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Study of Intravenous Vitamin C Effects on Serum Level of Phosphor in Hemodialysis Patients

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A B S T R A C T

Hyperphosphatemia is a common complication in patients with end stage renal failure that underwent hemodialysis, which, if untreated, can lead to renal osteodystrophy bone disease and vascular calcification, which is followed by cardiovascular complications in these patients has caused to increase cardiovascular mortality in these patients. The aim of this study was determine the intravenous vitamin C effects on serum level of phosphor in hemodialysis patients. In a double blind randomized clinical trial that performed in Internal Department of Medicine and Nephrology ward of Tabriz University of Medical Sciences on patients underwent hemodialysis, the effect of intravenous vitamin C on serum level of phosphor in hemodialysis patients evaluated. In this study, 60 patients with ESRD on hemodialysis were selected and the effect of intravenous vitamin C on serum level of phosphor in hemodialysis patients evaluated. Mean age of case group patients were 55.23±13.16 and in control group patients were 58.47±5.29 year. Mean calcium level case group patients at before intervention was 8.43±1.06 and in after intervention was 8.26±1.14. Mean calcium level of patients who underwent Vitamin C in after intervention was significantly decreased into the before intervention(P=0.049). Mean phosphor level case group patients at before intervention was 5.6±0.93 and in after intervention was 4.92±0.98. Mean phosphor level of patients who underwent Vitamin C in after intervention was significantly decreased into the before intervention (P<0.001). Significant difference was not found in calcium level of control group patients in after intervention into the before intervention (P=0.531). Significant difference was not found in phosphor level of control group patients in after intervention into the before intervention (P=0.492).

Introduction

Hyperphosphatemia is a common condition among patients with end-stage renal disease (ESRD) under hemodialysis, which could cause bone complications, renal osteodystrophy, vascular calcification, and consequently, severe cardiovascular complications, if left untreated (1). It also increases the rate of cardiovascular morality in these patients (2).

Considering that controlling the phosphorus level is difficult to achieve in dialysis patients, and that little progress has been made in controlling phosphorus level in the last 2 decades by (non)pharmaceutical means, and due to the fundamental significance of such a matter in dialysis patients, the present study was designed in search of a satisfactory way of controlling phosphorus levels in these patients.

Due to dietary restrictions, malnourishment, and vitamin C clearance from dialysis coils, hemodialysis patients are deficient in vitamin C, with a 50-70% decrease in the level of this vitamin after each dialysis session, which increases the need of body to get this vitamin. Considering that vitamin C could reduce C-Reactive Protein (CRP) levels, and that, the effect of reducing CRP on phosphorus reduction has been demonstrated in some studies (4), we sought to investigate the effect of this vitamin on the phosphorus levels of hemodialysis patients.

The objective behind this study was to investigate the effect of intravenous vitamin C in treating Hyperphosphatemia in patients under hemodialysis.

Materials and Methods

In a clinical trial conducted on patients under hemodialysis in Tabriz, the effect of intravenous vitamin C in treating Hyperphosphatemia was investigated.

After obtaining informed consents from the dialysis patients, 60 of them whose phosphorus levels were higher than 5.5 were included in the study using simple random sampling.

Both case and control groups were matched up in terms of age, gender, the time from which dialyses began, number of received dialyses, parathyroid hormone (PTH) level, duration of dialysis, calcium carbonate intake, and basic data.

The two groups, each consisting of 30 individuals, were determined randomly, using RandList software.

Informed consents were obtained from the patients, the forms of which are provided in the appendices.

In order to study the effect of intravenous vitamin C in reducing serum phosphorus levels in patients under hemodialysis, 60 patients whose phosphorus levels were higher than 5.5 (P>5.5) and who received hemodialysis for at least a period of 6 months, were selected without any age or gender restriction, and were randomly and double-blindly divided into two "case" and "control" groups. Patients from the case group received 500 mg of intravenous vitamin C after each dialysis session for a period of 2 months, and in control group, used placebo(water).

Inclusion Criteria

P > 5.5;

Receiving 6 months of dialysis or more.

Exclusion Criteria

- Patients with malignancy;
- Heart diseases;
- Respiratory illnesses;
- Liver diseases;
- Patients with weakened immune systems;
- Patients with a history of vitamin C consumption.

