The Response to Recombinant Human Erythropoietin in Patients with the Anemia of End-Stage Renal Disease Is Correlated with Serum Carnitine Levels

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Dear Sir,

The anemia of end-stage renal disease (ESRD) has a multifactorial origin [1]. This is reflected by large variations in the dose of recombinant human erythropoietin (rhEPO) needed to treat patients with this disorder [2–5]. Apart from blood loss and hemolysis, rhEPO therapy may be impaired by inflammation [5], insufficient body iron stores or transferrin saturation [5–7], and aluminium toxicity [4]. Theoretically, hyperparathyroidism might cause a reduced response to rhEPO, but so far, this has not been shown to be of clinical importance.

Carnitine metabolism may be involved in the synthesis of erythrocytes [8, 9], and L-carnitine administration has been shown to result in an increase in hematocrit (Ht) in patients with ESRD anemia who were not known to be carnitine deficient [10]. We wanted to investigate whether the development of ESRD anemia and the efficacy of treatment with rhEPO are influenced by the carnitine status. Therefore, we measured serum total (TC) and free (FC) carnitine levels before dialysis in 42 patients with ESRD who are maintained on chronic intermittent hemodialysis treatment with biocompatible high-flux artificial kidneys. None of these patients received L-carnitine substitution.

In these patients, TC was $45.6 \pm 10.5 \mu\text{mol/l}$ (mean $\pm$ SD) and FC $24.4 \pm 7.1 \mu\text{mol/l}$. We defined two subgroups: the first group of 11 patients in whom Ht was > 0.30 and who were not treated with rhEPO ('non-anemic group'), and the second group of 31 patients whose Ht was < 0.30 ($n = 15$) or who were treated with rhEPO because of previous ESRD anemia ($n = 16$) ('anemic group'). In the anemic group, TC and FC were significantly lower than in the nonanemic patients

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75

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TC, $\mu\text{mol/l}$

Fig. 1. Dose of rhEPO in relation to TC levels in 16 patients with ESRD anemia who are in the maintenance period of treatment.

($43.4 \pm 8.2 \mu\text{mol/l}$ versus $52.3 \pm 14 \mu\text{mol/l}$ mean $\pm$ SD; $p < 0.02$, Students t test, and $23.0 \pm 6.0 \mu\text{mol/l}$ versus $28.5 \pm 8.9 \mu\text{mol/l}$; $p < 0.03$, respectively).

All 16 patients treated with rhEPO were in the maintenance period of the therapy, and Ht had been stabilized between 0.30 and 0.35 since several months. In this group, we found a large variation in the rhEPO dose needed to maintain steady-state erythropoiesis. For instance, in the 20th week of treatment, the dose was $119.4 \pm 103 \text{ U/kg body weight/week}$ (mean $\pm$ SD). Linear regression analysis showed a Pearson's correlation coefficient of -0.58 ($p < 0.05$) between weekly rhEPO dose and TC (fig. 1). There was no significant correlation coefficient between rhEPO dose and FC. In 14 rhEPO-treated patients, we repeated the determination of TC and FC after 6 months. At this time, Pearson's correlation coefficient between weekly rhEPO dose and TC was -0.59 .

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These data suggest that patients with ESRD anemia or who are treated with rhEPO have lower serum carnitine levels than nonanemic patients. Furthermore, in patients with low carnitine levels higher rhEPO doses seem to be needed. This might explain partly the variance in the rhEPO dose needed to maintain target Ht. Further investigation is needed to clarify whether L-carnitine substitution improves the response to rhEPO treatment.

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