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Impact of vitamin C supplementation on serum ferritin level in hemodialysis patients

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ABSTRACT

Background: Iron deficiency anemia is common in patients on maintenance hemodialysis (HD). Serum ferritin is increased in HD patients. Vitamin C supplementation has shown to improve functional iron deficiency and anemia in HD patients.

Objectives: In this study we aimed to evaluate the effect of vitamin C supplementation on serum ferritin level.

Patients and Methods: In this randomized clinical trial, 39 HD patients were randomly assigned to receive routine therapy with (n = 24) or without (n = 15) vitamin C 500 mg IV twice a week after each dialysis session for 2 months. Changes in serum ferritin, iron, total iron-binding capacity (TIBC) and transferrin saturation (TS) before and after treatment were measured in each group.

Results: Serum ferritin levels before treatment in case and control groups were 1859 ± 1398.5 and 2567.5 ± 1907.8 ng/mL which was significantly decreased to 1084.8 ± 727.9 and 1313.5 ± 1151.5 ng/mL, respectively ($P=0.006$ and $P=0.007$). Serum iron, TIBC and TS did not change significantly in each group after treatment. Comparing the mean changes in serum ferritin, iron, TIBC and TS, there was no significant difference between groups.

Conclusions: Vitamin C had no effects on serum ferritin, iron and TS.

Implication for health policy/practice/research/medical education:

Iron deficiency anemia is common in patients on maintenance hemodialysis (HD). Serum ferritin is increased in HD patients. We observed that administration of vitamin C 500 mg IV twice a week had no effects on serum ferritin, iron and TS and might not improve anemia.

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1. Background

Iron deficiency anemia is common in patients on maintenance hemodialysis (HD) and may be associated with poor outcome, including higher death risk (1). The pathogenesis of anemia in chronic kidney disease is multifactorial. It can occur in HD patients due to shortened erythrocyte survival, continuing blood loss in the dialysis circuit, iron and other nutritional deficiencies, hemolysis, the presence of uremic inhibitors of erythropoiesis, and inadequate iron stores. Additionally frequently laboratory testing, interventional procedures

and gastrointestinal bleeding are responsible for anemia in HD patients (2,3).

Common laboratory tests used to diagnose iron deficiency in HD patients are serum ferritin and transferrin saturation (TS) (2). Serum ferritin is both an iron storage protein and an acute phase reactant. Serum ferritin concentration increases in the presence of inflammation, especially in HD patients (4,5).

Vitamin C plays an important role in the kinetics of iron metabolism and the utilization of iron for red blood cell formation. Low vitamin C levels have been reported

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in HD patients (6). Previous studies have shown improvement of anemia using vitamin C in HD patients (7,8). Vitamin C can decrease inflammatory markers (9) and hence by improving inflammation, it would improve ferritin level which results to improve anemia.

2. Objectives

In this study we aimed to evaluate the effect of IV vitamin C supplementation on ferritin, iron, TIBC and TS levels and anemia in HD patients.

3. Patients and Methods

In this randomized clinical trial, 39 HD patients for more than three months were randomly assigned to receive vitamin C (n=24) or no treatment (n=15). HD patients with serum ferritin >500 ng/mL were selected. Patients with a history of malignancy, active infection (hepatitis, tuberculosis), hyperparathyroidism (intact parathyroid hormone >3 upper limit normal) or evidence of hemolysis (reticulocyte count >2%) were excluded.

Patients in the intervention group received vitamin C 500 mg IV twice a week after each dialysis session for two months and group control received no injections. Before and after two months following treatment, serum ferritin, iron, total iron-binding capacity (TIBC) and TS were measured. Erythropoietin treatment as well as oral or IV iron treatment were similar between groups during the study period.

Before and after treatment, serum levels of iron and ferritin, TIBC and TS were measured and compared between groups. Mean percent changes in laboratory findings were also measured and compared between groups.

3.1. Ethical issues

The research followed the tenets of the Declaration

of Helsinki and its later amendments. Patients gave their written and informed consent to participate in this investigation by completing the consent form. This research has been granted by Ardabil University of Medical Sciences regarding financial budget, and has been approved by the university (ethics code # 0212).

3.2. Statistical analysis

All data were analyzed using SPSS 17 (version 17; SPSS Inc., Chicago, IL). Results are expressed as mean \pm SD or percentage. The chi-squared test was applied to compare categorical variables and independent t test to compare continuous variables. Laboratory findings before and after treatment in each group were analyzed using paired samples t test. Additionally, P values of less than 0.05 were considered statistically significant.

