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The effect of erythropoietin on glomerular filtration rate in patients with chronic kidney disease and mild anemia in terms of diabetic nephropathy

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Abstract

Introduction: Chronic kidney disease refers to the progressive and irreversible loss of renal function that ultimately results in ESRD (end-stage renal disease) and calls for conducting one of the alternative diseases or transplantation. Given the contradictory findings of the studies conducted previously and the lack of precise information on the effects of erythropoietin on the renal function of CKD patients and its effect on GFR, the present study was conducted to investigate these effects in CKD patients.
Method: The present study is a randomized clinical trial that was conducted to investigate the effect of prescribing erythropoietin on CKD patients' GFR. For this purpose, as many as 60 patients diagnosed with CKD entered the present study. These patients were in the second stage of CKD (with the GFR of 60-89). The patients were well explained and justified about the purpose and conditions of the study.
Findings: The mean of GFR levels in CKD patients was as follows: 74.95±5.81 two months after prescribing erythropoietin, 74.10±5.70 four months after prescribing erythropoietin, and 72.80±5.18 six months after prescribing erythropoietin. The comparison of the mean of GFR before the intervention, and the intervals of two months, four months, and six months after the intervention indicated that there was no significant statistical difference in these rates (P=0.089).
Discussion and conclusion : The general conclusion of the present study is that the reduction of GFR over a six-month study in patients receiving erythropoietin was less than that of the patients who did not receive erythropoietin. This indicates that the anemia treatment reduces GFR reduction rate in patients suffering from CKD.

Keywords: erythropoietin, glomerular filtration, anemia, diabetic nephropathy

Introduction

Chronic kidney disease refers to the progressive and irreversible loss of renal function that ultimately results in ESRD (end-stage renal disease) and calls for conducting one of the alternative diseases or transplantation. At the end stage of the renal disease, the patient is not able to conduct metabolic actions and maintaining the balance of fluids and electrolytes of the body, and a dangerous and deadly situation arises which is called uremia and it is followed by numerous complications (1, 2). The mortality rate of patients with chronic renal failure is much higher than that of the general population. Anemia is one of the most important complications of chronic renal failure, and its role as a mortality predictive factor in patients with hemodialysis and peritoneal dialysis has been well recognized (3-5). Anemia is one of the mortality

predictive factors in patients suffering from advanced chronic renal failure that leads to numerous pathophysiological disorders in these patients and brings about problems such as reduced tissue oxygenation, left ventricular hypertrophy, angina pectoris, heart failure, and immune system disorders. The most important reason of anemia in chronic renal failure is reduced erythropoietin. In the last fifteen years, owing to the wide use of *recombinant human erythropoietin in the treatment of* chronic renal failure patients, the complications of anemia have significantly reduced among these patients. Given the contradictory findings of the studies conducted previously and the lack of precise information on the effects of erythropoietin on the renal function of CKD patients and its effect on GFR, the present study was conducted to investigate these effects in CKD patients.

Method

The present study is a randomized clinical trial that was conducted to investigate the effect of prescribing erythropoietin on CKD patients' GFR. For this purpose, as many as 60 patients diagnosed with CKD entered the present study. These patients were in the second stage of CKD (with the GFR of 60-89). The patients were well explained and justified about the purpose and conditions of the study. They entered the study after providing informed consent, and their demographic information was recorded in the information forms. Then, as much as 5 cc of blood was drawn, and it was sent to the laboratory for measuring creatinine, BUN, and serum albumin. The patients were then randomly divided into two equal groups. The patients of the one group were prescribed erythropoietin for six months (the dose of erythropoietin was 25 U/Kg and it was subcutaneously every other day). The patients of the other group were not prescribed any erythropoietin (control group). The prescription of erythropoietin was conducted until the hemoglobin level reached 13 in males and 12 in females. The patients were followed up for 6 months. Each patient's GFR was measured every other two months by using the same method. Then the GFRs of before and after the prescription of erythropoietin as well as the GFRs of patients receiving erythropoietin and those of the control group were compared by using SPSS-22. For describing the data, descriptive statistics including frequency, percentage, mean, and standard deviation were used. For comparing the mean of GFR levels before and after the prescription of erythropoietin, dependent t-test was applied. For comparing the mean of GFR in both genders before and after the treatment, repeated analysis of variance was applied.

Findings

As many as 60 patients participated in the present study; 21were females and 39 were males, and their mean age was 58.85±6.20.

