KLİNİK ARAŞTIRMALAR

TREATMENT OF RENAL ANAEMIA WITH RECOMBINANT HUMAN ERYTHROPOIETIN

RENAL ANEMİNİN REKOMBİNAN HUMAN ERİTROPOETİN İLE TEDAVİSİ

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SUMMARY

Ten patients with end-stage renal failure and anaemia on three times weekly haemodialysis were treated with recombinant human erythropoietin (r-HuEPO) for six weeks. Erytropoietin was given as an intravenous bolus after each dialysis in increasing doses within 30-120 U/hg.

In all ten patients mean haemoglobin concentration, haematocrit and corrected reticulocyle counts increased from 6.28 ± 0.58g/dl, 19.2 ± 2.04 % and 0.26 ± 0.15 to % 9.2 ± 1 g/dl, 27.8 ± 3.11 % and 1.67 ± 0.3 % (P < 0.05).

Mean iron and total iron binding capacity didn't change with treatment (P> 0.05).

None of the patients had required transfusions during treatment. Only one patient had an increase in blood perssure with r-HuEPO. No organ dysfunction or other toxic effects were observed.

These results demonstrate that r-HuEPO is effective for treating anaemia of the end stage renal failure and can eliminate the need for transfusions with their risks of iron overload, infection and immunologic sensitization.

(Key Words: r-Hu EPO, Renal Failure.)

ÖZET

Renal yetmezlik nedeniyle haftada 3 kez hemodializ uygulanan 10 hastanın anemisi human eritopoetinle 1.5 ay süreyle tedavi edildi.

Eritropoetin, her dializden sonra IV bolus şeklinde 30-120 Ü/kg dozlarında uygulandı. Hastaların hemoglobin ve hemotokrit değerleri 6.28 ± 0.58g/dl, % 19.2 ± 2.04 dan 9.2 ± 1 g/dl ve % 27.8 ± 3.11'e yükseldi. (P < 0.05). Ayrıca retikulosit değerleri % 0.26 ± 0.15 den % 1.67 ± 0.3'e yükseldi (P < 0.05). Tedavi öncesi ve sonrası serum demir ve demir bağlama kapasiteleri arasında önemli bir fark yoktu (P> 0.05). Hastaların hiçbiri tedavi sırasında kan transfüzyonuna ihtiyaç göstermediler. Sadece bir hastanın kan basıncında yükselme dışında, ilaca bağlı yan etki gözlenmedi.

Sonuç olarak eritropoetin tedavisinin renal anemide etkin ve güvenli olduğu gözlendi.

(Anahtar Sözcükler: r-Hu EPO, Böbrek Yetmezliği.)

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Ane mia is a major and predictable complication of chronic renal failure. The pathogenesis of the renal anaemia is multifactorial. The factors that may contribute to this anaemia include shortened red-cell survival, marrow supression by uraemic toxins, repeated blood loss on dialysis, aluminium toxicity, and decreased erythropoetin production. The patients with renal anaemia require regular blood transfusions with their attendant risks of hepatitis, iron overload, and sensitisation to histocompatibility antigens (1-6).

It this study, we want to determine the efficacy of recombinant human erythropoietin in end stage renal failure patients with anaemia.

MATERIALS AND METHODS

During nine months, eleven patients receiving haemodialysis (at least 2 months, mean 5.66 ± 2.62 months) enrolled in the study. One patient was excluded because of disfunctional vaginal bleeding. Insulin-dependent diabeties mellitus and steroid, taking androgen or immunosuppressive medication were not included the study.

The ages of patients ranged from 17 to 55 (mean 33 ± 14.98) years. 4 (40 %) of them were female and 6 (60 %) were male. They were anaemic with haematocrits of less than 25 to and haemoglobin of less than 7 g/dl, no additional cause for anaemia.

They were not hypertensive, nor they had hypertension that was medically controlled. Vital sings (body temperature, blood pressure, pulse and respiration rate) were measured before and 30 min after injection of r-HuEPO.

Plasma urea. electrolyte, creatinine, protein, albumin, bilirubin and transaminase activities were checked weekly. Serum iron and total iron binding capacity were checked at the baseline state and at the end of treatment. Prothrombin time and partial thromboplastin time were assessed every week. Samples for haemoglobin concentration, haematocrit, red cell, platelets and reticulocyte count were taken before each dialysis. Reticulocytes were counted by standard methods and corrected for haematocrit value. The characteristics of all the patients are shown at table 1.

TABLE 1: Characteristics of Patients

Patient	Sex	Age (Yr.)	Dialysis Duration (month)	Nephropaty	Blood Pressure (mmHg)
1	F	54	10	NS	14/B
2	F	24	24	CGH	12/8
3	F	22	10	CGN	13/8
4	M	22	36	CPN	14/8
5	M	55	6	NS	10/7
6	M	30	7	CGN	14/9
7	F	23	5	CGN	12/8
8	M	53	6	CPN	13/8
9	M	17	8	CPN	14/8
10	M	30	84	CPN	14/9

- CGN Chnonic Glomenalo Nephritis
- CPN Chronic Pyelo Nephritis
- NS Nephrosclevosis

r-HuEPO was administered three times weekly as an intravenous bolus at the end of each routine dialysis treatment. The dose range studied was 30-120 U/kg. Each dose was administered for eleven days. In addition to each patient was given 50 mg daily oral iron.

Student's test was used for statistical analysis.

RESULTS

Before and after treatment findings of the patients are shown at table 2.