4. Results

Thirty-nine HD patients were enrolled in the study (vitamin C administration [n=24] or without using vitamin C [n=15] following dialysis sessions). Patients in case and control groups had similar age (54.29 ± 16.62 versus 52.20 ± 16.21 years, $P=0.11$) and gender distribution (males: 14 [58.3%] versus 9 [60%], $P=0.9$). Iron profile before and after treatment in each group is demonstrated in Table 1. Comparing the results before and after treatment in vitamin C and control group, only serum ferritin levels were significantly decreased ($P=0.007$ and $P=0.006$, respectively). Before treatment, ferritin levels were significantly higher in control group, but after treatment there was no significant difference between groups. Also, TIBC levels had no significant difference between groups before treatment, but following treatment, there was a significant difference. Changes in serum iron, ferritin, and TIBC and TS between groups also had no significant difference.

Table 1. Iron profile before and after treatment and mean percent change in each group

		Vitamin C, (n = 24)	Control, (n = 15)	P value
Serum Iron	Before	100.8 \pm 50.3	91.1 \pm 48.6	0.5
	After	108.6 \pm 26.4	101.9 \pm 48.00	0.27
TIBC	Before	309.4 \pm 237.2	294.9 \pm 185.6	0.08
	After	283.4 \pm 49.4	272.9 \pm 39.2	0.04*
Ferritin	Before	1859 \pm 1398.5	2567.5 \pm 1907.8	0.01
	After	1084.8 \pm 727.9	1313.5 \pm 1151.5	0.4
Transferrin saturation	Before	0.41 \pm 0.29	0.40 \pm 0.28	0.9
	After	0.42 \pm 0.09	0.41 \pm 0.14	0.7
Serum Iron change (%)		13.67 \pm 2.91	12.39 \pm 1.20	0.7
TIBC change (%)		-14.51 \pm 5.28	-17.27 \pm 11.09	0.3
Ferritin change (%)		-46.59 \pm 17.23	-47.52 \pm 17.36	0.8
Transferrin saturation change (%)		2.50 \pm 0.41	2.52 \pm 0.28	0.8

*P value is two-sided significant.

5. Discussion

Anemia is an important complication of CKD and HD which is multifactorial. It is recommended that vitamin C supplementation could improve anemia in HD patients. Vitamin C has multiple roles including antioxidant, immune function and improvement of the absorption of non-heme iron (10).

In this study we evaluated the effect of vitamin C supplementation on serum ferritin level and other markers. We found no significant difference of serum ferritin, iron, TIBC and TS among groups with and without vitamin C treatment.

Similar to our findings, Petrarulo et al and Ogi et al reported the improvement of functional iron deficiency anemia by vitamin C administration, which it had no significant effect on levels of ferritin, iron, TIBC and TS (11,12). Other studies were also unable to show any benefit in the administration of vitamin C (13).

However, recent studies have indicated that vitamin C reduces ferritin levels and improves anemia and increases iron utilization. Jalalzadeh et al (14) showed that intravenous vitamin C 500 mg following after each dialysis session reduces ferritin and improves TS. Similarly, Shahrbanoo and Taziki (15) reported vitamin C 300 mg intravenously following each dialysis session reduces ferritin levels, increases TS and improves responsiveness to erythropoietin therapy.

Reducing ferritin levels is important in HD patients to improve anemia and response to erythropoietin. Ogawa and colleagues (16) reported, serum ferritin levels <90 ng/mL and TS >20% provides proper iron status. They showed better results in anemia therapy in HD patients. Hence, finding the proper treatments to reduce serum ferritin in HD patients is important. It is possible that using constant doses of vitamin C and not increasing to the maximum dose could be a reason for our insignificant findings. Additionally, it is possible that vitamin C could not show its effects on the low duration of the therapy and longer duration may be necessary.

6. Conclusions

To conclude, vitamin C administration 500 mg IV twice a week had no effects on serum ferritin, iron and TS. Further studies are needed to evaluate the effective dosage of vitamin C on improving anemia and ferritin levels.

Study limitations

Small proportion of patients with high ferritin was the main limitation of our study.

Authors' contribution

BB contributed to study design, data collection, drafting

and clinical revision of article; AH contributed to data collection, data analysis, final approval of the version to be published; AZ contributed to study design and critical revision of the article; MJ contributed to data collection, data analysis and drafting the article; FA contributed to data collection, data analysis; and FK contributed to drafting the article, critical revision of the article and final approval of the version to be published. All authors read and signed the final manuscript.

Conflicts of interest

The authors declare no conflict of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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