r-HuEPO treatment may improve abnormalities of anterior pituitary hormone in the hemodialysed patients with chronic renal failure

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We investigated the levels of anterior pituitary hormones including prolactin. LH, FSH and TSH in the hemodialysis patients with chronic renal failure (CRF) and in the healthy subjects before and after r-HuEPO treatment. In the patients with CRF we investigated the correlation between levels of hemoglobin and hematocrit and levels of anterior pituitary hormones after r-HuEPO treatment. We detected a significant decrease in the levels of prolactin and a significant increase in the levels of LH and FSH; but there was no significant change in the levels of TSH. We concluded that r-HuEPO treatment may improve the endrocrinological abnormalities in the patients with CRF. [Turk J Med Res, 1994; 12(5): 196-199]

Key Words: Hemodialysis, Chronic renal failure (CRF), r-HuEPO treatment, Anterior pituitary hormone levels

Anemia is the leading symptom of chronic renal failure (CRF) (1). It is possible that correction of anemia may also improve some of the endocrine dysfunction that is frequently found in the patients with CRF (2). Finally, recombinant human erythropoietin (r-HuEPO) treatment is known to improve anemia in the patients with CRF. This effect results in improvement in various conditions associated with renal failure including subjective symptoms, exercise tolerance, cardiac functions and sexual disorders (1-3). Many different factors associated with Improvements in anemia are assumed to be involved in such changes in sexual functions including increases in tissue oxygen concentration, nutritional recovery and increases in exercese capacity (3). It was reported that r-HuEPO treatment improves the anemia in the patients with CRF (4). In our study, we examined the levels of prolactin, luteinizing hormone (LH), follicule-stimulating hormone (FSH) and thyroid-stimulating hormone (TSH) before and after r-HuEPO treatment in the hemodialysed patients with CRF. Compared the results with those of healthy subjects.

MATERIALS AND METHODS

We conducted this investigation at the Division of Nephrology, Internal Medicine Department, Research Hospital, Medical School of Atatiirk University between February and August in 1992. Seventeen patients with CRF (9 males, 8 females) on chronic hemodialysis and ten healthy subjects (8 males, 2 females) were examined. All of patients with CRF were hemodialysed.

Levels of hemoglobin and hematocrit were measured by authoanalyser (Cell-Dyn 1500 Sequoia-Turner, USA), levels of prolactin (Coat-A-Count Prolactin IRMA, catolog number IKPR2, DPC, USA), LH (Coat-A-Count LH IRM, catolog number IKLH5, DPC, USA), FSH (Coat-A-Count FSH IRMA, catolog number IKFS5, DPC, USA) and TSH (IRMA-Count TSH, catolog number RKTS5, DPC, USA) were measured by radioimmunoassay.

The patients with anemia associated with CRF, r-HuEPO (EPREX from Cilag) received 50U/kg received r-HuEPO intravenously, three times in a week, at the end of after each dialysis session. After 3 months or r-HuEPO treatment hemoglobin, hematocrit and the above mentioned hormone levels were detected in the patient and control groups.

Student's t-test and linear regression analysis were used for statistical evaluation.

RESULTS

Our results are summarized in Table 1.

Seventeen patients with CRF (9 males, 8 females; mean age 40.5±15.8 years; range 17-65 years) and ten healthy subjects (8 males, 2 females; mean age 31.6±8.2 years; range 25-48 years) were

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Table 1. Results of hematologic and hormonal parameters prior to and after r-HuEPO treatment in the patients with C R F

	Patients	Control
Number of cases (n)	17	10
Mean age (year)	40.5±15.8	31.618.2
Duration of r-HuEPO treatment (day)	42.2±20.7	
Hemoglobin levels (gr/dl)		
Before	6.81 ±0.65	14.3±3.1
After	9.76±0.76	
Hematocrit levels (%)		
Before	20.9+1.98	44.914.1
After	29.5li .87	
Prolactin levels (ng/ml)		
Before	33.79±8.17	10.46±2.99
After	13.79±3.39	
LH levels (mlU/ml)		
Before	5.85±3.79	8.39+0.99
After	28.27H9.51	
FSH levels (mlU/ml)		
Before	11.42±7.13	10.64ı 1.28
After	43.61 ±24.40	
TSH levels (**fiU**/ml)		
Before	2.30±0.62	1.8510.69
After	1.22±0.30	

examined. There was no significant difference in the mean age between patient and control groups (t-1.66 p>0.05).

