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Effect of r-HuEPO Treatment in Hemodialysis Patients

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Abstract

This study aimed to investigate the effects of recombinant human erythropoietin (r-HuEPO) on hemodialysis patients. r-HuEPO was administered to 38 patients receiving chronic hemodialysis treatment. After hemodialysis, the effects of erythropoietin on the hematologic and biochemical parameters of the patients were analyzed. r-HuEPO treatment was carried out for 16 weeks, three times a week, after hemodialysis. Each patient received a dose of 150 u/kg r-HuEPO subcutaneously after hemodialysis. During the period of the research, each patient received a total of 5000 units of r-HuEPO. Hematologic and biochemical analysis was performed before the r-HuEPO treatment and after the fourth, eighth, twelfth, and sixteenth week. The results of the research indicated that erythrocyte levels in patients increased from 3.1 to 31.6 percent, hematocrit levels increased from 9.1 to 31.5 percent, and hemoglobin levels increased from 7.1 to 32.3 percent, in the fourth to sixteenth week, respectively. In addition to the r-HuEPO treatment, iron deficiency was also treated. This treatment contributed to an observed increase in iron levels of 1.6 and 10.9 percent in the fourth and twelfth weeks, respectively. 16 weeks of r-HuEPO treatment played an important role in the recovery of end-stage chronic hemodialysis patients suffering from anemia problems; in addition, their health-related quality of life improved.

Key words: Erythropoietin (r-HuEPO), hemodialysis, hematologic analysis, biochemical analysis.

INTRODUCTION

Healthy kidneys clean blood and remove extra fluid in the form of urine. They also make substances that keep our body healthy. Dialysis replaces some of these functions when our kidneys no longer work. In chronic renal failure patients, anemia is a very real health problem. Recombinant human erythropoietin (r-HuEPO), a glycoprotein hormone that stimulates erythropoiesis, is a hemopoietic growth factor and a primary regulator of erythropoiesis that is used for the treatment of anemia. Chronic renal failure is an important health problem all over the world. Hemodialysis is a useful system for the recovery of patients to achieve longer and better quality of life. At the end of renal failure, the kidneys cannot function properly and toxic materials cannot be filtered by the kidneys. This results in toxic effects for the human body [1] There are two different types of renal failure, one of them is acute and the other chronic. Anemia is common in people with kidney disease. Erythropoietin (EPO) is a hormone that prevents anemia by helping produce red blood cells. Almost all the body's EPO is made in the kidneys. However, kidney disease may damage the cells that make EPO, leading to anemia [2]. Diseased kidneys do not make enough EPO; as a result, the bone marrow makes fewer red blood cells. Other common causes of anemia include loss of blood from hemodialysis and low levels of iron and folic acid. These nutrients from food help young red blood cells make hemoglobin (Hgb), their main oxygen-carrying protein [3]. 90% of renal failure patients have an anemia problem. r-HuEPO has been widely administered for recovery from this kind of anemia. A lot of factors play a role in the development of renal anemia, such as erythropoietin deficiency, blood loss, shortening of erythrocyte life-span, and pressure on the erythropoiesis [4]. The growth of anemia depends on an insufficient endogenous erythropoietin level in chronic renal failure patients. Except for erythropoietin deficiency, erythropoiesis and erythrocyte loss can help renal anemia [5]. Erythropoietin (EPO) is a glycoprotein hormone that is the primary inducer of erythrocyte formation in mammals [6]. Since the human EPO gene was cloned in 1985, r-HuEPO has been widely administered for treatment of chronic complications, including anemia, which is a common feature of renal disease [7]. Before EPO was synthesized and made available for injection, many patients with kidney disease had to receive blood transfusions to treat anemia. Now that it is possible to make EPO, persons with kidney disease can be given this form of EPO to correct anemia. The injectable form is called recombinant human erythropoietin and is almost identical to what a normal kidney makes [8]. r-HuEPO treatment can be administered intravenously, subcutaneously, or intraperitoneally [9]. The objective of our research was to determine the effects of r-HuEPO treatment on recovery from anemia in hemodialysis patients.

