Long-Term Persistence of Improvement of Renal Anaemia in Spite of Discontinued Erythropoietin Treatment

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partially dependent on blood transfusions (one blood unit per month). The plasma EPO concentration before rHuEPO therapy was 23.5 mU/ml and 3 months after withdrawal of rHuEPO treatment 82.0 mU/ml (in healthy subjects the mean serum EPO level is 18.1 ± 1.0 mU/l). 10 months after withdrawal of rHuEPO treatment, catheter-ization of renal veins was performed. EPO levels were estimated in plasma samples withdrawn from both renal veins and from the vena cava inferior below and above the

Dear Sir

Recombinant human erythropoietin (rHuEPO) is widely used in the treatment of renal anaemia [1]. Discontinuance of rHuEPO therapy is usually followed by a progressive decline of the haematocrit value to pretreatment levels [2]. However, as shown in our previous studies, in spite of discontinued rHuEPO treatment for 1 year, patients' need for blood transfusions was less, and blood haemoglobin (Hb) concentration higher as compared with respective values found before rHuEPO therapy [3].

We would like to present a 54-year-old male anuric patient, haemodialyzed since March 1989. The cause of chronic uraemia was chronic glomerulonephritis. Severe renal anaemia (Hb concentration = 4.5 mmol/l, erythrocyte count = $2.45 \times 10^{12}/l$) was the indication for rHuEPO treatment. The starting dose of rHuEPO was 20 U/kg subcutaneously three times a week administered before each dialysis session. In spite of only 16 weeks of low-dose rHuEPO therapy, a brisk and unexpected increase in blood Hb concentration up to 9.8 mmol/l was noticed (fig. 1). During rHuEPO treatment, blood pressure and body weight did not change significantly. The unexpected increase blood Hb concentration was the reason for discontinuation of rHuEPO treatment. Surprisingly, during the subsequent 29 months without rHuEPO therapy, the Hb concentration showed only a moderate decrease. After 27 and 36 months of discontinued rHuEPO treatment the respective values of Hb concentration were 8.8 and 6.5 mmol/l (fig. 1). Before rHuEPO therapy, the patient was

12-

rHuEPO

10-

16-

4-

-i i 1 i 1-T r~! 1 r-i 1 r-i 1 t

-6-3 0 3 6 9 12 15 18 21 24 27 30 33 36 39

Months

Fig. 1. Hb concentration before, during and after withdrawal of therapy with rHuEPO. orifices of the renal veins. As can be seen in figure 2, the plasma EPO level in blood withdrawn from the right renal vein was 2.5 times higher than in vena cava inferior blood withdrawn distally from the orifices of the renal veins. Renal sonography and computerized tomography (CT) performed 10 months after the beginning of rHuEPO treatment did not reveal presence of renal cysts in the residual kidneys.

The reason of long-term persistence of normalized erythropoiesis for more than 2

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EPO (mU/ml)

Fig. 2. EPO concentration in plasma withdrawn from renal veins and from the vena cava inferior above and below the orifices of the renal veins 10 months after withdrawal of rHuEPO treatment.

years after withdrawal of rHuEPO therapy remains unclear. As shown in figure 2, 10 months after discontinuation of rHuEPO therapy, the concentration of EPO in venous blood from the right kidney was inappropriately high taking into account the presence of an almost normal Hb concentration, but normal in blood serum from the left kidney. This seems to indicate the presence of an autonomously functioning mechanism of EPO secretion in the right kidney. As the presence of cysts in the right residual kidney could be excluded by sonography and CT, synthesis of endogenous EPO by renal tissue other than cysts seems to be highly likely. It remains to be elucidated whether, or to what extent, administration of exogenous EPO was the triggering mechanism for excessive production of EPO by the right but not the left kidney. Improved responsiveness of the bone marrow to endogenous erythropoietin induced by the administration of supraphysiological doses of this hormone cannot be excluded in the mechanism of long-term improvement of erythropoiesis in our patient.

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Improved Renal Anaemia after Stopping rHuEPO Treatment