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An Assessment of Erythropoietin Levels in Haemodialysis Patients in Addington Hospital Durban, South Africa

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Abstract

Objective: Anaemia being one of the most severe complications of end stage renal disease is presently being managed with treatment by recombinant erythropoietin (RHuEPO). The assessment of native erythropoietin (EPO) and haemoglobin blood levels was carried out in this study on a sample of patients with renal failure on haemodialysis. This monitoring of erythropoietin levels in haemodialysis patients has been one of the first done in our population group in South Africa.
Design: Controlled clinical trial.
Setting: Haemodialysis unit at Addington Hospital, Durban, South Africa.
Subjects: Forty patients with renal failure on haemodialysis receiving recombinant erythropoietin (RHuEPO) EPO Beta (Recormon) for treatment of anaemia via the subcutataneous route in weekly doses of 2000 IU, 4000 IU, 6000 IU, 8000 IU, 12000 IU, or 18000 IU according to the severity of the anaemia. Also included in the study were 10 haemodialysis patients not on RHuEPO therapy and 10 healthy individuals. The subjects were representative of the population pool and their number was statistically representative of the population size.
Outcome Measures: Haemoglobin (Hb%) levels were monitored monthly over a trial period of six months during the RHuEPO therapy. Ferritin, transferrin saturation (TSATS), transferrin and EPO levels were monitored

simultaneously. Enzyme Linked Immunossorbant Assay (ELISA) was used to measure EPO levels.

Results: The haemodialysis patients receiving RHuEPO presented with higher EPO levels as compared to the haemodialysis patients not receiving RHuEPO and the healthy individuals. However, in the study the (Hb%) levels were not increased over the trial period with higher RHuEPO doses.

Conclusion: Higher doses of RHuEPO therapy showed no clear increase in haemoglobin levels in patients with renal failure on haemodialysis.

Keywords: Erythropoietin, Human Recombinant erythropoietin, Haemodialysis.

Introduction

Anaemia in chronic kidney disease is due to the decreased production of the glycoprotein hormone erythropoietin (EPO). Although EPO can be produced in many of the body tissues, it is mostly produced by endothelial cells in proximity to renal tubules[1]. The administration of recombinant erythropoietin results in significant improvement of the anaemia associated with renal failure based on increase haemoglobin level.[2] According to Kharagjitsingh et al, resistance to recombinant EPO therapy was observed in haemodialysis patients. Patients who did not respond to high doses of EPO were referred to as hyporesponsive or EPO resistant. The causes for EPO resistance have been identified, and the most important have been iron deficiency, infection and inflammation. One of the rare causes of EPO resistance has been the antibody formation against EPO[3]. The aim of this study was to monitor erythropoietin levels (EPO) and status of anaemia in a sample of patients with End Stage Renal Disease (ESRD). The patients were not scheduled for renal transplantation, some were receiving RHuEPO therapy to treat their anaemia, and, others did not need RHuEPO therapy. Another second group was studied which were normal healthy volunteers.

Methods

After ethical approval of the Institutional Research Ethics Committee of the Durban University of Technology patient recruitment started. Fifty male (n=25) and female (n=25) patients with ESRD (group I) on haemodialysis not scheduled for renal transplantation who granted informed consent were recruited from the haemodialysis unit at Addington Academic Hospital, Durban, South Africa. Forty patients of group I received RHuEPO to treat their anaemia and 10 pateints of group I did not receive RHuEPO. The other group consisted of 10 healthy individuals (group II).

The RHuEPO used in this study was the EPO Beta (Recormon) given through the subcutaneous route in weekly doses of 2000 IU, 4000 IU, 6000 IU, 8000 IU, 12000 IU, or 18000 IU. During the study an attempt was made to keep the Hb level between 11-12g/l, depending on the severity of the anemia The EPO Beta injections were given during the last hour of each patients' dialysis session.

Patients with parathyroid dysfunction were excluded from the study. The Aluminium concentration in the dialysis water was also monitored to exclude it as a possible cause of EPO resistance.

For six consecutive months blood samples were collected before the dialysis session commence. The analysis performed on the blood samples were haemoglobin, ferritin, iron, EPO and transferrin. Patients who required weekly dosages of iron received supplementation accordingly. Furthermore, iron supplementation was strictly monitored during the trial to ensure that adequate iron levels were maintained. All the ferritin levels were within the target range for haemodialysis. The adequacy of Haemodialysis was monitored by the Kt/V formula which was kept at a target of at least 1.2.