MATERIALS AND METHODS

Blood samples were taken from a private dialysis center in Canakkale, Turkey. The blood from forty end-stage chronic hemodialysis patients was used for this research. Two of the forty patients were died during the period of the research, therefore, the blood parameters of thirty-eight patients were analyzed.

r-HuEPO treatment

r-HuEPO was administered to end-stage chronic renal failure patients after hemodialysis. r-HuEPO treatment was carried out for 16 weeks, three times per week. Each patient received a

dose of 150 u/kg r-HuEPO subcutaneously after hemodialysis. During the research, each patient received a total of 5000 units of r-HuEPO.

Hematology Analysis
An MS9 blood counter was used for hematology analysis. Acti DIFF, iso-flux (dilute solution), HEMOREF (hemoglobin reference solution), and Transflux (cleaner solution) were used as kit solutions.

Biochemical Analysis
Blood samples were loaded into vacutainer gel biochemical test tubes for biochemical analysis, left for 30 minutes to prevent hemolysis, then centrifugated for 15 minutes at 25000 rpm. The dissociated serum of blood samples was analyzed spectrophotometrically. Every parameter was determined with special kits.

RESULTS

In this research, the hematological and biochemical parameters of 38 hemodialysis patients were checked at baseline and after the fourth, eighth, twelfth, and sixteenth weeks of r-HuEPO treatment. The results given in Table 1 and Table 2 shows the total hematologic and biochemical parameters for the 38 patients over sixteen weeks.

Effect of r-HuEPO Administration on Hematologic Parameters
When we compare the results of the analysis before and after r-HuEPO treatment, Erythrocyte levels increased by 3.1%, 11.9%, 21.1%, and 31.6% at the end of 4, 8, 12, and 16 weeks, respectively. Hematocrit levels were increased by 9.1%, 15.7%, 24.8%, and 31.5% after the 4th, 8th, 12th, and 16th weeks, respectively. Hemoglobin levels were increased by 7.1%, 14.6%, 23.6%, and 32.3% at weeks 4, 8, 12, and 16, respectively. Leukocyte levels increased 6% at the end of fourth week and then decreased by 20.4%, 7.9% and 9.5% in the eighth, twelfth, and sixteenth weeks, respectively. At the same time intervals, MCV levels slightly increased by 6.1%, 3.4%, 3.0% and 1.3%, respectively. Thrombocyte levels increased by 13.2%, 34.1%, and 13.2% in the fourth, eighth, and twelfth weeks of r-HuEPO treatment but decreased 3.5% in the sixteenth week. Changes in hematologic parameters are given in Table 1.

Table 1. Effect of r- HuEPO treatment on hematologic parameters

	Baseline	**4th week**		**8th week**		**12th week**		**16th week**	
	38 patients	38 patients		38 patients		38 patients		38 patients	
	Total value	Total value	% impact	Total value	% impact	Total value	% impact	Total value	% impact
Rbc ($10^{12/L}$)	112.83± 38.2	116.33±39.4	3.1	126.1±41.3	11.9	136.64±48.6	21.1	148.45±35.3	31.6
Hct (%)	1052.1±112.8	1147.5±121.6	9.1	1217.1±117.4	15.7	1313.5±135.9	24.8	1383.5±143.4	31.5
Hgb(mg/dL)	344.4±60.4	368.8±63.2	7.1	394.8±68.7	14.6	425.6±72.4	23.6	455.6±74.6	32.3
Wbc ($10^{9/L}$)	298.3±45.2	316.1±46.8	6.0	237.3±41.7	-20.4	274.7±44.7	-7.9	269.89±42.9	-9.5
Mcv (fL)	3568.7±112.7	3785.4±124.9	6.1	3688.3±120.8	3.4	3676.5±135.4	3.0	3615.6±143.2	1.3
Plt (($10^{9/L}$)	8578±778.9	9712±801.5	13.2	11500.8±942.3	34.1	9710±843.1	13.2	8281±765.2	-3.5

