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

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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 (200 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 B₁₂ 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 recommendation 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, $\mu\text{mol/l}$	n=51 $\pm$ 3			20	30.5	41	41
Total carnitine, $\mu\text{mol/l}$	n=58 $\pm$ 3			34.6	57.7	71	67.5
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, $\mu\text{mol/l}$	n=51 $\pm$ 323			32.3	48	39.9
Total carnitine, $\mu\text{mol/l}$	n=58 $\pm$ 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

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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 decreasing 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

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. *Ne-phron* 1991;57:127-128.

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.
Bellinghieri G, Savica V, Mällamace A, Di Ste-fano 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 hemo-dialyzed patients. *Am J Clin Nutr* 1983;38: 523-531.

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

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

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

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

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

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.

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