lactate serum levels. Our results seem to confirm the importance of carnitine in improving metabolism of the energy-giving substrate in patients receiving TPN.

Key words: carnitine – lipid metabolism – carbohydrate metabolism – total parenteral nutrition

Introduction

In multiple injury patients, it is necessary to correct the negative nitrogen balance resulting from the rapid, intense increase in catabolism which is the body's metabolic reaction to stress [Kinney et al. 1970]. Total parenteral nutrition is an excellent therapeutic measure to achieve this. It is, on the other hand, a known fact that parenteral administration of carbohydrate solutions, amino acids, electrolytes, multiple vitamin compounds and lipid emulsions can interfere with the body's normal metabolic processes and even with the activity of some of the endocrine glands [Pietropaoli et al. 1984].

It may be surmised that at least some of the clinical and metabolic changes observed during total parenteral nutrition are induced by a lack of carnitine.

In this respect, hepato-steatosis with altered cholestasis indices and reactive hypoglycemia, observed during TPN or after its discontinuation, are typical symptoms of carnitine deficiency [Dudrick et al. 1972, Engel 1980, Sheldon et al. 1978]. The hypothesis is further borne out by the fact that blood, urine and tissue concentrations of carnitine have been found to be below the norm in patients receiving TPN [Hann et al. 1982, Penn et al. 1981, Tanpharchitr and Lerdvuthisonpon 1981].

It is probable that, without supplementing such nutrition, endogenous production will not be sufficient to meet the body's demand for carnitine during TPN [Worthley et al. 1984].

The main metabolic role of carnitine is to allow the passage of long-chain fatty acids from the cytosol across the mitochondrion in order for beta-oxidation to take place [Fritz 1959]. It has also been postulated that carnitine improves the peripheral utilization of glucose [Long et al. 1971] and contributes indirectly

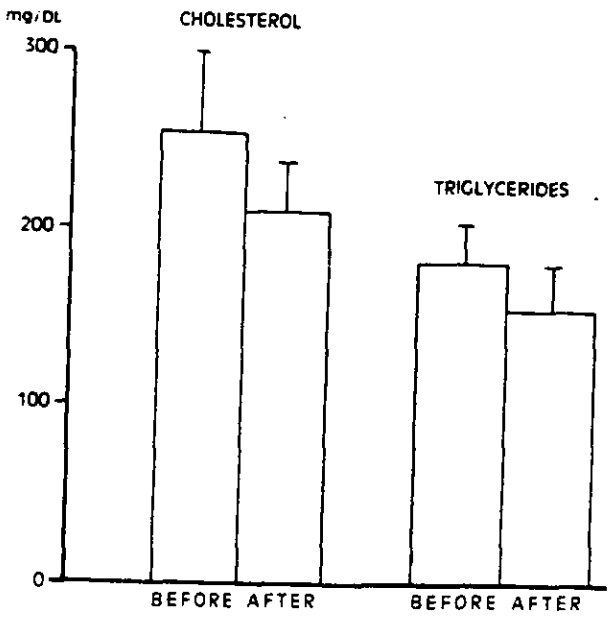

Fig. 1 Trend for blood cholesterol and triglyceride levels before and after carnitine supplementation of TPN.

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Table 1 Clinical data

Patients (20)	Age (years)	Sex	Diagnosis
S. S.	16	M	Head injury. Diencephalic coma
T. R.	20	F	Multiple injuries
B. G.	49	M	Multiple injuries
F. G. E.	18	M	Head injury. Cortical and subcortical coma
C. R.	67	M	Head injury. Cortical and subcortical coma
S. M.	16	M	Head injury. Diencephalic coma
A. N.	74	M	Multiple injury
G. G.	17	F	Multiple injury
F. A.	24	F	Multiple injury
M. M.	24	F	Multiple injury
C. L.	73	F	Multiple injury. Mesencephalic coma
B. E.	62	M	Multiple injury
P. G.	68	M	Head injury. Meso-diencephalic junction coma
B. F.	16	F	Head injury. Diencephalic coma
L. T.	47	M	Multiple injuries
C. R.	65	F	Multiple injuries
P. C.	61	F	Multiple injuries
T. S.	69	M	Multiple injuries
G. D.	86	F	Head injury. Cortical and subcortical coma
S. A. R.	15	F	Head injury. Mesencephalic coma

to the process of glycolysis, thereby increasing pyruvate dehydrogenase activity [Hansford 1976].

The use of carnitine during TPN thus seems necessary in order to supplement both blood and tissue concentrations of the compound and to make possible better utilization of the substances administered by TPN.

This study was conducted with the purpose of evaluating the trend of certain parameters taken as an index of lipid and intermediary metabolism in multiple injury patients receiving TPN.

Materials and methods

The study population comprised 20 patients (10 male and 10 female) with an average age of 47.5 years (range 15–86 years).

All patients had been admitted to the Intensive Care Unit in a state of coma following multiple injuries (11 cases) or brain injury (9 cases). Details of patient's age and sex, together with the diagnosis and subsequent course of the illness for each case, are presented in Table 1.

All patients were subjected to mechanical respiration by means of naso-tracheal intubation or tracheoctomy, anti-edema therapy with glycerol and dexamethasone, antibiotic and gastroprotective treatment.

