EFFECT OF INJECTABLE ERYTHROPOIETIN AND HEMODIALYSIS ON BLOOD HEMOGLOBIN, SERUM CREATININE AND BLOOD UREA LEVELS IN CHRONIC RENAL FAILURE PATIENTS

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ABSTRACT

The administration of recombinant human erythropoietin (r-HuEPO) is in trials all over the world to stimulate the process of erythropoiesis and hence to cover the state of anemia. In this study two-month treatment of erythropoietin (EPO) was administered subcutaneously along with hemodialysis to chronic renal failure (CRF) patients and found it very effective in raising blood hemoglobin levels and to cure anemia. After two-month treatment, blood Hb levels increased from 7.20±0.43 g/dl to 9.60±0.47 g/dl while blood urea and serum creatinine levels decreased from 202.9±29.9 mg/dl to 147.4±4.48 mg/dl and 7.37±2.24 mg/dl respectively.

Key words: Erythropoietin, chronic renal failure, anemia, blood hemoglobin

INTRODUCTION

Glomerulonephritis is the inflammation of nephron, which is a functional unit of kidney (Guyton and John, 1996). In glomerulonephritis there is acute shut down of kidneys, which result in anurea followed by diuratic, phase in which there is excessive formation of urine (Eschbach, 2000). Glomerulonephritis is of two types. Acute glomerulonephritis and chronic glomerulonephritis. Chronic glomerulonephritis is the major reason of chronic renal failure. Chronic renal failure consists of a persistent impairment of both glomerular and tubular functions of the kidney (Dewardner, 1996). Major problem to patients of chronic renal failure is the disturbed excretory function of kidneys, less production of erythropoietin (EPO) that decreased the erythropoiesis resulting in low levels of blood hemoglobin (Hb), high levels of blood urea and serum creatinine (Vanella et al., 1983). Chronic renal failure (CRF) requiring dialysis or transplantation is known as end-stage renal disease. Erythropoietin is a glycoprotein and it behaves like a hormone (Bain, 1995). It is produced primarily in the kidneys in adults and to a lesser extent, in the liver (Koury et al., 1991). Hypoxia is the sole physiological stimuli for erythropoietin production (Piros et al., 1989). In the kidneys, erythropoietin production of the hormone occurs on an all-or-none basis in each cell, normally there is constitutive production of the hormone that is commensurate with its role as a survival factor (Spivak et al., 1991). EPO acts in several ways to increase the number of circulating red cells. The primary action of EPO is to increase the number of developing erythroid precursors within the marrow by including terminal differentiation of EPO responsive stem cells (Giblett et al., 1956). The high efficacy of recombinant human erythropoietin (r-HuEPO) in therapy of anemia was first demonstrated in uremic patients on hemodialysis. In the mean time it became clear that all renal failure patients including, pre dialysis and renal transplanted ones, regardless the way of dialysis and etiology of renal disease, benefit of r-HuEPO therapy. EPO proved to be effective in reversing the anemia of CRF and all its divers’ consequences (Stojimirovic and Vera, 2000).

Optimal use of r-HuEPO should achieve the greatest benefits at the lowest cost. The challenge now is to optimize the r-HuEPO treatment and to provide a wider spectrum of patients to use it. This study was planned to see the effect of injectable erythropoietin and elevation of blood Hb levels in CRF patients on hemodialysis.

MATERIALS AND METHODS

Anemic patients (16 males and 4 females) of CRF on hemodialysis were registered in this study. The patients mean age was 41±10.22 years. Quantitative variables blood hemoglobin (Hb), blood urea and serum creatinine were determined before starting the treatment. Erythropoietin in a dose of 2000U / Kg body weight was administered subcutaneously thrice a week for two months. After completion of treatment hematological parameter blood Hb and biochemical parameters blood urea and serum creatinine were determined again.
**Determination of Blood Hemoglobin**

Concentration of Hb in whole blood was determined by calorimetric method (Kampen and Zijlstra, 1965). Hemoglobin reagent was taken in a test tube and 20 µl of the fresh blood (sample) was added into Hb reagent mixed and let stand for 5 min. to ensure complete cell lyses. Measure the absorbance of each sample and standard of known concentration.

\[
\text{Hb g/dl} = \frac{\text{Absorbance of sample x concentration of standard}}{\text{Absorbance of the standard}} \times 1000
\]

**Determination of Blood Urea**

Blood urea was determined by Berthelot modified method (Hallette, 1971). 10 µl of each sample serum was mixed with 1250 µl of urease and incubate at 37 ºC for 5 minutes. Read the absorbance of sample and standard of known concentration.

\[
\text{Urea mg/dl} = \frac{\text{Absorbance of sample x concentration of standard}}{\text{Absorbance of the standard}}
\]

**Determination of Serum Creatinine**

Creatinine was determined by Jaffei Method (Bartels et al. 1972). The 100 µl of the sample and standard was mixed with 1000 µl of working solution and read the absorbance of the sample and standard.

\[
\text{Creatinine mg/dl} = \frac{\text{Absorbance of sample x concentration of standard}}{\text{Absorbance of the standard}}
\]

**Statistical Methods**

All the variables were described by mean ± standard deviations. The T-test was used to compare these variables in paired samples (before and after treatment). Significant differences were defined by P< 0.001.

