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Relationship between diet and calcium-phosphorus disorders in maintenance hemodialysis patients

Związek pomiędzy dietą a zaburzeniami gospodarki wapniowo-fosforanowej u chorych przewlekle hemodializowanych

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Keywords

chronic kidney disease, hemodialysis, diet, hyperphosphatemia

Słowa kluczowe

przewlekła choroba nerek, hemodializa, dieta, hiperfosfatemia

Summary

Introduction. Calcium-phosphorus disturbances and related cardiovascular complications are one of the causes of increased morbidity and mortality in patients with chronic kidney disease (CKD). Hyperphosphatemia, and elevated calcium-phosphorus products are considered to be independent risk factors for mortality. A diet with limited phosphate content is an element in the prevention and treatment of calcium-phosphate disturbances.

Aim. The aim of this study was to evaluate the relationship between diet and calcium-phosphorus disturbances in patients with chronic kidney disease treated with hemodialysis.

Material and methods. The study was conducted at the Department of Nephrology, Transplantology and Internal Diseases MUG. The study included 45 hemodialysis (HD) patients aged 24 to 84 years (mean 56.9). In all patients serum concentrations of phosphorus, calcium, parathyroid hormone (PTH) and alkaline phosphatase were measured. The calcium-phosphorus product, and Kt/V were calculated. The diet of patients was assessed by 24-hour recall. Statistical analyzes were performed using Statistica vs 10.

Results. In 66.7% of patients hyperphosphatemia was observed. In 17.7% of patients normal levels of serum calcium, and in 77.78% hypocalcaemia was observed. Elevated calcium-phosphorus products were found in 26.67%, and the recommended level of PTH was observed in only 24.44% of patients. There was no relationship between diet and calcium and phosphorus concentration in the study group. In the study, a negative correlation between Kt/V and the serum concentration of phosphorus and the value of the calcium-phosphate product was observed. In addition, the results showed a positive correlation between the low intake of phosphates and an inadequate intake of protein and energy.

Conclusions. Adequate dialysis improves calcium and phosphorus disorders. Dietary restrictions have a marginal effect on serum phosphorus levels in patients on hemodialysis. A significant reduction of phosphates in the diet may be a risk factor for low calorie and protein intake, which in turn can lead to malnutrition.

Conflict of interest
Konflikt interesów

None
Brak konfliktu interesów

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Streszczenie

Wstęp. Zaburzenia gospodarki wapniowo-fosforanowej i związane z nimi powikłania sercowo-naczyniowe stanowią jedną z przyczyn zwiększonej chorobowości i śmiertelności u chorych na przewlekłą chorobą nerek (PChN). Hiperfosfatemia oraz podwyższony iloczyn wapniowo-fosforanowy są uznawane za niezależne czynniki ryzyka zgonu. W celu zmniejszenia śmiertelności wdrażana jest profilaktyka i leczenie zaburzeń gospodarki wapniowo-fosforanowej, których częścią jest dieta z ograniczeniem fosforu.

Cel pracy. Celem pracy była ocena wpływu diety na zaburzenia gospodarki wapniowo-fosforanowej u chorych na PChN leczonych powtarzanymi hemodializami.

Materiał i metody. Badanie zostało przeprowadzone w Klinice Nefrologii, Transplantologii i Chorób Wewnętrznych GUMed. Uczestniczyło w nim 45 pacjentów w wieku średnio 56.9 +/- 17,5 lat (zakres 24-84). W badaniu wykonano następujące oznaczenia biochemiczne, takie jak stężenie w surowicy: fosforu, wapnia, parathormonu i aktywność fosfatazy

alkalicznej. Obliczono również iloczyn wapniowo-fosforanowy oraz uwzględniono wskaźnik adekwatności dializy (Kt/V). Badania biochemiczne, iloczyn wapniowo-fosforanowy oraz wskaźnik adekwatności dializy porównano do wyników analizy diety pacjentów ocenionej za pomocą wywiadu 24-godzinnego. Analizę statystyczną przeprowadzono za pomocą programu Statistica vs 10.

