

Once Weekly Subcutaneous Administration of Erythropoietin in Haemodialysis Patient

Pages with reference to book, From 88 To 90

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Abstract

Twenty-five anaemic patients of End Stage Renal Disease (ESRD) on maintenance haemodialysis at the Kidney Centre were studied. Recombinant human erythropoietin (EPO) 50-units/kg body weight was given once a week subcutaneously to see the response to therapy. In 21 cases haemoglobin increased significantly from 7.5 to 9.5 g/dl and haematocrit from 23 to 30.5 I/I with success rate of 84% and marked improvement in their quality to life. Once a week subcutaneous administration of erythropoietin is convenient and cost effective in reversing renal anaemia with minimal complications (JPMA 44:88, 1994).

Introduction

Anaemia is an important sequelae of chronic renal failure which effects the quality of life and limits rehabilitation in many patients. About 60% of patients undergoing haemodialysis require intermittent or regular blood transfusion to treat symptoms associated with anaemia¹. The etiology of anaemia is multifactorial but the primary cause is diminished production of erythropoietin². Previous attempts to correct anaemia were based on supplements of iron, folic acid, vitamin B12 androgens, adequate dialysis and blood transfusions³, but the results were not satisfactory and there were many side effects and complications like hepatic dysfunction, hirsutism, iron overload, infections (hepatitis B, C, HIV), reaction to leucop antigen and the development of cytotoxic antibodies⁴. The efficiency of recombinant human erythropoietin in correction of anaemia of ESRD is now well established and subcutaneous route for administering EPO is rapidly gaining popularity⁵. The aim of present study was to investigate the effectiveness of once weekly subcutaneous administration of erythropoietin in anaemia of ESRI) patients on maintenance haemodialysis and to evaluate the convenience and cost effectiveness of the treatment.

Patients and Methods

Twenty-five patients of ESRD on maintenance haemodialysis at the Kidney Centre Karachi who had anaemia of renal origin, adequately controlled blood pressure with no history of convulsions or systemic infection were included in the study. Informed consent was taken from all patients. Serum iron, TIBC, transferrin saturation and serum ferritin were estimated before initiating the therapy and then after every three months (serum ferritin 100 ug/l and transferrin saturation atleast 20%). Haematocrit was assessed initially and then weekly for atleast 2-6 weeks. Urea, creatinine, electrolytes, inorganic phosphorus were monitored monthly. Pre and post dialysis blood pressure was also recorded. Erythropoietin was given in a dose of 50 unit/kg body weight subcutaneously once a week at the end of dialysis.

Results

Fourteen females and 11 males with a mean age of 44 years were studied. All patients were on maintenance haemodialysis twice a week for more than six months under stable condition. The cause of uraemia in 10 patients was chronic glomerulonephritis, in 9 diabetic nephropathy, 3 had chronic pyelonephritis, 2 hypertensive nephropathy and in 1 polycystic kidneys. The most common associated illness was hypertension in 18, diabetes mellitus in 9 and ischaemic heart disease in 4 patients. In 10 patients blood transfusion was needed (2 units of blood per month) before initiating EPO therapy while in 15 blood was not required although they were anaemic (Hb 7-8 g/dl). No patient required transfusion after the initiation of EPO therapy. Six were normotensive and 19 were on antihypertensives. In only 3 of 19 cases antihypertensives were increased during the course of treatment. However, no episode of hypertensive crisis was observed. Mean haemoglobin before EPO therapy was 7.48 g/dl and haematocrit 23 l/l. In 21 of 25 patients target response (Hb 9-10 g/dl, haematocrit 28.30 l/l) was achieved within three months of therapy (Figure).