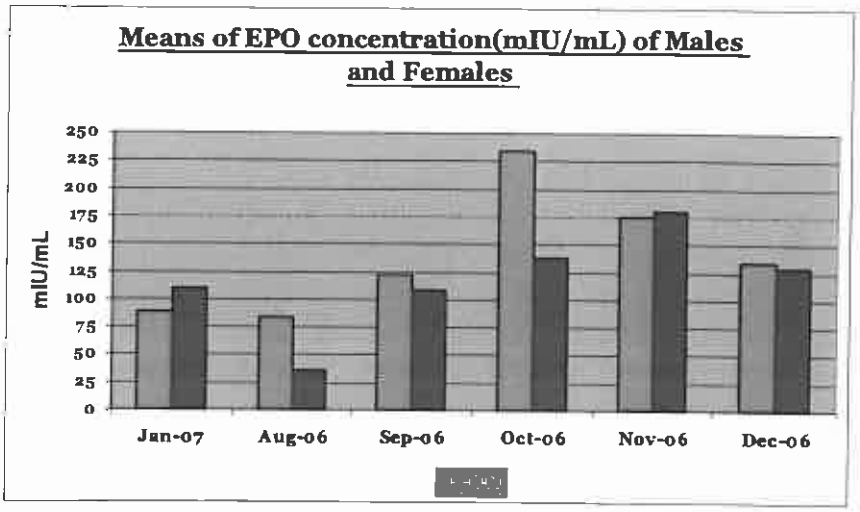

Figure 1: Erythropoietin concentrations of male and female haemodialysis patients (*p<0.05).

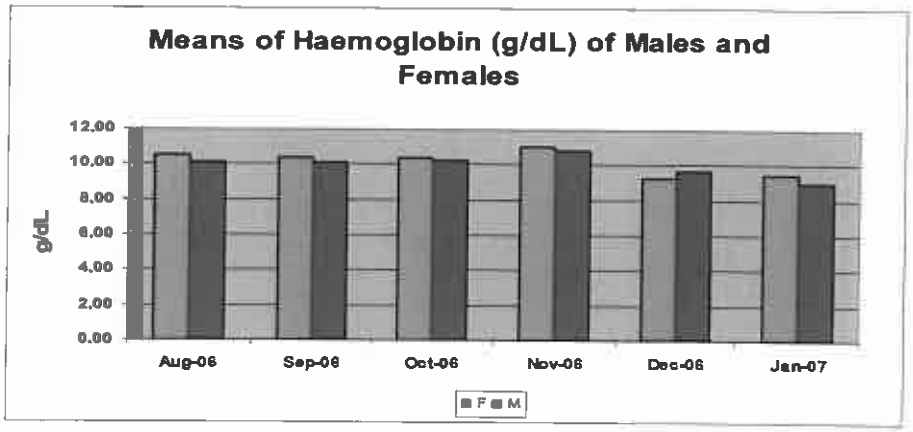

Figure 2: Haemoglobin levels of male and female haemodialysis (group I) patients.

Patients with parathyroid dysfunction were excluded from the study. Dialysis water concentrations of Aluminium was monitored to exclude these as possible causes of EPO resistance.

Enzyme Linked Immunosorbent Assay (ELISA) was used for measurement of erythropoietin (EPO) levels in blood.
In the normal healthy group (group II) and in the haemodialysis group(group I) who were not on RHuEPO treatment ELISA measured the native erythropoietin in blood, while in the haemodialysis group (group I) on RHuEPO treatment ELISA measured both native and exogenous EPO. Statistical analysis was carried out by the Instat 3 computer programme. (Graphpad, San Diego, CA, US).

Results

The mean erythropoietin (EPO) concentration in the haemodialysis patients (group 1) varied over the trial period. The mean EPO concentration of the female haemodialysis patients was higher than the male haemodialysis patients (139.42+/-15.24m IU/m L versus 119.49+/-7.54m IU/m L) Table 1. The mean Hb level for the female haemodialysis patients was 10.07+/-0.26 g/dL and 9.87+/-0.27 g/dL for the male hemodialysis patients (Table .2) and did not reveal any statistical significant differences (p=0.19; Table 2).

Table 1: Mean +/- SEM values of EPO concentration of group I males and females with statistical analysis.

Mean of epoconc (m iu/m l)	**Gender**	
Months	**F**	**M**
Aug 06	84.15	35.45
Sep 06	121.63	107.91
Oct 06	234.51	137.32
Nov 06	174.52	179.30
Dec 06	133.71	129.57
Jan 07	88.64	109.57
MEAN TOTAL	139.42	119.49
SEM ±	15.24	7.54
P(T<=t) one tail	0.02	