The patients' and control group's levels of PTH, Ca, CRP, urea, Cr, serum ph, and Hb were measured before the consumption of vitamin C and 2 months after it. No dietary change was made in the diets of patients under hemodialysis, and none of them were deprived of their prescribed medications during the administration of the study.

No change was made in the diet or medication of patients undergoing hemodialysis.

Ethical Considerations

Informed consents were obtained from the patients in writing, after providing them with the necessary information in a plain, intelligible language. The patients were assured that participation in the study was optional and confidential, and that the patients' names would not be mentioned under any circumstances. It should be noted that, full renal profile, parathyroid hormone (PTH), as well as blood cell functionality tests were carried out on the patients undergoing dialysis, monthly or quarterly. They were documented in patients' hospital records, with no new trial conducted. Furthermore, considering that these patients are deficient in vitamin C, no complications would arise as a result of the administration of vitamin C. Moreover, all vitamin C injections were offered to patients by the researcher, free of charge. This research project has not been presented at Tabriz University of Medical Sciences; rather, it was proposed as a thesis, the administration costs of which were covered entirely by the researcher.

Statistical Analysis

The collected data were analyzed by SPSS-17 statistical software. The collected data were expressed as percentage and mean ± SD. Continuous (quantitative) variables were compared by Independent samples and Paired t test. Categorical (qualitative) variables were compared by contingency tables and Chi-square test or Fisher's exact test. P-value ≤ 0.05 was considered statistically significant.

Results and Discussion

In this study, 60 patients with ESRD under hemodialysis were selected, and the effect of vitamin C on their phosphorus levels was examined.

The mean age of case and control groups' patients were 16.13±23.55 and 29.5±47.58 years, respectively (P = 0.330).
The case and control groups consisted of 20 and 21 male patients, respectively (P = 0.871).

The mean duration of hemodialysis for the case and control group patients were 31.3±5.25 and 63.2±5.25, respectively (P = 0.845).

The results from the clinical laboratory tests done on both groups of patients before and

after the study are presented in tables 1 and 2.

Hyperphosphatemia occurs in early stages of renal failure (RF) due to a decreased renal excretion of phosphorus (5).

In the early stages of renal failure, Hyperphosphatemia is mild; yet, as in continues to progress, and due to vitamin D deficiency and a reduction in the level of ionized calcium, parathyroid glands are activated, resulting in bone resorption and an eventual release of calcium and phosphorus from bones. The released calcium and phosphorus will be accumulated in body due to inadequate renal excretion of phosphorus (6). Hyperphosphatemia is one of the common conditions in dialysis patients, which could lead to secondary hyperparathyroidism. Hyperphosphatemia could be observed in 90% of dialysis patients, the lack of treatment of which could cause such complications as vascular calcification, phosphate deposition under the skin, and various bone diseases arising from hyperparathyroidism (7).

A single hemodialysis session is not significantly effective in removing phosphorus. Therefore, in addition to maintaining a dietary regimen, phosphate binders are used, which contain calcium acetate and calcium carbonate. However, the main complications of phosphate binders are hypercalcemia, the bonding of calcium and phosphorus, the aggravation of vascular calcification, and bone diseases with low degrees of reconstruction. Unfortunately, however, merely 44% of dialysis patients enjoy reasonable levels of phosphorus (6). Since phosphorus restriction in dialysis patients are not usually sufficient, phosphate binders are often prescribed to reduce dietary phosphorus absorption; which, despite being effective, cause numerous side effects, including increasing blood calcium levels and increasing the risk of aluminum toxicity. Furthermore, some of them, such as Sevelamer (Renagel/Renvela), and lanthanum carbonate (Fosrenol) are expensive (8-9). Therefore, some methods are required to reduce phosphorus levels in patients with RF.

Despite the advent of modern phosphate binders, filters with more adequate clearance, and quality enhancement of dialysis techniques, the elevation of blood calcium level is still regarded as one of the therapeutic complications in hemodialysis patients (10).

In a study conducted by Bower et al, NA resulted in a considerable decrease in serum phosphorus levels after 8 months of treatment; yet, it had no effect during the first 4 months of treatment. Consequently, they concluded that, the effective dose to achieve a significant effect is probably 1000 mg/daily, as nearly all patients had reached the 1000 mg/daily level after merely 8 months of treatment (11). In other studies, the minimum amount of consumed dose was in the range of 1000 mg/daily (12-14).