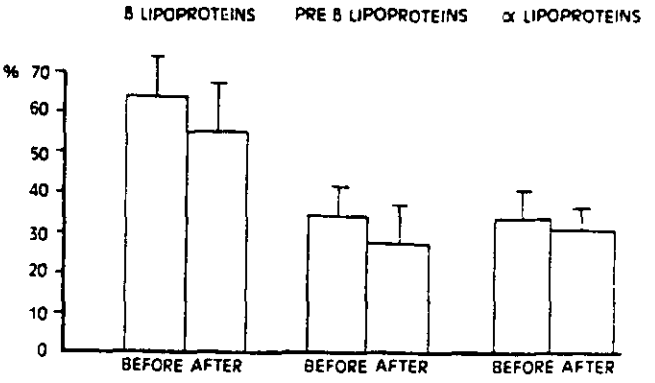

Fig. 2 Trend for lipoprotein levels before and after carnitine supplementation of TPN.

From the 2nd day the TPN regime was started with hypertonic polycarbohydrate solutions, 7% amino acid solutions and 10% lipid suspensions (for about 40% of the total calory count). Starting from the 7th day, carnitine was administered on a daily dosage basis varying from 3 to 8 g daily, injected intravenously as a single bolus each morning.

At the beginning and end of the treatment, blood samples were taken in order to evaluate the plasma levels of lipids (cholesterol, triglycerides and lipoproteins), pyruvic acid and lactic parameters were also evaluated throughout the TPN treatment.

Results

Figure 1 shows the trend for blood cholesterol and triglyceride values before and at the end of carnitine supplementation of TPN. Both parameters showed a decrease, cholesterol from 252 ± 49 mg/dl to 219 ± 46.6 mg/dl and triglycerides from 181.7 ± 19.2 mg/dl to 156 ± 23.3 mg/dl. Lipoproteins also showed a tendency to decrease, particularly beta- and pre-beta lipoproteins (Figure 2).

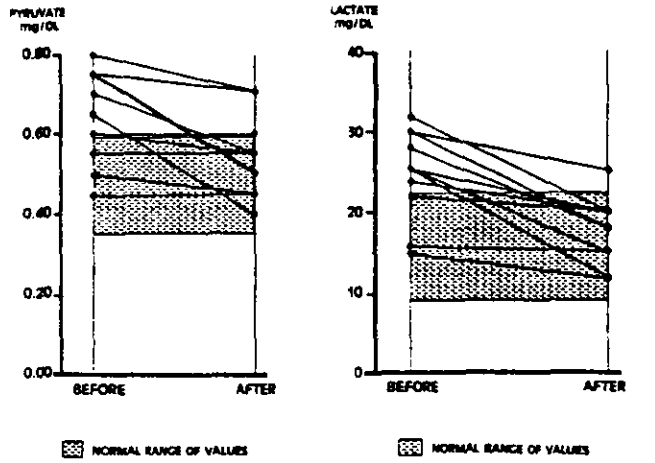

Fig. 3 Trend for blood levels of pyruvic acid and of lactate before and after carnitine supplementation of TPN in 11 patients.

Pyruvate levels were high in 8 out of 11 patients in whom they were determined (Figure 3). On completion of carnitine-supplemented TPN, this parameter returned within the normal range of values in 5 cases. A similar trend was observed for lactate (Figure 3), which, from initially high values in 8 out of 11 patients, was normalized at the end of the treatment in all but one.

Discussion

Total parenteral nutrition is a vital form of therapy in various forms of diseases. Its use requires, however, that various blood chemistry parameters be carefully observed in order to forestall possible alterations to the metabolism.

It has, in fact, been proved that TPN without lipid supplementation induces a progressive depression of blood cholesterol levels [Zanello et al. 1982], while the addition of lipid emulsions such as long-chain fatty acids (Intralipid®) induces an increase, albeit temporary, of blood lipid levels [Pola et al. 1983]. It may be surmised that this effect is heightened by the relative lack of carnitine in patients receiving TPN [Hann et al. 1982, Penn et al. 1981, Tanpharchitr and Lerdvuthisonpon 1981].

The results of this study show that blood cholesterol levels during carnitine-supplementated TPN show no increase, tending, if anything, to drop.

These findings are in agreement with those of other authors [Montanini et al. 1983, Sheldon et al. 1978] and seem to justify carnitine supplementation of TPN, particularly in dyslipidemic patients. Triglyceride, beta- and pre beta-lipoprotein blood levels also tend to decrease, bearing out the findings of other authors [Pola et al. 1983] and confirming that carnitine supplementation during TPN is conducive to full metabolic utilization of the lipids administered.

The trend for pyruvate and lactate levels is also worthy of comment, both parameters tending, from an initially high level in most patients, to normalize during the course of treatment. This normalization is an indication of good utilization of the energy-giving substrate, probably indicating that carnitine exerts a direct or indirect effect on pyruvate kinase and determines a higher rate of glucose utilization and a lower pyruvate level.

Our results thus tend to confirm the favourable effects of carnitine on carbohydrate metabolism, as observed by other authors in studies conducted on patients receiving continuous 5% of glucose infusion [Dudrick et al. 1972, Kinney et al. 1970, Peatson 1974, Pietropaoli et al. 1984].

It may be remarked in conclusion that our results, despite the limited number of patients studied and the varied nature and extent of injuries suffered, seem to confirm the importance of carnitine in improving metabolism of the energy-giving substrate in patients receiving TPN.

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