Long-Term Treatment with Recombinant Human Erythropoietin in Haemodialysis Patients: Effects on Left Ventricular Performance

S. Casati, G. C. Ambrosio, C. Ponticelli, A. Pierini, R. Mangiarotti, and C. Pini

Introduction

Left ventricle enlargement and dilation is a frequent result of the hyperdynamic circulatory condition induced by anaemia in the uraemic patient [1-3]. Thus, an adequate correction of anaemia may improve the haemodynamic status in these patients.

Studies on cardiovascular changes during therapy with recombinant human erythropoietin (rHuEPO) are now becoming available [3-7]. However, only short-term follow-ups have been reported.

In the present paper we report the long-term effects of the correction of anaemia with rHuEPO on cardiovascular function, evaluated by M-mode echocardiography, in a group of chronic haemodialysis patients.

Patients and Methods

Twenty-two chronic haemodialysis patients were selected for treatment with rHuEPO because of severe anaemia (mean haemoglobin 6.5±0.8 g/dl). No causes other than uraemia accounted for the anaemia. The drug was given as an intravenous bolus at the end of dialysis, three times a week. The starting dose was 24 U/kg body weight. During the follow-up, rHuEPO doses were adjusted as described elsewhere [8] to maintain haemoglobin (Hb) between 10 and 12 g/dl.

Patients with clinical, electrocardiographic or echocardiographic signs of valvular diseases, past or current evidence of pericarditis or congestive heart failure, as well as obese, diabetic patients and all those with “inadequate echocardiographic window” were excluded from the study. Thus, six patients mean age 42±12 years (range 21-60) on chronic haemodialysis for a mean 9±6 years were considered eligible for the study. Their pre-rHuEPO mean Hb was 6.5±0.8 g/dl. Four of the six were on maintenance antihypertensive therapy (beta-blockers, calcium antagonists, converting enzyme inhibitors).

Echocardiographic examinations were performed both before and immediately after mid-week dialysis. To minimize the influence of water load, the test was performed only if the patients’ interdialytic weight gains differed by
less than 10% from weight gains at baseline. The time schedule was: (a) before rHuEPO treatment (baseline); (b) after short-term correction of anaemia (3 and 6 months); and (c) after long-term correction of anaemia (1, 2 and 3 years). M-mode echocardiographic examinations were performed according to the recommendations of the American Society of Echocardiography [9] employing a two-dimensional sectorial image for correct positioning of the transducer and careful measuring. A Sigma 1 SC (Kontron) with a 3.5 MHz transducer and an MSV 110 (Piker) with a 3.0 MHz transducer were used. Echocardiograms were tape recorded and afterwards data were obtained with an image analysing computer (Cardio 200, Kontron) from an average of at least three consecutive cardiac cycles.

Left ventricular end-diastolic diameter (LVED) and left ventricular fractional shortening (SHRT) (normal values: 40±1.5%) were measured and calculated. The mean velocity of circumferential fibre shortening (MVCF) was estimated using the method of Cooper et al. [10]. Stroke volume was calculated from a regression equation as described by Teichholz et al. [11]. Left ventricular systolic work (LVSW) (normal values: 110±15 g-m/beat) was calculated and assumed to equal external cardiac work (i.e., the product of stroke volume and mean aortic pressure) [12]. Diastolic arterial pressure (DAP) was recorded and considered an index of after load to evaluate peripheral perfusion [13].

For the statistical analysis, we used a statistical software for data description and comparison of groups with paired t-tests and multiple linear regression, looking for correlations between haemoglobin and haemodynamic parameters. The functions for cubic spline interpolation were also computed using a statistical software program. All data are expressed as mean ± standard deviation.

Results

Hb changes between baseline (6.5±0.8 g/dl) and subsequent times were always statistically significant (p<0.001) (Table 1). The highest Hb level (12±0.9 g/dl) was reached after 6 months of treatment (mean dose of rHuEPO: 400±75 U/kg per week), while at third year the mean Hb was 10.5±0.4 g/ml (mean rHuEPO dose: 135±45).

Pre-dialysis heart rates tended to be lower at 3 and 6 months of treatment and significantly higher at 2 years (Table 1).

Pre-dialysis DAP rose significantly between 3 months and 1 year. Post-dialysis DAP was higher at 3 months than at 6 months and 1 year (Table 1). As a consequence, antihypertensive drug prescription had to be increased for all hypertensive patients when the Hb rose from 6.5±0.8 to 11.9±0.6 g/dl. In contrast, at 3 years, when the Hb level was 10.5 g/dl, antihypertensive drugs had to be reduced by 50% from that before rHuEPO treatment, to keep blood pressure values unchanged.