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ORIGINAL ARTICLE

Association of Intradialytic Hypertension and Dietary Elements: A Case-Control Study

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ABSTRACT

Background: Intradialytic hypertension (IDH) is defined as a rise in blood pressure during or immediately after hemodialysis that is associated with increased mortality in these patients. This study aimed to evaluate the association between IDH and the nutritional intake of trace and micromineral elements in maintenance hemodialysis patients.

Methods: Patients with chronic renal failure treated with maintenance hemodialysis were assessed in this case-control study. The participants who had IDH were selected as the case group. The Food Frequency Questionnaire (FFQ) was used to collect nutritional data; and then, the diets of the two groups were analyzed. Totally, 23 patients with IDH and 23 without IDH were included in the analysis.

Results: Although there was no significant difference in daily calorie intake between the two groups, the mean dietary intake of sodium, calcium, phosphorus, and total fat was significantly higher in the IDH group than the control group (p<0.05). In the group with IDH, the phosphorus intake was higher than the recommended amount, while the control group consumed significantly less oral phosphorus.

Conclusion: Advising limiting oral phosphorus and sodium consumption along with low-fat diet may help to reduce blood pressure in IDH patients and the subsequent mortality.

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Introduction

The incidence of chronic kidney disease (CKD) and end-stage renal disease (ESRD) is rising worldwide. Patients with ESRD finally need peritoneal dialysis or hemodialysis before a kidney transplant. Hemodialysis has serious complications such as intradialytic hypotension with an incidence of 5-40% (1), anaphylactoid reaction, transient ischemic events or stroke, and hemostasis problems (2). Although hemodialysis is life-saving for renal

failure patients, variability in blood pressure (BP) measurement during and between dialysis is a risk factor for increased cardiovascular mortality in patients with ESRD (3). More studies have investigated decreasing BP during dialysis, but few studies have been conducted on intradialytic hypertension (IDH). IDH is defined as a paradoxical rise in systolic blood pressure (SBP) of at least 10 mmHg from pre- to post-dialysis (4) or elevation in mean arterial blood pressure of 15 mmHg during or immediately after hemodialysis (5); it is associated with higher home BP, measured by ambulatory blood pressure monitoring (6), hospitalization, and death in hemodialysis patients.

There are three mechanisms in the pathophysiology of IDH. The first one is extracellular volume overload in IDH patients (7). The second one, which is investigated as a predominant mechanism of IDH, is vasoconstriction mediated by endothelin (1ET-1) (8), and the last mechanism is fluctuations of dialysate sodium composition that induce fluid movement from various intracorporal compartments (9). The association between dietary intake and BP was revealed in previous studies. For example, some researches confirmed the relationship between high dietary sodium and hypertension (10, 11) and the beneficial effect of a potassium-rich diet on atrial blood pressure and cardiovascular outcome (12). Also, there is an inverse association between dietary calcium intake and BP (13). These investigations eventually led to creating a nutrition guideline called Dietary Approaches to Stop Hypertension (DASH). DASH is an eating pattern; a diet rich in fruits, vegetables, whole grains, and low-fat dairy with reduced sodium, and saturated and total fat content is introduced as an appropriate diet for hypertension (14). Also, DASH includes advances in consuming food rich in vitamin C and folate; minerals like potassium, calcium, magnesium, phosphorus; and amino acids such as arginine and different substances with organic movement in human cells (flavonoids and inorganic nitrate) (15, 16). Researches revealed that DASH diet intervention would decrease up to 13% in the 10-year Framingham risk score for cardiovascular events in hypertension patients (17). To the best of our knowledge, no studies have assessed the relationship between IDH and dietary mineral intake. Therefore, the objective of this study was to evaluate the effect of dietary minerals such as sodium, potassium, and calcium on IDH as an increased mortality risk in hemodialysis patients.

Materials and Methods

All patients with chronic renal failure treated with maintenance hemodialysis for at least six months at various dialysis centers affiliated with Shiraz University of Medical Sciences (SUMS) from September 2019 to February 2020 were eligible for inclusion in this cross-control study. Exclusion criteria were age >70 or <18 years; malignancy; acute infectious diseases; evidence of heart failure, or acute cardiovascular and cerebrovascular diseases. Also, those whose antihypertensive medication or erythropoietin stimulating agents changed in the past month were excluded.

Brachial artery from a side that did not have an arterio-venous fistula (AVF) was measured before, during, and after dialysis via a mercury sphygmomanometer. Participants were asked to have an at least a 5-minute rest in a seated position before BP measurement. Systolic and diastolic pressures were recorded to the nearest 5 mmHg. Patients with SBP of at least 10 mmHg from pre- to post-dialysis or elevation in mean arterial blood pressure of 15 mmHg during or right after hemodialysis in at least 4 out of 6 sessions of dialysis were selected as the IDH group. The participants whose SBP did not rise were chosen as the control group (participants without IDH).

