Nephron 1992;62:368–369

E. Bérard[a]
A. Iordache[b]

[a] Pediatric Dialysis Unit,
Department of Pediatrics,
Hôpital de Cimiez,
Nice University Hospital, and
[b] Department of Biochemistry,
Hôpital Pasteur,
Nice University Hospital, Nice, France

Effect of Low Doses of *L*-Carnitine on the Response to Recombinant Human Erythropoietin in Hemodialyzed Children: About Two Cases

Dear Sir,

We read with great interest the article of Kooistra et al. [1] in a recent issue of your review. These authors noted that adult hemodialyzed patients who are resistant to recombinant human erythropoietin (rhEPO) have low carnitine levels. Since the studies of Trovato et al. in 1982 [2], different authors have shown the effect of high doses of *L*-carnitine (20–40 mg/kg/day) on anemia in dialyzed patients [3–6]. The existence of myocarditis bound to low levels of carnitine in dialyzed people and the possibility of its decline after treatment have been widely discussed [7].

In 1990, we observed 2 children, 13 and 15 years old, hemodialyzed for 2.5 and 3 years, who, in spite of treatment by rhEPO over 12 months at doses as high as 240–360 U/kg/week, had hematocrit between 20 and 23% (with normal levels of iron, vitamin B_{12} and folic acid, and no hyperparathyroidism). In addition, these patients suffered from bad cardiac contractility at ultrasonic examinations and severe tiredness. Their carnitine levels (measured by a spectrophotometric method [8]) were low (table 1). Following the recommandation of Wanner and Hörl [7] and

Table 1. Evolution of carnitine levels, hemoglobin and hematocrits after treatment with L-carnitine in our patients

A. Patient 1					
Time, months	0	3	6	9	12
Treatment, mg/kg/session	0	1.5	3	2	3
Free carnitine, μmol/l n=51±3	20	30.5	41	41	60
Total carnitine, μmol/l n=58±3	34.6	57.7	71	67.5	97.5
Hematocrit, %	22.3	26.8	28.1	24.3	29.3
Hemoglobin, mmol/l	4.5	5.4	5.8	5.2	5.8
B. Patient 2					
Time, months	0	3	6	9	
Treatment, mg/kg/session	0	1.5	2	2	
Free carnitine, μmol n=51±3	23	32.3	48	39.9	
Total carnitine, μmol n=58±3	38	46	70	63.5	
Hematocrit, %	20.9	23.8	28.4	28.6	
Hemoglobin, mmol/l	4.4	4.6	5.9	5.8	

E. Bérard, MD
Department of Pediatrics
Hôpital de Cimiez, 4, avenue Reine Victoria, BP179
F-06003 Nice Cedex (France)

0028–2766/92/
0623–0368$2.75/0

Wanner et al. [9], we started treatment with low doses of *L*-carnitine (1–3 mg/kg intravenously at the end of dialysis sessions) without any modifications of rhEPO doses. During the following weeks, hematocrit reached 27–31%, carnitine levels being normal or high, and this effect remained after 6 and 9 months. Fearing a therapeutic overdose in patient 1, we decreased the doses of treatment to 2 mg/kg/session. The hematocrit decreased and later increased again after resumption of 3 mg/kg/session. We observed no cardiac modification on ultrasonic examinations, but the doses we used were lower than those used in studies describing this effect. Under treatment, our patients describe improvement of tiredness, although it is impossible to know if this is linked to an effect on hematocrit, to possible myocardiac effects or other muscular effects.

Our observations on only 2 cases need to be confirmed by a study involving a wider population, but several questions remain unanswered concerning dose and duration of treatment and the validity of carnitine levels as a means of therapeutic follow-up. It may also be asked whether, as has been described for other effects of carnitine in dialyzed patients, there are good and bad responders and we could have a descreasing therapeutic effect after a few months of treatment. Finally, considering that carnitine levels are only imperfectly representative of tissular storage, we could wonder whether, in subjects with normal carnitine levels, treatment with *L*-carnitine would permit a reduction in rhEPO doses.

References

1 Kooistra MP, Struyvenberg A, van ES A: The response to recombinant erythropoietin in patients with the anemia of end-stage renal disease is correlated with serum carnitine levels. Nephron 1991;57:127–128.

2 Trovato GM, Ginardi V, Di Marco V, Dell Aira AE, Corsi M: Long term *L*-carnitine treatment of chronic anaemia of patients with end stage renal failure. Curr Ther Res 1982;31-6:1042–1049.

3 Bellinghieri G, Savica V, Mallamace A, Di Stefano C, Consolo F, Spagnoli LG, Villaschi S, Palmieri G, Corsi M, Macari F: Correlation between increased serum and tissue *L*-carnitine levels and improved muscle symptoms in hemodialyzed patients. Am J Clin Nutr 1983;38:523–531.

4 Vacha GM, Giorcelli G, Siliprandi N, Corsi M: Favorable effects of *L*-carnitine treatment on hypertriglyceridemia in hemodialysis patients: Decisive role of low levels of high density lipoprotein-cholesterol Am J Clin Nutr 1983;38:532–540.

5 Ahmad S, Golper TA, Hirschberg R, Kopple JD, Katz LA, Kurtin P, Ashbrook DW, Wolfson M: Efficacy of *L*-carnitine in hemodialysis: A multicenter controlled clinical trial (abstract). Kidney Int 1987;31:226.

6 Albertazzi A, Capelli P, Di Paolo B, Pola P, Tondi P, Vaccario O: Endocrine metabolic effects of *L*-carnitine in patients on regular dialysis treatment. Proc Eur Dial Transplant Assoc 1982;19:302–307.

7 Wanner C, Hörl WH: Carnitine abnormalities in patients with renal insufficiency. Nephron 1988;50:89–102.

8 Cederblad G, Harper P, Lindgren K: Spectrophotometry of carnitine in biological fluids and tissue with a COBAS bio centrifugal analyzer. Clin Chem 1986;32:342–346.

9 Wanner C, Wäckerle B, Boeckle H, Scollmeyer P, Hörl WH: Plasma and red blood cell carnitine and carnitine esters during *L*-carnitine therapy in hemodialysis patients. Am J Clin Nutr 1990;51:407–410.