Mean haemoglobin concertration increased from 6.28 ± 0.58 g/dl to 9.2 ± 1 g/dl. There was significant difference between these values ($P < 0.05$) (Fig, 1).

Mean haematocrit was 19.2 ± 2.04 % before the study. By r-HuEPO, it had risen to 27.8 ± 3.11 %, the values of post treatment

was significantly higher than the baseline ($P < 0.05$) (Fig, 2).

Pretreatment mean reticulocyte count was 0.26 ± 0.15 %.

After 44 days mean reticulocyte count reached 1.67 ± 0.3 %.

There was a significant increasing in reticulocyte count ($P < 0.05$) (Fig, 3)

The haemoglobin concentration, haematocrit and reticulocyte count increased gradually during the treatment.

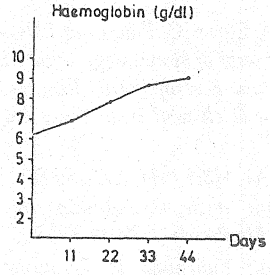

Figure 1: Haemoglobin concentration vs days of treatment with r-HuEPO

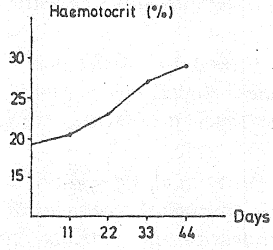

Figure 2: Mean haemotocrit vs days of treatment with r-HuEPO

Mean serum iron concentration and mean total iron binding capacity were 0.78 ± 0.16 Ug/dl and 2.9 ± 0.32 Ug/dl in the baseline state and were 0.76 0.35 Ug/dl, 2.79 0.63 Ug/dl at the end of the study.

Serum iron and total iron binding capacity were not statistically significant ($P < 0.05$) (Fig, 4)

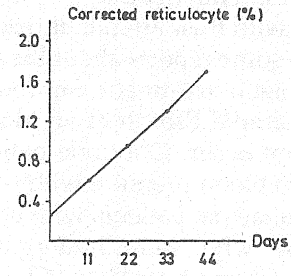

Figure 3: Mean corrected reticulocyte counts vs days of treatment with r-HuEPO

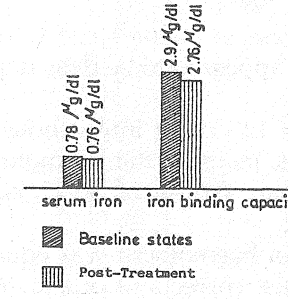

Figure 4: Mean serum iron and iron binding capacity in pre-and post treatment state with r-HuEPO

TABLE 2: Haematologic Changes Before and After Treatment

Patient	Haemoglobin g/dl		Haemotocrit %		Corrected Reticulocyt %		Serum Iron µg/dl		Serum Total Iron binding µg/dl	
	B	A	B	A	B	A	B	A	B	A
1	6,7	9,2	22	28	0,2	1,6	0,7	0,6	3,0	2,5
2	6,5	10,0	20	30	0,3	1,5	0,8	0,9	3,0	2,5
3	5,2	8,0	16	24	0,2	1,2	0,7	0,6	3,0	3,5
4	5,5	8,2	16	25	0,0	1,6	0,8	1,6	2,5	2,5
5	7,0	11,0	21	33	0,5	2,2	0,5	0,9	3,5	2,0
6	6,2	9,2	19	27	0,3	1,5	1,0	0,9	3,0	4,0
7	6,0	8,1	18	24	0,0	1,2	0,7	0,7	2,5	3,0
8	6,2	8,9	19	28	0,1	1,6	0,9	0,9	3,0	2,0
9	6,8	9,0	21	27	0,3	1,9	1,0	0,9	3,0	2,9
10	6,7	10,4	20	32	0,3	1,9	0,6	0,4	2,5	3,0

B: Before A: After

DISCUSSION

Anemia is one of the most distressing complications of chronic renal failure and is particularly severe in patients treated by long-term maintenance haemodialysis. Many of these patients may require blood transfusions with their attendant risks (1.7).

There are some reports about the benefits of erythropoietin treatment for renal anaemia. For example Esbach et al. Major side effects did not occur. Only one patient had an increase in blood pressure with r-HuEPO reported 25 anaemic patients with end stage renal disease who were undergoing haemodialysis, treated by r-Hu EPO and their anaemia improved with treatment (2). Nayir, Karakullukçu, Ayaz and Cozma also reported same results (Turkish Congress of Nephrology, 1991).

The increase in haemotocrit in response to treatment appeared to be dose dependent (2, 8, 9).

A dose of 120 U/kg intravenously three times a week increase the haemotocrit significiantly than a dose of 30 U/kg three times a week.

The rise in haemotocrit was equally significant. Partial corrections of anaemia with haematocrit values ranging between 30 and 35 %, regressed the symptoms associated with anaemia (3).

The rise in blood pressure during erythopoietin treatment may be attributable to the increased blood viscosity and total red cell mass, inducing an increase in peripheral resistance (2, 7, 9, 10).

But in our study hypertension has occured in only one patient. No other side effect was observed. We found that serum iron and total iron binding capacity of our patients did not change with r-HuEPO treatment. Some clinical trials have been reported in which these values decrease with treatment. Its cause may be the exhaustion of the iron stores as iron was mobilized for haemoglobin synthesis (1.7).

We found that haemoglobin, haematocrit and reticulocyte count had increased with r-HuEPO in increasing doses. These findings are in accordance with many other trials (11-13).

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