In another study conducted by Gholipour et al. at Gorgan University of Medical Sciences on patients with RF under hemodialysis, the effect of vitamin C on their blood phosphorus levels was investigated. The results suggested that the consumption of vitamin C in hemodialysis patients resulted in a significant decrease in their blood phosphorus levels (1).

In our study, the mean phosphorus levels in patients treated by vitamin C were 5.64±0.93 and 4.92±0.98 before and after intervention, respectively; pointing to a significant decrease in the mean phosphorus

level of patients under vitamin C after the intervention was made (P < 0.001). This suggests that, the administration of vitamin C has a significant effect in reducing the blood phosphorus level of these patients, which corresponds to the results obtained from the abovementioned study.

Table.1 Laboratory Finding of Patient at Between Two Groups

	Group		P
	Intervention	Control	
Ca Before	8.44±1.06	8.27±1.27	0.577
Phosphor Before	5.65±.94	5.36±1.47	0.368
ALK-P Before	456.14±359.71	359.83±218.14	0.217
iPTH Before	326.73±271.62	338.37±265.02	0.867
Hb Before	10.81±1.76	11.86±1.63	0.019
Serum Iron Before	54.85±17.53	71.40±30.24	0.014
TIBC Before	291.03±33.85	284.03±61.34	0.587
Cr Before	8.93±2.04	8.72±1.88	0.681
Ca After	8.26±1.15	8.20±1.37	0.855
Phosphor After	4.92±.98	5.49±1.45	0.081
ALK-P After	367.79±178.71	391.60±241.98	0.668
iPTH After	362.03±296.95	398.90±298.23	0.633
Hb After	11.21±1.82	12.00±1.89	0.107
Serum Iron After	85.59±36.74	75.97±40.77	0.355
TIBC After	293.37±53.33	317.20±110.30	0.291
Cr After	9.03 ±2.17	8.74±1.92	0.585

Table.2 Laboratory Finding of Patient in Two Groups at Before-After of Study

	Intervention Group		P
	Before	After	
Ca	8.44±1.06	8.26±1.15	0.049
Phosphor	5.65±.94	4.92±.98	<0.001
ALK-P	456.14±359.71	367.79±178.71	0.183
iPTH	326.73±271.62	362.03±296.95	0.291
Hb	10.81±1.76	11.21±1.82	0.146
Serum Iron	54.85±17.53	85.59±36.74	<0.001
TIBC	291.03±33.85	293.37±53.33	0.811
Cr	8.93±2.04	9.03 ±2.17	0.639
	Control Group		
	Before	After	
Ca	8.27±1.27	8.20±1.37	0.531
Phosphor	5.36±1.47	5.49±1.45	0.492
ALK-P	359.83±218.14	391.60±241.98	0.157
iPTH	338.37±265.02	398.90±298.23	0.223
Hb	11.86±1.63	12.00±1.89	0.414
Serum Iron	71.40±30.24	75.97±40.77	0.567
TIBC	284.03±61.34	317.20±110.30	0.074
Cr	8.72±1.88	8.74±1.92	0.935

In a study carried out by Aramwit et al. (2012) at Chulalongkorn University in Bangkok, Thailand, the effect of NA on hemodialysis patients' blood phosphorus levels was examined. The results revealed that, the consumption of NA resulted in a decrease in the blood phosphorus levels of these patients (15).

Yet in another study done by Locatelli at al. (2010) at the hemodialysis department of the Manzoni hospital in Lecce, Italy, the effects of different methods of reducing blood phosphorus levels, including MCI-196 (a phosphate binder), were investigated. The results indicated that, the consumption of MCI-196 resulted in a decrease in the blood phosphorus levels of these patients (16).

Various methods are available in order to control the phosphorus level in hemodialysis patients, among which are, controlling dietary regimens, and the consumption of phosphorus-level-reduction medications. In our study, the beneficial effects of intravenous vitamin C in reducing the phosphorus level in hemodialysis patients were demonstrated, in that, it resulted in a significant decrease in the blood phosphorus level in these patients.

Few suggestions includes for this study that considering the obtained results, it is suggested that intravenous vitamin C be used in hemodialysis patients in order to control their phosphorus levels, and that more studies be conducted using bigger sample sizes and longer periods of examination.

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