Before r-HuEPO treatment, hemoglobin and hematocrit levels were detected as 6.81 ±0.65 gr/dl and 20.9±1.98 percent in the patient group, respectively and 14.3±3.1 gr/dl and 44.9±4.1 percent in the control group, respectively. There were significant differences in the hemoglobin and hematocrit levels between patient and control groups (t-31.15 p<0.0001; t-39.15 p<0.0001, respectively).

In the patient group, r-HuEPO treatment was continued 42.2±20.7 days until hemoglobin and hematocrit levels reached optimal values. After r-HuEPO treatment period, hemoglobin and hematocrit values were 9.76±0.76 gr/dl and 29.5±1.87 percent, respectively in the patient group. There were statistically significant differences between hematocrit and hemoglobin values measured before and after the treatment (t-18.68 p<0.0001 and t-16.93 p<0.0001, respectively).

Mean prolactin level were 33.79±8.17 ng/ml in the patient group and 10.46±2.99 ng/ml in the control group before r-HuEPO treatment. The difference was statistically significant (t-11.03 p<0.0001). After r-HuEPO treatment, prolactin levels decreased to 13.79±3.39 ng/ml (t-9.31 p<0.0001). There was a negative correlation between hematocrit and prolactin levels (r--0.682 p<0.0001) (Fig 1).LH levels were 5.85±3.79 mIU/ml in the patient group and 8.39±0.99 mIU/ml in the control group prior to r-HuEPO treatment, LH levels increased to 28.27±19.51 mIU/ml (t-4.51 p<0.0001). There was a positive correlation between hematocrit and LH levels (r=0.7924 p<0.001) (Fig 2).

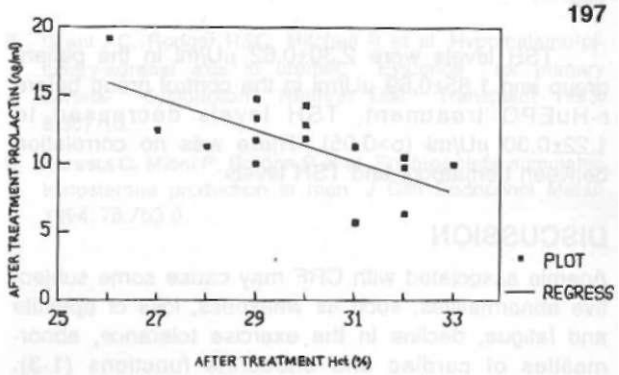

Figure 1. Negative correlation between hematocrit and prolactin levels after r-HuEPO treatment

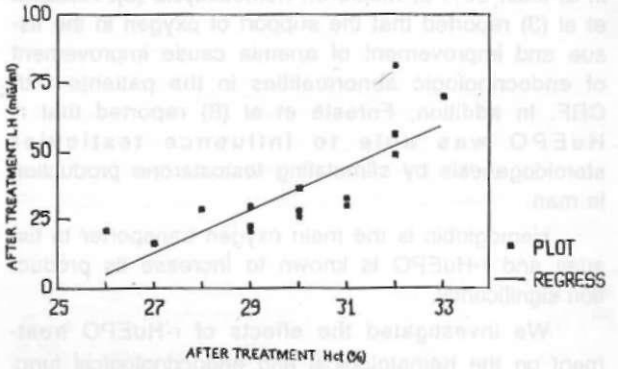

Figure 2. Positive correlation between hematocrit and LH levels after r-HuEPO treatment

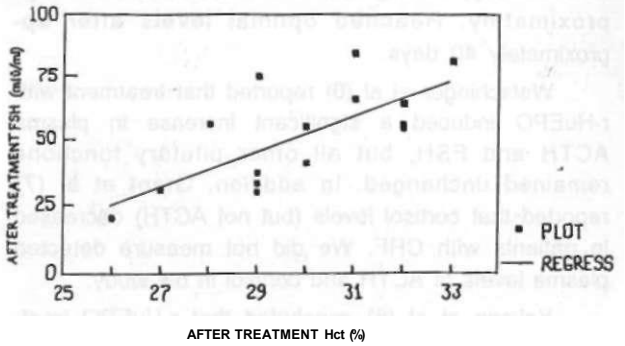

Figure 3. Positive correlation between hematocrit and FSH levels after r-HuEPO treatment

FSH levels were 11.42±7.13 mIU/ml in the patient group and 10.64±1.28 mIU/ml in the control group prior to r-HuEPO treatment. The difference was not significant (t-1.64 p>0.05). After r-HuEPO treatment, FSH levels increased to 43.61 ±24.40 mIU/ml (t-5.22 p<0.0001). There was a positive correlation between hematocrit and FSH levels (r-0.7003 p<0.001) (Fig 3).