Effect of r-HuEPO Administration on Biochemical Parameters

When we compare the results of analysis before and after r-HuEPO treatment, Alkalen phosphatase levels decreased 2.1% and 0.4% in the fourth and eighth weeks respectively, increased 8.4% in the twelfth week, then decreased 19.4% in the sixteenth week. Total cholesterol levels decreased by 3.7%, 4.7%, 1.5%, and 1.7% in the tested weeks, sequentially. Total protein levels increased 2% in the fourth week, decreased 2.2% in the eighth week, increased 2.6% in the twelfth week, and decreased 4.7% in the sixteenth week. Triglyceride levels decreased 2.1%, 8.5%, 9.5%, and 0.3% in the 4^{th}, 8^{th}, 12^{th}, and 16^{th} weeks respectively. Serum ferritin levels increased 1.6% in the fourth week, decreased 5.1% in the eighth week, increased 10.9% in the twelfth week, and decreased 1.1% in the sixteenth week. Changes in biochemical parameters are given in **Table 2**.

Table 2. Effect of r-HuEPO treatment on biochemical parameters

	Baseline	**4th week**		**8^{th} week**		**12^{th} week**		**16^{th} week**	
	38 patients	38 patients		38 patients		38 patients		38 patients	
	Value (mg/dl)	**Value (mg/dl)**	**% impact**	**Value (mg/dl)**	**% impact**	**Value (mg/dl)**	**% impact**	**Value (mg/dl)**	**% impact**
Alkalen phosphatase	52.5±5.5	51.39±6.3	-2.1	52±7.2	-0.9	56.9±8.7	8.4	42.3±6.5	-19.4
Total cholesterol	6478±437.6	6236±336.2	-3.7	6174±345.8	-4.7	6378±456.9	-1.5	6370±453.7	-1.7
Total protein	288.6±56.7	294.3±62.3	2	282.4±74.2	-2.2	296.1±72.4	2.6	275.1±68.6	-4.7
Triglyceride	7492±654.1	7331±595.4	-2.1	6858±656.8	-8.5	6784±702.3	-9.5	7469±775.8	-0.3
Serum ferritin	3562.5±158.4	3619.1±165.7	1.6	3382.1±156.3	-5.1	3951±179.6	10.9	3522.1±185.3	-1.1

DISCUSSION

Research on the end-stage renal failure patients has showed that the basic indications of anemia are low hemoglobin, erythropoietin and erythrocytes levels. The best way for recovering these patients is treatment with EPO [10]. Anemia is one of the basic symptoms of chronic kidney disease and it increases when renal function is lower than 50% of its normal function. According to research, 40% of renal failure patients have an anemia problem [11]. The most important factor which plays a role in renal anemia pathogenesis is insufficient production of EPO. The discovery of r-HuEPO has been very important in treating the problem of renal anemia. Researchers have evaluated the impact of recombinant human erythropoietin (r-HuEPO) therapy on the health-related quality of life (HRQL) in predialysis chronic renal disease patients with anemia. Patients entered a randomized, parallel-group, open-label clinical trial with follow-up evaluations over 48 weeks. Hematocrit levels were measured at baseline and monthly. HRQL was assessed at baseline and at weeks 16, 32, and 48 [12]. In Spain, a dialysis health quality group carried out research on 156 hemodialysis patients. At the end of the assessment, the health-related quality of life (HRQL) was found to have increased, which included measures of physical function, energy, cognitive function, social function, and life satisfaction, due to an increase in hematocrit levels [13]. In the present study, similar results were obtained in the patients. In vivo and in vitro research showed that r-HuEPO has maximum effects on the stimulation of erythroid burst-forming units and erythroid colony-forming units from bone marrow [14].

CONCLUSION

In conclusion, the effects of r-HuEPO treatment for 16 weeks increased the erythrocyte, hemoglobin, hematocrit levels and cured the anemia in hemodialysis patients. According to the results of our research, the health-related quality of life assessment included measures of renal anemia, physical function, energy metabolism and life satisfaction recovery in all patients.

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