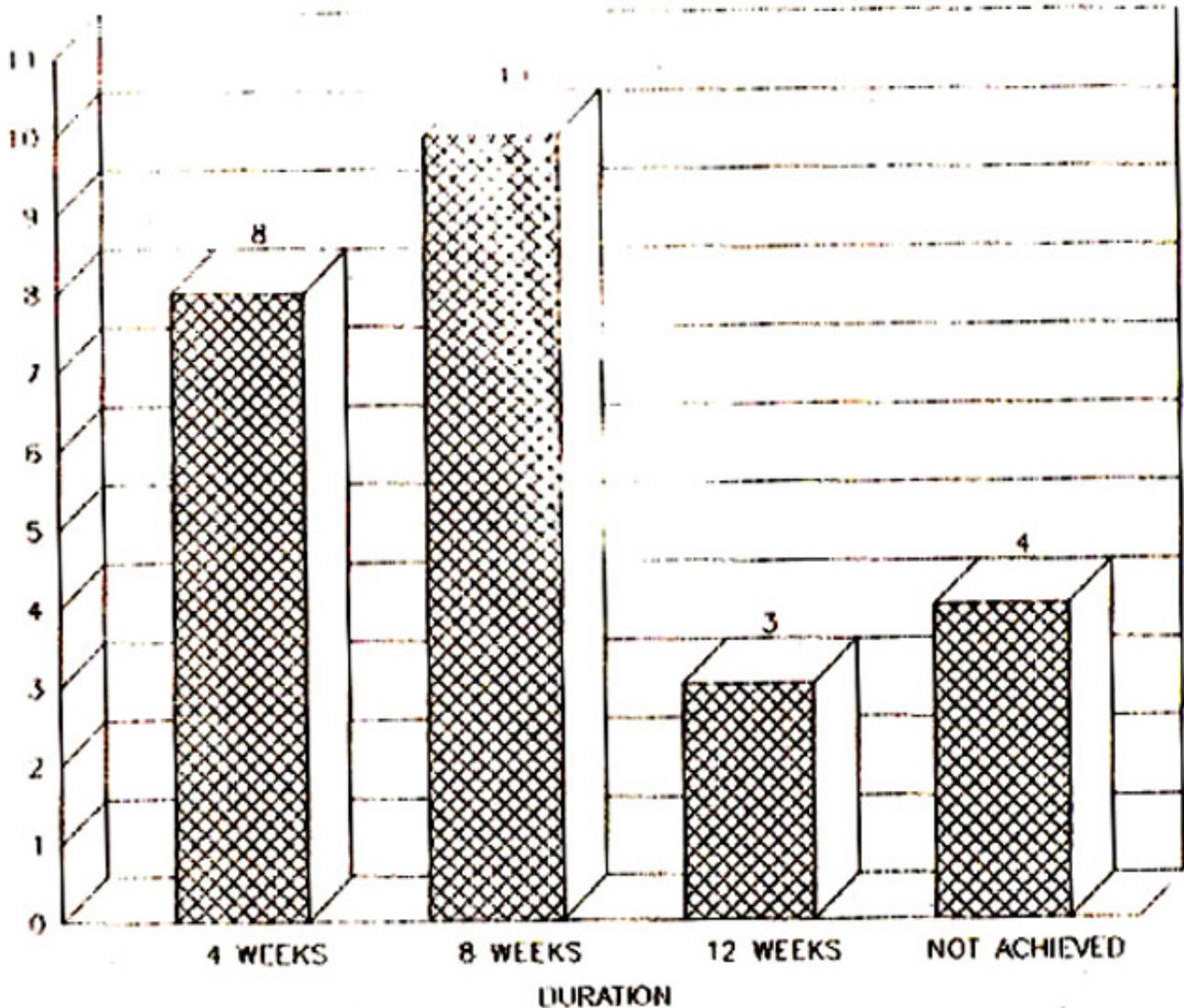


Figure. Response to EPO therapy.

Two patients were found iron deficient at the end of study even though they were on iron supplements. Subjective improvement in their general condition, appetite, sense of well-being and exercise tolerance were observed. None of the major complications of EPO therapy were observed except in 3 where doses of antihypertensive had to be increased, 3 had hyperkalaemia and 5 hyperphosphatemia. Once

weekly subcutaneous administration of EPO was as convenient, effective and as good as twice weekly therapy.

Discussion

Recombinant human erythropoietin is of proven benefit in treatment of renal anaemia and preliminary results suggest that it may have a role in the management of other anaemic conditions⁶. Pharmacokinetic and therapeutic studies have examined the use of EPO administration intravenously and subcutaneously, there is an accumulating evidence that the latter route has several advantages⁶. After intravenous administration EPO is distributed with a half life of between 4-12 hours, while after subcutaneous administration the plasma EPO level increases maximally during the first 12-24 hours and decreases very slowly over several days. Consequently more than hundred hours after a single subcutaneous injection, EPO level continues to be elevated⁷. Our previous study has shown that twice weekly administration of EPO is effective for the treatment of renal anaemia in patients on haemodialysis⁸. However, the optimal frequency of administration has not yet been established. We initiated this study with the dose of 50-unit/kg body weight subcutaneously post-dialysis once a week. The target response (Hb 9-10 g/dl pcv 28.30 l/l) was achieved in less than three months in 21 patients and in 4 response was not satisfactory. However, their haemoglobin increased from 6.7 to 8.6 g/dl within three months of study and the general condition remained stable during therapy. The altered response in 2 of 4 was due to iron deficiency in 1 hyperparathyroidism and in another due to thalassaemia trait. Iron deficiency was corrected by dietary counselling and increase in iron supplementation. In others dose of EPO was increased. In our study once weekly dose of EPO represents better results with slightly higher haemoglobin level and low average dose of EPO, i.e., 50 units/kg per week than the results observed by Lui et al in 1992¹⁰. There was slight delay in response with once weekly regimen as compared to twice weekly but the success rate was 84%. Hyperkalemia in 3 and hyper phosphatemia in 5 were also observed during therapy; it was due to dietary indiscretion¹¹. No major complication was observed during therapy possibly due to low dose of EPO and low target haemoglobin level. In summary once weekly subcutaneous administration of EPO is equally effective than twice weekly. Monthly cost of therapy on once weekly programme was in the range of Rs.4200-8400, which was almost half of twice weekly (Rs.8400-16800). It is more convenient and cost effective with almost no complication. The need for transfusion was significantly reduced with marked improvement in quality of life.

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