Successful trial of steroids in two haemodialysis patients with inflammatory disease and anaemia unresponsive to recombinant erythropoietin

Sir,

Resistance to erythropoietin (rHuEpo) therapy in patients with uremia treated by dialysis may be due to many reasons such as deficiency of haemopoietic factors (iron, B12, folic acid), inadequate dialysis, hyperparathyroidism, aluminium toxicity, infections, neoplastic diseases, primary haematological disorders and inflammatory diseases [1]. The management of these patients consists of the detection and correction, if it is possible, of the cause, in combination with a further increase in the dose of rHuEpo in some cases [2]. In a recent article published in Nephrology Dialysis Transplantation, Macdougall suggests 'a blind trial of steroids' in patients with inflammatory diseases and poor response to rHuEpo therapy [3].

We administered low doses of prednisolone to two patients on haemodialysis with anaemia refractory to rHuEpo, who had autoimmune diseases (rheumatoid arthritis and vasculitis), which resulted in a marked increase in their haematocrit (Ht).

Patient 1, a 67-year old female, started regular haemodialysis at the age of 63 (chronic pyelonephritis). She had rheumatoid arthritis for 18 years and she intermittently received salicylates. Her Ht at the start of haemodialysis was 18%. She was treated with rHuEpo for 12 months in doses gradually increased to 120 U/kg intravenously thrice weekly (this maximum dosage for 4 months), but without any improvement. The laboratory data were as follows: Ht 18%, Hb 6 g%, ferritin 850 µg/l, Fe 38 µg/dl, iPTH 125 pg/ml (10-65), Al 28 µg/l, Al/DFO 118 µg/l, ESR 135 mm/1St, RA test positive (+ + + +), cryoglobulins negative. An examination of bone marrow was typical of 'anaemia of chronic disease' [4].

At this time we decided to administer prednisolone 25 mg i.v. at the end of each dialysis session and progressively the Ht increased to 32% over 8 weeks. Now, 13 months later, the dose of rHuEpo and prednisolone have been tapered to 35 U/kg thrice weekly and 8 mg/daily respectively and the patient's Ht has been stabilized at 30–32%.

Patient 2, a 74-year old male, started HD on January 1994. The origin of his renal failure was a microscopic form of polyarteritis nodosa, which was diagnosed in April 1992 and resulted in terminal renal failure, despite therapy with corticosteroids and cyclophosphamide. During this period he did not manifest any haematological disorder, which could be attributed to the cyclophosphamide. At the initiation of HD, the patient's Ht was 24%, but subsequently it declined to 17% in the first 3 months. He started therapy with rHuEpo, the dosage of which was increased gradually to 150 U/kg thrice weekly over 8 months (this maximum dosage for 3 months), but without any response and he was transfused with packed red cells to maintain an Ht at 16–18%. His laboratory data were as follows: Ht 16–18%, Hb 5.5 g%, WBC 6500/mm3, PLTS 180 000/mm3, ferritin >1000 mg/ml, Fe 62 µg/dl, iPTH 95 pg/ml, AL 15 µg/l, Al/DFO 85 µg/l. Two examinations of bone marrow were the same as in patient 1. At this time we started therapy with steroids and progressively his Ht increased to 26% after 10 weeks and it maintained at this value 1 year after the institution of steroids. The current doses of rHuEpo and prednisolone are 150 U/kg thrice weekly and 8 mg/daily respectively.

Our two patients were rHuEpo resistant since they received an adequate dose of rHuEpo for a long time without any alteration in Ht. There were no other apparent cause EPO resistance, but both suffered from autoimmune diseases, which may cause anaemia by affecting iron utilization (reticuloendothelial block), by elevated inflammatory cytokines [5]. The dose of rHuEpo which we administered to our patients could have been further increased but their quick response to steroid therapy, dramatic in the first case, indicates that the effect of prednisolone on the inflammatory disease possibly increased the sensitivity of bone marrow to the rHuEpo.

To our knowledge there are inadequate data in the literature about the subject of rHuEpo therapy plus steroids in cases of anaemia caused by renal failure and autoimmune diseases and this issue needs further evaluation.
48-h analysis is much smaller than the number that embarked patient co-operation (and indeed this can be inferred from associated with a decline in sleep quality, quantity, and experience, continuation of recording much beyond 24 h is the present study, as the number of patients achieving a full finally excluding interdialytic weight gain as important in this context: first, a significant association between IDWG it seems unattractive to reject extracellular fluid volume changes. It is difficult to see why one should analyse and use the potential mechanisms to explain this finding one would really need to see whether this phenomenon was simply the consequence of a positive relationship between cardiovascular mortality and BP levels, i.e. the longest survivors having the lowest BP. If patients 'tracked' over 5–10 years could be shown to have a steadily falling BP over this dialytic time period, this would be more persuasive evidence of a 'diary effect'. Also, in dissecting the potential mechanisms to explain this finding one would ideally need to see whether in accounting for the fall in mean BP, both the diastolic and the systolic BP changed pari passu, or one changed significantly more than the other (in health, diastolic BP does reach a plateau in the 6th to 7th decades then start to fall in the very elderly, while systolic BP rises with age progressively)—it is likely that patients dialysed for a long time will be older than those dialysed for a short time. In our study we did not see such an inverse relationship between SBP or DBP in patients dialysed from 10 to 25 years. One of the criticisms that can be levelled at Chazot's study is the use of several criteria for interpretation of diurnal BP changes. It is difficult to see why one should analyse and use the results from all of the systolic, mean and diastolic BP changes. It is true that there is little common methodological ground in the other studies in secondary hypertension, but such presentation only serves further to confuse the issues. Analysis of mean BP, an unattractive 'short-cut', should really be abandoned, as its use could for example mask opposite changes in systolic and diastolic BP (as above, i.e. alteration in pulse pressure); thus it is regrettable that a 5% change in MBP between day and night was chosen as significant. Most of 'renal' hypertension is systolic rather than diastolic, perhaps the best day to night analytical tool is day to night BP ratio average (as used in the Staessen meta-analysis [5]), or a 10% fall in systolic BP at night.

Whatever method is used, the central message, of significant impairment of normal diurnal BP variability, is clear. Thus at all stages of renal disease (pre-dialysis, short and long-hours haemodialysis, CAPD, and transplantation)