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Original Article

Comparison of the Therapeutic Effect of Erythropoietin Alone and with the Combination of L-Carnitine on Hemoglobin Levels in Hemodialysis Patients

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Abstract

Background: L-carnitine deficiency causes various pathological conditions such as muscle weakness and erythropoietin-resistant anemia in hemodialysis patients. The present study was conducted to compare the therapeutic effect of erythropoietin alone and with the combination of L-carnitine on anemia in hemodialysis patients

Method: In this clinical trial, 24 patients undergoing hemodialysis at Imam Ali Hospital were selected for the study. The eligible participants were randomly assigned into two equal groups: one group received erythropoietin treatment alone, while the other group was treated with a combination of L-carnitine and erythropoietin. Blood samples were collected from all patients for a complete blood count (CBC), and their hemoglobin levels were measured both before and after the treatment.

Results: The mean age of patients in the erythropoietin-only treatment group was 18.66±3.70 years, while in the group receiving both erythropoietin and L-carnitine, it was 23.83±5.70 years. A significant difference in age was found between the two groups (P=0.015). However, there was no significant difference in hemoglobin levels between the groups before treatment (P=0.327). After treatment, the mean hemoglobin levels in the erythropoietin group and the combination therapy group were 9.8±1.6 and 10.6±3.9 g/dL, respectively, with no significant difference observed between the two groups in terms of hemoglobin (P=0.324).

Conclusion: Our findings indicated that treatment with erythropoietin alone, as well as in combination with L-carnitine, did not lead to a significant improvement in blood parameters in hemodialysis patients with anemia.

Keywords: Erythropoietin; Hemoglobin; Hemodialysis; L-Carnitine

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Introduction

Chronic kidney disease (CKD) is considered as a permanent, stable and debilitating disease that is associated with many complications and problems (1, 2). In general, the goal in modern treatment is to establish kidney replacement therapy by dialysis or kidney transplant. Before the patient finds advanced symptoms of uremia (3).

Anemia is commonly seen in chronic kidney failure, which is caused by the accumulation of toxins in the bone marrow and the presence of erythropoietin inhibitors and hemolysis caused by uremia or blood remaining in the dialysis lines, bleeding events caused by vascular pathways, Sampling is for tests and elimination of blood caused by bleeding in the digestive tract (4, 5).

Anemia caused by chronic renal failure intensifies from the middle stage of chronic renal failure and becomes worse in parallel with the progress of renal failure (6). In the past, transfusion was used as the only major method of anemia treatment in hemodialysis patients despite the risks involved (7).

However, in 1989, Recombinant Human Erythropoietin (eHuEpo) or (Erythropoietin, EPO) became available to patients for the treatment of anemia caused by chronic kidney failure (8).

EPO is an effective and tolerable treatment with documented clinical benefits, which is recommended for hemoglobin less than 10-11 and hematocrit less than 30 (9). Timely diagnosis and treatment of anemia with erythropoietin and iron significantly reduces the mortality rate of patients and improves their quality of life (10).

Carnitine (trimethylaminobutyric acid) is an essential vitamin-like substance for the human body, which is involved in many metabolic processes such as regulating ketogenesis, controlling mitochondrial energy, and transferring long-chain fatty acids from the cytoplasm to the mitochondria for beta-oxidation (11).

Metabolic disorders such as oxidative stress and phospholipids transformation caused by carnitine deficiency can cause or develop anemia in ESRD patients (12).

Small molecule L-carnitine is filtered from the glomerular membrane and reabsorbed by the proximal tubule. Renal clearance of carnitine in normal conditions is 1-3 mm/min, but in hemodialysis its clearance is 100 ml/min. As a result, with the start of hemodialysis and the increase in its duration, carnitine decreases rapidly (13, 14).

According to research, taking carnitine supplements in hemodialysis patients reduces C-reactive protein (CRP) and low density lipoprotein (LDL) (15). Despite the studies, the effect of supplemental carnitine administration on dyslipidemia, cardiovascular function, muscles and anemia in people with ESRD and chronic hemodialysis is not clear. Hence, the present study was conducted with the aim of comparing the therapeutic effect of erythropoietin alone and with the combination of L-carnitine on anemia in hemodialysis patients.

Materials and Methods

In this clinical trial study, 24 hemodialysis patients were admitted to the dialysis department of Imam Ali Hospital. The inclusion criteria were being an adult with a history of at least 6 months of chronic dialysis, the absence of an active infectious or inflammatory disease, and age under 30 years. Dissatisfaction to participate in the study was the exclusion criterion. After obtaining written informed consent from the patient, the samples were selected according to the available method until the desired volume was reached and they were placed in two groups of treatment with erythropoietin alone and the combination of L-carnitine and erythropoietin.