Table 1. The mean of GFR level before prescribing erythropoietin

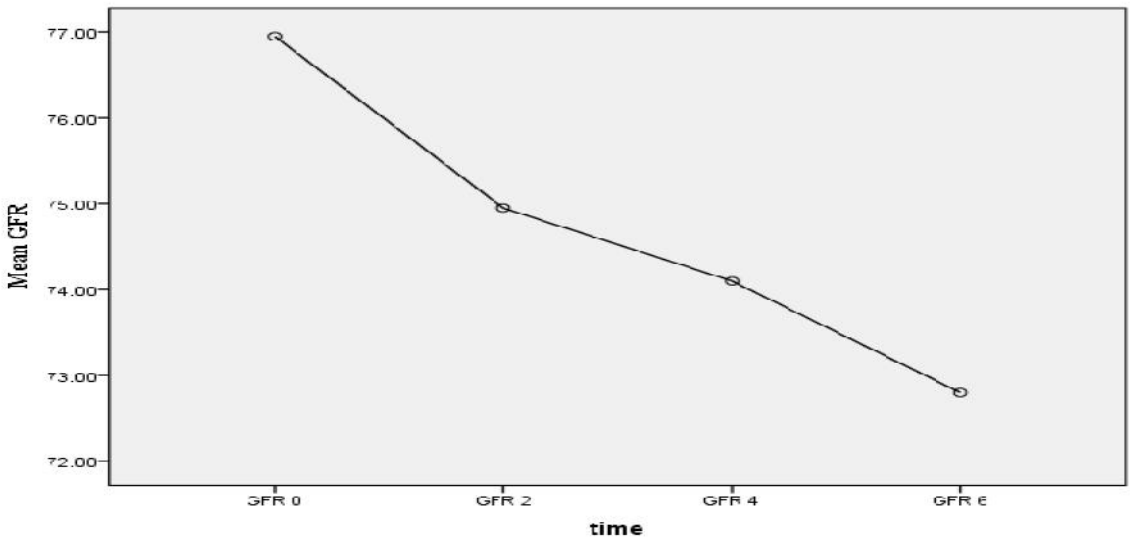
	Number	Minimum	Maximum	Standard Deviation±mean
GFR(mL/min/1.73 m^2)	60	65	85	76.95±5.97

According to the findings obtained, the mean of GFR levels in CKD patients was as follows: 74.95±5.81 two months after prescribing erythropoietin, 74.10±5.70 four months after prescribing erythropoietin, and 72.80±5.18 six months after prescribing erythropoietin (table 2).

Table 2. The mean of GFR in CKD patients after the prescription of erythropoietin

Index Intervention stage	GFR(mL/min/1.73 m^2) Standard Deviation ±mean
Before the intervention	76.95±5.97
Two months after the intervention	74.95±5.81
Four months after the intervention	*74.10*±5.70
Six months after the intervention	*72.80*±5.18

The comparison of the mean of GFR before the intervention, and the intervals of two months, four months, and six months after the intervention indicated that there was no significant statistical difference in these rates (P=0.089). However, reduced GFR level is higher and more remarkable after the first two months of intervention than that of the second and third two months (6).



Discussion

Anemia is one of the most important complications of chronic renal failure (7).Anemia is also one of the mortality predictive factors in patients suffering from advanced chronic renal failure that leads to numerous pathophysiological disorders in these patients and brings about problems such as reduced tissue oxygenation, left ventricular hypertrophy, angina pectoris, heart failure, and immune system disorders. The most important reason of anemia in chronic renal failure is reduced erythropoietin. Applying recombinant human erythropoietin in the treatment of these patients reduce the complications of anemia in such patients (8). In the present study, it was indicated that CKD patients' GFR was 76.95±5.97 before the prescription of erythropoietin. Michio et al (2015) conducted a study in Japantitled "Responsiveness to erythropoiesis-stimulating agents in non-dialysis CKD patients". In their study, the mean of GFR in the patients was 18.0±11.1 mL/min/1.72 m^2 before the treatment. Rossert et al (2006) conducted another study titled "Effect of early correction of anemia on the progression of CKD". In their study, the mean of GFR was 18.6±8.3 at the onset of the treatment (9). In the study conducted by Kazuhiko (2015) titled "Erythropoiesis-stimulating agent slows the progression of chronic kidney disease: a possibility of a direct action of erythropoietin", the mean of basic GFR was 12.6 in the patients (10). In the study conducted by Niles Videndal (2010) in Denmark titled "Erythropoietin down-regulates proximal renal tubular reabsorption and causes a fall in glomerular filtration rate in humans", the mean of GFR was 108 before the prescription of erythropoietin"(11). The present study was conducted on healthy individuals without underlying diseases (12). The findings of the present study indicate that the mean of GFR in CKD patients was as follows: 74.95±5.81 two months after prescribing *erythropoietin*, *74.10*±5.70 four months after prescribing erythropoietin, and 72.80±5.18 six months after prescribing erythropoietin. In the study conducted by Kazuhiko, the mean of GFR was 10.0 after 6 months of treatment. In the study conducted by Niles Videndal, the mean of GFR was 98 on the fourth day of erythropoietin prescription (13). The findings of the present study indicate that GFR level reduced after six months of prescribing erythropoietin in comparison to the period before the prescription of erythropoietin. However, this reduction is not statistically significant. In the study conducted by Niles Videndal, after prescribing erythropoietin, GFR level reducedon the fourth day in comparison to the basic level; it was 108 before the prescription, but reached 98 after prescribing erythropoietin.

In the study conducted by Kazuhiko, the GFR reduced after prescribing erythropoietin in comparison to that of the pre-prescription; it was 12.6 before the prescription, but reached 10 after prescribing erythropoietin(14 and 15)). Thus, the findings of the abovementioned studies are consistent with those of the present study.

Conclusion

The general conclusion of the present study is that the reduction of GFR over a six-month study in patients receiving erythropoietin was less than that of the patients who did not receive erythropoietin. This indicates that the anemia treatment reduces GFR reduction rate in patients suffering from CKD.

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