A total of 235 patients with chronic renal failure and on maintenance hemodialysis were assessed for this study; finally, 46 participants were enrolled in the analysis; 23 participants had IDH. This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all research protocol, informed consent form, and the questionnaires were approved by the Ethics Committee of the Shiraz University of Medical Science, Shiraz, Iran (IR.SUMS.MED.REC.1397.452). All information was collected after obtaining the permission of the participants. Data of demographic characteristics and personal medical history, such as the participants' age, sex, smoking habits and alcohol consumption; history of diabetes mellitus, hypertension and cardiovascular diseases; length of the dialysis session, and administration of any type of drugs, were collected by trained physicians. Anthropometric measurements were taken by a trained nutritionist using a standard protocol. Both pre- and post- hemodialysis weight was measured to the nearest 0.1 kg using mechanical scales and height to the nearest 0.5 cm using a stadiometer; while the participants were wearing light clothes with no shoes. Subsequently, body mass index (BMI) was calculated as the ratio of weight/hight^2 (kg/m^2).

To study the participants' diet in terms of daily intake of energy and nutrients (carbohydrates, proteins, fats, water- and fat-soluble vitamins, and minerals), a 168-food-item dish-based food frequency questionnaire (FFQ) was used (18).

The questionnaire provided information about the frequency of the participant's consumption of dietary items over the previous year and was completed through face-to-face interviews conducted by expert dietitians. The FFQ was then analysed by Nutritionist IV diet analysis software modified for Iranian foods (version 3.5.2; 1994, N-Square Computing, First Data Bank Division, The Hearst Corporation, San Bruno, CA, USA). The daily intakes of nutrients were finally compared with the relevant recommended daily intakes (RDAs) and tolerable upper limit (UL) intakes provided for this age group. Previous researches have shown that the Food FFQ is valuable for assessing dietary intakes in dialysis patients (19, 20).

In order to justify several blood parameters related to the CKD in both groups, the data of blood flow rate, ultrafiltration, hemoglobin, blood urea nitrogen, creatinine, sodium, potassium, calcium, phosphorous, serum albumin, para thyroid hormone, and 25-hydroxyvitamin D3 from the previous documented history of all patients were obtained. All analyses were performed using the Statistical Package for the Social Sciences (SPSS, software, version 21, SPSS Inc., Chicago, IL, USA). The results were shown as mean±SD. Shapiro-Wilk test was used to test the normal distribution in each group. Descriptive statistics and independent t-test or its nonparametric Mann-Whitney-U-test were used to analyze quantitative variables. The one-sample t-test was utilized for comparing the mean intake with the RDA of the daily dietary elements. Fisher's exact test was applied for qualitative variables. In all analyses, P values <0.05 were considered indicative of statistical significance.

Results

Out of 46 participants, 33 (71.7%) were male, and 13 (28.3%) were female. The mean age of the patients was 53±11.3 years, and the causes of renal failure in the participants were high blood pressure (N=21), diabetic nephropathy (N=16), polycystic kidney disease (N=4), and other diseases or unknown etiology (N=5). There was no significant difference in the causes of renal failure between the two groups (p>0.05). Demographic, clinical, biochemical, and hemodialysis session characteristics of the study population were listed in Table 1. The mean SBP after hemodialysis in the IDH group (160±8.2 mmHg) was significantly higher than SBP in the control group (p<0.001). The mean serum level of 25-hydroxy vitamin D (25OHD) was considerably lower in the patients with IDH (32.20±17.44 ng/mL) than those without IDH (43.50±16.20 ng/mL).

Table 1: Baseline characteristics of enrolled participants.

Variable[a]	IDH group	Control group	*P* value
Male/Female	16/7	17/6	0.5
Age (y)	50±13.32	56±8.07	0.071
Hypertension (N, %)	23(100%)	20(87%)	0.117
Diabetes mellitus (N, %)	8(34.8%)	10(43.5%)	0.382
Cardiovascular diseases (N, %)	2(8.7%)	1(4.3%)	0.5
Pre-hemodialysis SBP (mmHg)	144.13±8.3	136.52±15.4	0.062
Pre-hemodialysis DBP (mmHg)	88.26±7.8	84.5±14.37	0.284
Post-hemodialysis SBP (mmHg)	160±8.2	120.6±11.5	<0.001
Post-hemodialysis DBP (mmHg)	96.52±8.31	77.4±11	<0.001
Blood flow rate (mL/min)	277.8±23.7	285.2±30.7	0.366
Ultrafiltration (L)	2.32±0.8	1.8±0.9	0.066
eKt/V	1.34±0.16	1.4±0.18	0.183
Dialysis session length (h)	3.7±3.6	3.5±2.9	0.301
Pre-hemodialysis weight (Kg)	71±16.1	74.5±18.8	0.518
Post-hemodialysis weight (Kg)	69±16	72.5±19	0.453
Hemoglobin (g/dL)	10.65±1.7	11.4±1.6	0.129
Blood urea nitrogen (mg/dL)	53.7±19.75	50±17.2	0.502
Creatinine (mg/dL)	7.1±2.5	6.71±2.11	0.574
Sodium (mmol/L)	138.04±3.21	138.04±3.21	>0.5
Potassium (meq/L)	4.82±0.75	4.95±0.54	0.489
Calcium (mg/dL)	8.7±0.91	8.6±0.7	0.725
Phosphorous (mg/dL)	5.34±2	4.54±0.93	0.08
Serum albumin (g/dL)	3.7±0.7	4±0.4	0.068
Para thyroid hormone (ng/L)	381.34±389.22	322.3±259.5	0.548
25-hydroxyvitamin D3 (ng/mL)	32.20±17.44	43.50±16.20	0.028