**RESULTS AND DISCUSSION**

Blood Hb ranged between 6.1 - 7.9 g / dl before treatment and 8.2 - 10.2 g / dl after treatment. Normal blood Hb values are 12-16 g / dl for females and 14-18 g / dl for males (Kampen and Zijlstra, 1965). The values of blood urea and serum creatinine ranged between 159-263 mg / dl and 7.95 - 13.15 mg / dl respectively before treatment. Two month treatment of r-HuEPO + hemodialysis decreased the levels of blood urea and serum creatinine to 87- 234 mg / dl and 4.35 - 12.0 mg / dl respectively. Normal blood urea values are 10-55 mg / dl (Bartels et al., 1972). Normal serum creatinine values are 0.5 -1.0 mg / dl for females and 0.7-1.2 mg / dl for males (Hallette, 1971).

<table>
<thead>
<tr>
<th></th>
<th>Blood Hemoglobin (g / dl)</th>
<th>Blood Urea (mg / dl)</th>
<th>Serum Creatinine (mg / dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ±SD before treatment</td>
<td>7.20 ± 0.43</td>
<td>202.0 ± 29.9</td>
<td>10.06 ± 1.44</td>
</tr>
<tr>
<td>Mean ±SD after treatment</td>
<td>9.60 ± 0.47</td>
<td>147.4 ± 4.48</td>
<td>7.37 ± 2.24</td>
</tr>
<tr>
<td>Difference of two means</td>
<td>-2.40</td>
<td>55.4</td>
<td>55.4</td>
</tr>
<tr>
<td>Standard error of difference</td>
<td>0.144</td>
<td>12.03</td>
<td>0.596</td>
</tr>
<tr>
<td>P</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Level of significance</td>
<td>Highly significant</td>
<td>Highly significant</td>
<td>Highly significant</td>
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</tbody>
</table>

Statistically significant rise in mean Hb levels (7.20 g / dl ± 0.43 – 9.60 ± 0.47 g / dl) after two-month treatment of r-HuEPO were observed (Table 1, Fig. 1). The value of Hb should be the level at which normal quality of life is
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possible. Most patients with the anemia of chronic renal failure remained moderately anemic and have not achieved the target Hb (11 to 12 g /dl) (Eschbach, 2000). Exact normal levels of Hb is not achieved but it was quite better as reported earlier 7.10 ± 1.4 g /dl – 8.4 ± 1.8 g /dl (Okura, 1996) and 7.22 ± 1.26 g /dl – 8.60 ± 1.66 g /dl (Singh et al, 1999). It is revealed that 2000 IU/kg/week increase Hb concentration to 10-12 g/dl in 90% of hemodialysis patients and best marker of benefit of the introduction of r-HuEPO is the reduction in need for regular blood transfusion (Winearls, 1998). It is suggested that in CRF patients on hemodialysis r-HuEPO therapy is more effective in rising blood Hb levels. Adequate dialysis is of paramount importance in correcting anemia.

Fig. 1 Comparison of Blood Hemoglobin levels Before And After Treatment

![Blood Hemoglobin Before and After Treatment](image1)

Fig. 2. Comparison of blood hemoglobin levels before and after treatment.

Fig. 2 Comparison of Blood Urea levels Before And After Treatment

![Blood Urea Before and After Treatment](image2)

Blood urea and serum creatinine levels were high before treatment (202.9 ± 29.9 mg / dl and 10.06 ± 1.44 mg / dl) (Table, Fig. 2, and Fig. 3). After treatment the above levels were significantly decreased to 147.4 ± 4.48 mg / dl and 7.37 ± 2.24 mg /dl respectively (Table 1, Fig. 2, 3). High flux haemodialysis (HD) had recently been vigorously promoted as a novel standard and it can indeed efficiently reduces the occurrence of most uremic symptoms (Okada et al., 2000). Statistical analysis did not reveal any relationship between EPO and creatinine concentrations. A low negative correlation was found between creatinine and Hb values (Zadrazil et al., 1997). It clearly indicates that EPO therapy does not have any effect on blood urea and serum creatinine and this decrease is only due to
haemodialysis but it is reported that the direct effect of dialysis- adequacy on EPO therapy response is still not completely understood (Movilli et al., 2001, 2003).

![Fig. 3 Comparison of Serum Creatinine Levels before and after treatment.](image)

This suggests that dialysis adequacy can influence anemia independently and can reduce the r-HuEPO requirement but further intervention studies are needed to fully confirm this.

REFERENCES


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