TSH levels were 2.30±0.62 nU/ml in the patient group and 1.85±0.69 uU/ml in the control group before r-HuEPO treatment, TSH levels decreased to 1.22±0.30 uU/ml (p>0.05). There was no correlation between hematocrit and TSH levels.

DISCUSSION

Anemia associated with CRF may cause some subjective abnormalities, such as weakness, loss of appetite and fatigue, decline in the exercise tolerance, abnormalities of cardiac and endocrine functions (1-3). Menstrual abnormalities are seen in 30-50% of females, and decreased libido and impotence are seen in at least 50% of males on hemodialysis (3). Akizawa et al (3) reported that the support of oxygen in the tissue and improvement of anemia cause improvement of endocrinologic abnormalities in the patients with CRF. In addition, Foresta et al (8) reported that r-HuEPO was able to influence testiculer steroidogenesis by stimulating testosterone production in man.

Hemoglobin is the main oxygen transporter to tissues and r-HuEPO is known to increase its production significantly.

We investigated the effects of r-HuEPO treatment on the hematological and endocrinological functions in the hemodialysed patients with CRF and compared the results with those of healty subjects. In our study, hemoglobin and hematocrit levels approximately. Reached optimal levels after approximately 40 days.

Watschinger et al (6) reported that treatment with r-HuEPO induced a significant increase in plasma ACTH and FSH, but all other pitutary functions remained unchanged. In addition, Grant et al (7) reported that Cortisol levels (but not ACTH) decreased in patients with CRF. We did not measure detected plasma levels of ACTH and Cortisol in ow study.

Yeksan et al (5) concluded that r-HuEPO treatment decreased plasma levels of proiactin in uremic hemodialysis patients. Similarly detected to decrease plasma levels of prolactin on treatment r-HuEPO patients with CRF. In addition, decreased plasma prolactin levels was negatively correlated with increased plasma levels of hematocrit.

We detected increase in levels of LH and FSH levels increase after r-HuEPO treatment in the patients with CRF. In addition, increasing plasma gonadotrophins levels were positively correlated with plasma levels of hematocrit.

We concluded that improvement of plasma prolactin and gonadotrophins levels is due to improvement of hypophyseal O_2 support by increased plasma levels of hemoglobin and hematocrit by r-HuEPO treatment in the patients with CRF.

Circulating concentrations of erythropoietin concentration in blood is known to be inversely related to the hematocrit or oxygen tension (4). It still is not clear whether such a recovery is due to increase in tissue oxygen concentrations and improvements in the state of nutrition caused by improvements in anemia or is associated with the recovery of endocrinological functions (3).

Kokot et al (1) reported that TSH levels were not significantly different from normals. As such, we did not detect plasma levels of TSH. This results may be interest in chronically movement of the CRF. Because, we were known that thyroid status was nearly interested in such as diseases movement, malnutrition and medications.

Finally, we concluded that r-HuEPO treatment may improve plasma levels of prolactin and gonadotrophins with CRF.

r-HuEPO tedavisi kronik renal yetersizliği (KBY) olan hemodiyaliz hastalarında ön hipofiz hormonlarındaki anormallikleri iyileştirebilir.

r-HuEPO tedavisinden önce ve sonra, kronik böbrek yetmezliği (KBY) olan hemodiyaliz hastalarında prolaktin, LH, FSH ve TSH dahil olmak üzere ön hipofiz hormonlarının seviyelerini inceledik. Hasta grubunda r-HuEPO tedavisinden sonra hemoglobin ve hematokrit düzeyleri ile ön hipofiz hormonlarının düzeyleri arasındaki ilişkiyi inceledik, r-HuEPO tedavisinden sonra hasta grubunda prolaktin düzeylerinin önemli oranda azaldığını, LH ve FSH düzeylerinin ise önemli oranda arttığını, buna karşılık TSH düzeylerinde önemli değişiklik olmadığını tesbit ettik. Bu çalışmanın sonucunda, kronik böbrek yetersizliği olan hastalarda görülen endokrinolojik anormalliklerin r-HuEPO tedavisi ile düzelebileceğ kanaatini edindik. [Turk J Med Res 1994; 12(5): 196-199]

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