[a]Data were reported as mean±standard deviation or number. SBP: Systolic blood pressure. DPB: Diastolic blood pressure.

Table 2: Comparison of daily dietary elements among IDH and control groups.

Daily dietary elements[a]	IDH group	Control group	*P* value
Total calorie intake/day	1864.8±867.2	1538.5±694.7	0.16
Energy (Kcal/kg)	28.63±14.7	22.24±10.7	0.287
Protein (g)	55.55±26.75	43.02±20.64	0.082
Total fat (g)	77.48±35.2	56.85±37.1	0.019
Cholesterol (mg)	272.23±215.01	157.24±89.75	0.04
Saturated fat (g)	22.86±12.35	17.21±13.26	0.038
Oleic acid (g)	24.83±10.56	18.72±11.93	0.034
Sodium (mg)	4827.85±2321.26	2836.45±1748.88	0.002
Potassium (mg)	3538.18±1320.07	1976.81±1406.10	0.17
Calcium (mg)	948.81±400.78	699.48±343.94	0.029
Phosphorous (mg)	1003.32±444.16	762.61±309.64	0.039
Vitamin D (mcg)	1.52±1.55	0.71±0.73	0.01

[a]Data were reported as mean±standard deviation.

Table 3: Comparison of daily dietary elements with recommended values for hemodialysis patients.

Daily dietary elements[a]	Recommended value	IDH group	*P* value	Control group	*P* value
Sodium (mg)	2000	4827.85±2321.26	<0.001	2836.45±1748.88	0.047
Calcium (mg)	2000	948.81±400.78	<0.001	699.48±343.94	<0.001
Phosphorous (mg)	900	1003.32±444.16	0.267	762.61±309.64	0.045
Vitamin D (mcg)	15	1.52±1.55	<0.001	0.71±0.73	<0.001

[a]Data were reported as mean±standard deviation or number.

There was no significant difference between the two groups in hemodialysis session characteristics such as blood flow rate, ultrafiltration, eKt/V, dialysis session length, pre-hemodialysis weight, and post-hemodialysis weight (p>0.05).

Table 2 compares daily dietary elements between IDH and control groups. There was no difference in the total calorie intake as well as kcal/kg between the two groups (p=0.28 and p=0.16, respectively). There was a significant difference between the two groups in sodium, calcium, and phosphorus of the food. The average of these elements in the group with IDH was higher than that without IDH (p<0.05). There was no significant difference between the two groups in protein and potassium consumption. In addition, the difference in protein intake in the group with IDH with an average of 55.55 g/day was higher than the control group with an average of 43.02 g/day. In addition to total fat, which made a significant difference between the two groups (p=0.019), saturated fat, cholesterol, and oleic acid also had significantly higher means in the group with IDH. Vitamin D with a mean of 1.52 mcg/day in the IDH group was significantly different from the control group with an average of 0.71 mcg/day (p=0.01).

In both groups, the sodium intake was more than the recommended amount, but the amount eaten by the IDH group was significantly higher (p<0.001). In the group with IDH, the phosphorus consumption was more than the recommended amount, but there was no significant difference (p=0.267), but in the group without IDH, they consumed significantly less phosphorus (p=0.045) (Table 3).

Discussion

This study assessed two groups of hemodialysis patients with and without IDH for daily dietary elements. The results showed that the mean daily dietary intake of sodium, fat, and phosphorous was more than the control group. Similarly, daily protein intake was higher in the IDH group than in the control group; however, it was not insignificant. Meanwhile, the amount of daily calorie intake did not have a significant difference between the two groups.

A previous study suggested a close relationship between dietary sodium intake and blood pressure, and even more significantly in renal failure and dialysis patients (21).

