

Parenteral Use of Iron and Ascorbic Acid (Vitamin C) in Haemodialysis Patients

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Abstract: The aim of this work was to study the effect of supplementation of iron and vitamin C therapy to hemodialysis patients, hoping that this therapy is effective in the treatment of anaemia in these patients. In this work, 40 stable hemodialysis patients suffering from severe to moderate anemia not receiving any form of replacement therapy (i.e., neither erythropoietin (EPO) nor iron), were selected and divided into two groups: The first group was treated by injection with ferrosac 100 mg/5ml twice a week for 3 months, and the second group was treated by injection with 500 mg/2.5ml of vitamin C in combination with 100 mg/5ml ferrosac twice a week for three months. The results of this study indicated that: There was a significant decrease in both urea and creatinine in hemodialysis patients after i.v. treatment of ferrosac alone (100 mg/5ml) "group I" and combined ferrosac (100 mg/5ml) with ascorbic acid (500 mg/2.5ml) "group II" twice weekly for 3 months. There was a significant increase in hemoglobin concentration and serum iron in both hemodialysis patient groups (I&II) after treatment, the highly increase markedly occurred in group II rather than group I after treatment. Moreover, there was a significant decrease in serum ferritin concentration in group I and a more pronounced decrease in group II after treatment, indicating the importance of vitamin C in decreasing the serum ferritin level and therefore the better correction of anemia.

Key words: Ascorbic acid; ferrosac; ferritin; hemodialysis.

INTRODUCTION

The kidney is responsible for maintaining both volume and ionic composition of the body fluids excreting fixed or non-volatile metabolic waste products such as creatinine, urea, uric acid and eliminating exogenous drugs and toxins. It also catabolizes small molecular weight proteins and is responsible for most

metabolic functions⁽¹⁾. The kidney is a major endocrine organ, since it produces renin, erythropoietin, 1,25 dihydroxy cholecalciferol, prostaglandins, and kinins. It also serves as a target organs for many hormones⁽²⁾. Renal failure is a clinico-biochemical syndrome resulting from failure of the kidney function. Renal failure may be acute but more commonly it is chronic.⁽³⁾ It is essentially

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characterized by a sudden decline in renal function, leading to retention of nitrogenous and other waste products, disordered hydrogen ion hemostasis and disturbances of extra-cellular fluid volume and composition⁽⁴⁾. Chronic renal failure (CRF) is the result of long-standing, gradually progressing renal disease seen often in people with hypertension; diabetes; and chronic inflammatory diseases. When patients develop end-stage kidney disease, there are a number of treatment modalities available. Hemodialysis is presently the most commonly used treatment for these patients.⁽⁵⁾

Anemia may be the first clue to kidney disease. Together with uremia of advanced renal failure, anemia can cause marked fatigue and reduced exercise tolerance. Although the uremia is improved by adequate dialysis, it persists with the hematocrit value ranging between 15% and 30%. Severe anemia is one of the major barriers to rehabilitation in such patients.⁽⁶⁾ The goal of therapy for iron deficiency anemia

is to supply sufficient iron to correct the anemia and replenish storage iron. The fact that 150 mg of iron are required to synthesize 1 g of hemoglobin can be used to approximate the amount of parenteral iron necessary for heme synthesis during the correction phase⁽⁷⁾.

It is now well established that intravenous (i.v.) iron supplementation is essential in the majority of patients to maintain an optimal iron supply to the bone marrow for red blood cell production.^(8,9) Vitamin C may be involved in tyrosin metabolism, microsomal drug metabolism, synthesis of epinephrine and anti-inflammatory steroid by the adrenals, folic acid metabolism, and leukocyte functions^(10,11). Absorption of Fe^{2+} is enhanced by simultaneous ingestion of vitamin C. Ascorbic acid, a reducing agent, is able to release iron from ferritin and mobilize iron from the reticuloendothelial system to transferrin. This leads to an increased iron availability.⁽¹²⁾ Vitamin C is an antioxidant. It protects against the harmful effects of pollution, prevents cancer, protects against infection, and enhances immunity⁽¹³⁾.