First, a complete blood count (CBC) sample was taken from the patients and the hemoglobin level was measured in these patients. Then a group of patients (n=12) were treated with erythropoietin for three months. Erythropoietin was injected subcutaneously in the form of an ampoule of 2000 units in a volume of 0.5 cc during three dialysis sessions per week, and the patients received 6000 units of erythropoietin every week. In the second group (n=12), in addition to the 6000 units of erythropoietin they received per week, L-carnitine tablets in the amount of 20 mg based on weight with a maximum dose of one g daily for three months were given to the volunteers participating in the project. The changes in hemoglobin levels were recorded and analyzed monthly. The protocol of the study was approved by the ethics committee of Zahedan University of Medical Sciences with the ethics code of IR.ZAUMS.REC.1398.421.

Statistical analysis

Statistical analysis was performed by SPSS software version 22 (IBM, Chicago, USA). The quantitative and qualitative variables were indicated as mean±SD and number (percentage), respectively. Kolmogorov–Smirnov and Shapiro–Wilk tests were used to test for the distribution.

Fisher's exact test and t-test tests were used for analysis. *P*-value less than 0.05 was considered statistically significant.

Results

The distribution of gender in the treatment group with erythropoietin and the combination treatment group of oral erythropoietin and L-carnitine had no statistically significant difference with each other. This means that the two groups were homogeneous in terms of gender (*P*=0.5). The mean age of the patients in the erythropoietin treatment group and oral erythropoietin and L-carnitine combination treatment group was 18.66±3.70 and 23.83±5.70 years, respectively, and a significant difference was observed between the two groups (*P*=0.015) (**Table 1**).

Based on **Table 2**, the mean hemoglobin of hemodialysis patients before treatment, in the group treated with erythropoietin and group receiving erythropoietin with L-carnitine were 10.5±1.5and 9.9±1.4 g/dL, respectively, and there was no significant difference between the two groups in terms of hemoglobulin (*P*=0.327).

The mean hemoglobin of hemodialysis patients after treatment, in the group treated with erythropoietin and group receiving erythropoietin with L-carnitine were 9.8±1.6 and 10.6±3.9 g/dL, respectively, and there was no significant difference between the two groups in terms of hemoglobulin (*P*=0.324).

Table 1. Demographic data in two groups of patients

Variable	Group receiving erythropoietin	Group receiving erythropoietin with L-carnitine	*P*-value
Sex, female, n (%)	6 (50)	7 (58)	0.5
Age (year), mean±SD	18.66±3.70	23.83±5.7	0.015

N, Number; SD, Standard deviation

Table 2. Comparison between hemoglobin before and after treatment in two groups

Variable	Group receiving erythropoietin	Group receiving erythropoietin with L-carnitine	*P*-value
Hemoglobulin level before treatment	10.5±1.5	9.9±1.4	0.327
Hemoglobulin level after treatment	9.8±1.6	10.6±3.9	0.324

Discussion

The present study was conducted with the aim of comparing the therapeutic effect of erythropoietin alone and with the combination of L-carnitine on hemoglobin levels in hemodialysis patients.

According to our results, the hemoglobulin levels were not significantly different in the two groups receiving erythropoietin and the L-carnitine and erythropoietin group. Also, our findings showed that the mean hemoglobin after treatment with oral erythropoietin and L-carnitine is higher than before treatment.

Sedighi et al. conducted a study to investigate the frequency and causes of non-response to synthetic erythropoietin treatment in 530 patients with chronic kidney failure in 7 hemodialysis centers in Tehran. The results showed that receiving a sufficient dose of synthetic erythropoietin in patients with anemia undergoing hemodialysis did not affect the improvement of anemia in these patients(16), the findings of this study were consistent with the present study.

In the study of Tayibi Khosrowshahi et al., pa-

tients with chronic kidney failure were randomly divided into three groups. The first group was treated with subcutaneous erythropoietin 6000 units per week (erythropoietin group). The second group was treated with 500 mg of carnitine daily (carnitine group).

The third group was treated with subcutaneous erythropoietin 6000 units per week along with carnitine 500 mg daily (erythropoietin plus carnitine group). All three groups were treated for three months. The results of their study showed that a significant increase in hemoglobin was observed in the group receiving carnitine and erythropoietin (17).

Their results were inconsistent with current findings. Verrina et al. in a study that aimed to investigate the effect of carnitine supplementation on lipid profile and anemia in 24 children undergoing chronic dialysis, showed that receiving this dose of carnitine supplementation in patients improves the lipid profile and improves the symptoms of anemia (18), the findings of this study were contrary to our study.

The difference in sample size may be the cause of this discrepancy. Contrary to current findings, tthe results of the study by Higuchi et al, which was conducted to investigate the effect of levocarnitine on cardiac function and renal anemia in patients undergoing hemodialysis, showed that receiving levocarnitine in patients decreased red blood cell and hemoglobin(19). The difference in carnitine dosage and different methodologies in the two studies may be the possible cause of this discrepancy.

Conclusion

Our results showed that receiving erythropoietin alone and erythropoietin together with L-carnitine did not show a significant effect in improving blood indices in patients with anemia undergoing hemodialysis. Further multi-center studies with higher sample sizes are suggested in order to determine the effect of L-carnitine on blood hemoglobin levels in patients undergoing hemodialysis.

Conflict of interests

The authors declare that they have no conflict of interest.

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