A high salt diet could increase blood pressure by modulating the activity of the sympathetic nervous system, provoke an expansion in circulating volumes, and adverse remodeling of the arterial wall due to an increase in the wall tension resulting in arterial stiffness (22, 23). The present study revealed remarkable sodium intake in hemodialysis patients with IDH. Because the main causes of developing IDH are increased extracellular volume, and sodium intake (24), aggressive control of extracellular volume and dietary sodium intake can normalize blood pressure in patients with chronic hemodialysis. Also, it is essential to consider the simultaneous

effect of other elements of the diet like potassium, calcium, and magnesium to understand the impact of diet on blood pressure; because they may affect each other. For example, high sodium intake can alter calcium excretion by increasing intravascular volume, which is associated with an increase in SBP (24, 25). However, Stamler et al. and Weaver et al. showed small benefits of lower-sodium intakes in controlling BP (10, 26); it could be due to the effects of the minerals on each other and their different effects which are not easily discernible.

In this study, serum phosphorus level was higher in the IDH group than in the control group; however, it was not significant. Likewise, dietary phosphorus was significantly higher in the IDH group than in the control group. However, the blood level of calcium was not significantly different; as dietary calcium intake was significantly higher in the IDH group. Higher phosphorus intake in combination with higher dietary calcium intake is associated with calcium deposition and vascular stiffness in IDH patients, and it is an independent risk factor for resistant hypertension during hemodialysis and is associated with increased mortality (27). This relationship could be due to an increase in fibroblast growth factor-23 (FGF-23) levels, which are directly related to hemodialysis patients' mortality. FGF-23 increases the urinary phosphate excretion and inhibits renal production of 1,25-dihydroxy vitamin D, thus helping to reduce hyperphosphatemia in patients with kidney disease (28). Evaluation of vascular stiffness and calcification in IDH patients can help to clarify this relationship. Although a previous study showed that higher phosphorus intake is associated with lower blood pressure levels in hemodialysis patients, these potential benefits appear to be limited to nutritional phosphorus from dairy products (29).

There is a limitation in the consumption of dairy products in hemodialysis patients; therefore, phosphorus intake is not probably associated with reducing blood pressure in these patients. The relationship between the source of phosphorus intake and hypertension in dialysis patients should be investigated in future studies. Effective removal of phosphorus by hemodialysis depends on its biphasic excretion (rebound of plasma level after reaching nadir level) in the body, limitation of oral phosphorus intake, and elimination of protein malnutrition which increases the absorption of dietary phosphorus (30, 31). Therefore, patients with IDH are recommended to limit the consumption of dietary phosphorus; while improving malnutrition and increasing albumin levels, because serum albumin levels have an inverse association with high diastolic blood pressure and mortality in dialysis patients (32, 33).

Vitamin D has the potential effect on controlling blood pressure in several ways; inhibiting the Renin-Angiotensin-Aldosterone-System (RAAS), regulating the vascular tone, reducing the impact of glycation end products on endothelium, improving the effect of nitric oxide (NO) system, and increasing the production of prostacyclin (34-36). Vitamin D deficiency is prevalent in dialysis patients due to increased FGF-23 and decreased renal tissue function, so previous studies have supported using vitamin D supplements in these patients (36). The dietary vitamin D intake was significantly lower than the recommended amount in both groups in the current study. It was remarkable that although dietary vitamin D intake in the IDH group was higher than the control group, serum vitamin D levels were lower in the IDH group, so patients with IDH may have lower vitamin D absorption, or vitamin D production is reduced due to higher phosphorus intake and subsequent increased FGF-23. Notably, none of the patients received vitamin D supplementation as 25 hydroxyvitamin D3 (37). The mean of fat intake in the group with IDH was significantly higher than the control group. Several studies demonstrated higher intakes of total fat, saturated fat, and cholesterol to be risk factors for hypertension, and low-fat dairy foods to be associated with lower blood pressure (38, 39). The most important limitation of our study was the lack of correct answers about the food consumed by the patients at the time of completing the questionnaire. And the most important strength was that we investigated for the first time the relationship between the consumption of trace elements and minerals in the diet of patients under hemodialysis with IDH.

Conclusion

The present study showed that IDH patients consumed more dietary sodium, phosphorus, and fat; while limiting the consumption of these nutritional elements is recommended. The above findings suggest that adherence to a diet based on the DASH in dialysis patients with IDH is lower than in patients without IDH. Therefore, recommending the DASH to IDH patients could be an effective treatment strategy for reducing the risk of cardiovascular events.

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Authors' Contribution

P.M. Mahmoudi and M. Shafiee were responsible for designing and interpreting data and writing the manuscript. M. Ekramzadeh, S.A. Zomorodian and M. Ranjbar Zahedani contributed to writing the manuscript, and E.A. Dehkordi analyzed the data. M.H. Shirazi contributed to the data acquisition and drafting of the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

None declared.

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