The aim of this work is to study the effect of combined supplementation of iron and vitamin C therapy to hemodialysis patients, hoping that this therapy is effective in the treatment of anaemia in these patients.

MATERIAL and METHODS

This study was performed on forty end-stage renal disease patients (28 males and 12 females) undergoing maintenance hemodialysis. Mean age was 50 years (range 22-70 years). All the patients studied had been on hemodialysis for at least one year before being included in the study.

All patients were dialyzed in Nephrology Unit, Medical Research Institute (Alexandria University, Egypt). All patients were anemic, blood hemoglobin averaged 7.64 g/dl and serum ferritin was less than 300 ng/dl. They were divided randomly into two groups:

Group I: Comprising 20 hemodialysis patients were intravenously infused ferrosac, i.e., ferric-hydroxide saccharate complex, manufactured by SPIMACO, Saudia Arabia,

100 mg/5ml ferrosac twice a week for three months.

Group II: Comprising 20 hemodialysis patients were supplemented intravenous, 100 mg ferrosac combined with 500 mg/2.5ml vitamin C twice a week for three months.

Preparation of the samples: Blood samples were collected before dialysis session by routine venupuncture using silicon red evacuated blood tubes without anticoagulant and EDTA tubes. Separation of serum was obtained by centrifugation at 500 g for 10 min. Serum was divided into aliquots and frozen and stored at -20oC until analyzed.

The prepared samples were used to determine the following parameters:

- 1- Serum urea using the method of Orsonneau *et al.*,⁽¹⁴⁾
- 2- Serum creatinine using the method of Rosano *et al.*,⁽¹⁵⁾
- 3- Serum albumin using the method of Doumas,⁽¹⁶⁾
- 4- Blood haemoglobin using the method of Dacie and Lewis^{·(17)}
- 5- Serum iron using the method of Burtis

and Ashwood⁽¹⁸⁾, and 6- Serum ferretin using the method of Zanella *et al.* ⁽¹⁹⁾

Measurements were carried out on Labo Med, Inc. USA spectrophotometer.

Results

Table 1 shows the mean values \pm S.E of blood urea, creatinine, albumin, haemoglobin, iron, and ferritin levels in patients group receiving intravenous ferrosac for 3 months (group I).

It has been found that there was a significant decrease in urea and creatinine levels after treatment, while there was no significant difference in albumin concentrations before and after treatment. A significant increase was found in haemoglobin and iron concentrations together with a significant decrease in ferritin levels in haemodialysis patients after treatment than before treatment with ferrosac. Table 2 shows the mean values \pm S.E of the same parameters mentioned above in patients group

receiving intravenous ferrosac and ascorbic acid (group II).

It has been found that there was a significant decrease in levels of urea and creatinine after treatment. Also there was a significant increase in albumin, haemoglobin, and iron concentrations together with a significant decrease in ferritin levels after treatment than before treatment in haemodialysis patients receiving combined ferrosac and ascorbic acid.

DISCUSSION

Renal failure disease has been documented to be associated with excessive production of free radicals, which leads to a state of oxidative stress. This condition may be raised due to the decrease of serum level of antioxidants like vitamins C and E. At the same time, significant and debilitating anemia occurs in patients with end-stage renal disease⁽²⁰⁾. Anemia of chronic disease (ACD) is often occurring in subjects suffering from chronic inflammatory disorders.

The underlying diversion of iron traffic leads to a withdrawal of the metal from the sites of erythropoiesis and the circulation to the storage compartment in the reticuloendothelial system, thus resulting (at the same time) in hypoferremia and hyperferritinemia.⁽²⁰⁾

Table (1): The statistical analysis of the studied parameters in hemodialysis patients before and after intravenous treatment with iron therapy (group I).

parameters		No. of cases	Mean	SE	P
Urea (mg/dl)	B	20	190.35	10.58	0.01*
	A		165.94	9.55	
Creatinine (mg/dl)	B	20	12.14	0.61	0.004***
	A		11.31	0.57	
Albumin (gm/dl)	B	20	3.50	0.07	NS
	A		3.63	0.09	
Hemoglobin Gm%	B	20	8.28	0.37	0.000***
	A		9.61	0.41	
Iron (ug/dl)	B	20	69.18	5.52	0.047*
	A		94.18	6.57	
Ferritin (µg/dl)	B	20	31.61	1.6	0.000***
	A		17.81	1.01	

P: probability of error

B: before treatment

*: statistically significant difference at <0.05

A: after treatment

***: statistically significant difference at <0.001

NS: not significant

Table (2): The statistical analysis of the studied parameters in hemodialysis patients before and after intravenous treatment with combined iron and ascorbic acid therapy (group II).

parameters		No. of cases	Mean	SE	P
Urea (mg/dl)	B	20	191.47	9.29	0.042*
	A		173.40	10.26	
Creatinine (mg/dl)	B	20	11.85	0.53	0.000***
	A		10.65	0.48	
Albumin (gm/dl)	B	20	3.45	0.086	0.000***
	A		3.70	0.082	
Hemoglobin (gm%)	B	20	7.61	0.22	0.000***
	A		11.97	0.26	
Iron (µg/dl)	B	20	60.17	5.36	0.047*
	A		118.93	9.68	
Ferritin (µg/dl)	B	20	24.80	1.69	0.000***
	A		10.15	1.12	

P: probability of error

B: before treatment

*: statistically significant difference at <0.05

A: after treatment

***: statistically significant difference at <0.001

The present study was done to evaluate the effect of administration of iron alone (ferrosac, 100 mg/5ml twice a week for 3 months), as well as, combined iron and ascorbic acid (100 mg/5ml ferrosac + 500 mg/2.5 ml vitamin C twice a week for 3 months) on serum urea, creatinine, albumin, blood hemoglobin, serum iron and ferritin. The study reveals significant differences in serum urea and creatinine levels in hemodialysis patients after i.v. treated with ferrosac alone and more pronounced significance if combined with ascorbic acid. Intravenous ascorbic acid can effectively improve the functional iron deficient erythropoiesis associated with iron overload in hemodialysis patients⁽¹¹⁾.

This study indicated a significant increase in hemoglobin concentration and serum iron in hemodialysis patients after i.v. treatment with ferrosac (100 mg/5ml) twice weekly for 3 months. While, a highly significant increase in hemoglobin concentration and in serum iron in

hemodialysis patients after treatment with combined ferrosac (100 mg/5ml) and ascorbic acid (500 mg/2.5ml) twice weekly for 3 months occurred. The increase markedly occurred after the combined administration and it was highly significant. Since vitamin C is one of the most important antioxidants existing in plasma, it increases intestinal iron absorption and induces iron mobilization from inert tissue stores, including reticuloendothelial system, and may improve iron availability. It has also a role in the enzymatic incorporation of iron into protoporphyrin for heme synthesis⁽²¹⁾

This was in accordance with the results of Giancaspro *et al.*,⁽²²⁾ who obtained only a partial correction of anemia and functional iron deficiency together with a reduction of serum ferritin levels within the treatment with i.v. vitamin C (500 mg) 3 times per week for 3 months, which indicated the importance of vitamin C in decreasing the serum ferritin level. Tarng *et al.*,⁽²³⁾ found that some patients had a dramatic response to intravenous ascorbic acid (300 mg, 3 times/week) with a

significant decrease in serum ferritin and significant increase in their hemoglobin, reticulocyte index, and serum iron concentration.

From this study, we recommend the administration of iron combined with ascorbic acid in hemodialysis patients suffering from anemia to increase iron absorption and improve hemoglobin concentration.

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