Wyniki. U 66,7% badanych osób zaobserwowano hiperfosfatemię. Prawidłowy poziom wapnia w surowicy zaobserwowano jedynie u 17,7% osób. Dominującym odchyleniem w badaniach laboratoryjnych była hipokalcemia (77,8% badanych). Podwyższony iloczyn wapniowo-fosforanowy stwierdzono u 26,67%, a zalecany poziom parathormonu – jedynie u 24,4% pacjentów. Nie stwierdzono związku pomiędzy dietą a zaburzeniami gospodarki wapniowo-fosforanowej w badanej grupie. W przeprowadzonym badaniu zaobserwowano ujemną korelację między Kt/V a stężeniem fosforu w surowicy oraz wartością iloczynu wapniowo-fosforanowego. Dodatkowo stwierdzono dodatnią korelację pomiędzy niskim spożyciem fosforanów i nieadekwatną podażą białka i energii.

Wnioski. Adekwatna hemodializoterapia poprawia zaburzenia gospodarki wapniowo-fosforanowej. Restrykcje dietetyczne mają marginalny wpływ na stężenie fosforanów u chorych hemodalizowanych. Znaczne ograniczenie fosforanów w diecie może stanowić czynnik ryzyka niskiego spożycia białka i kalorii, co w konsekwencji może prowadzić do niedożywienia.

INTRODUCTION

Approximately 11% of the world's population suffers from chronic kidney disease (CKD). Maintenance hemodialysis (HD) is the dominant method of treatment of end stage renal disease in Poland. Cardiovascular diseases are one of the main causes of morbidity and mortality in patients with CKD. Bone mineral metabolism disorders and inflammation are pathological conditions that involve increased cardiovascular risk in hemodialysis patients. Both hyperphosphatemia and elevated calcium-phosphorus product (Ca-P) are independent risk factors for death. In addition, secondary hyperparathyroidism is associated with an increase in mortality. The pharmacology, adequate dialysis, and a low-phosphate diet, are elements of the treatment of calcium-phosphorus disturbances (1).

Maintaining a restricted intake of phosphorus is extremely difficult without the reduction of the content of protein and energy in the diet. This is extremely disadvantageous, especially in patients with risk factors for malnutrition. Recently, controversy was aroused around the benefits and risks resulting from dietary restrictions in hemodialysis patients. This has prompted us to examine the relationship between diet and the Ca-P disorders in a population of patients on hemodialysis (2).

AIM

The aim of this study was to evaluate the relationship between diet and calcium and phosphorus disorders in patients treated with hemodialysis.

MATERIAL AND METHODS

Patient characteristics

The study was performed in 45 patients treated with chronic hemodialysis in the Department of Nephrology, Transplantology and Internal Medicine MUG. The research obtained the consent of the Independent Ethics Commission MUG No. NKBBN/75/2013. The study was performed in a group of 45 patients (22m/23f), mean age 56.9 ± 17.5 (range 24-87) years. The causes of CKD in the study group were: glomerulonephritis (n = 14), diabetic nephropathy (n = 8), hypertensive nephropathy (n = 3), chronic pyelonephritis (n = 3), polycystic kidney disease (n = 3), ischemic nephropathy (n = 2), renal hypoplasia (n = 1), and others (n = 8). In the study group 13 patients suffered from insulin dependent diabetes mellitus. The patients were on maintenance hemodialysis for 93.9 ± 89.2 (range 2.3-317.3) months. The hemodialysis prescription was as follows: three times per week, mean dialysis session time 4.2 ± 0.5 (range between 3 to 5) hours, planned to achieve minimum Kt/V ≥ 1.2. In the study group, the mean BMI (body mass index) was 23.4 ± 4.7 kg/m^2 (tab. 1). According to BMI 5 people were underweight, 28 normal weight, 8 overweight and 4-obese.

Tab. 1. The characteristics of the study group

Parameters	n = 45
Age (years)	56.9 ± 17.5 (24-87)
Height (cm)	168.8 ± 12.2 (120-186)
Body mass (kg)	65.1 ± 18.1 (35-128.5)
BMI (kg/m^2)	23.4 ± 4.7 (16.5-37.6)

The data are presented as means ± SD and minimum and maximum

Among the patients, 41 subjects were administered calcium in supplement form: in 35 patients calcium carbonate (Calperos and Osteovit) – average dose of 4.2 ± 2.8 g/day; and in 6 patients calcium acetate (Calcifos) – an average dose of 4.3 ± 2.9 g/day. 29 patients received Alfacalcidol (Alfadiol) in average doses of 0.3 ± 0.132 μg/day; 2 patients received sevelamer (Renagel) in a dose of 1800 mg/day, and 8 patients – cinacalcet (Mimpara) (30 or 60 mg/day).

Diet assessment

For the diet assessment, a 24-hour diet interview was applied. Results were analyzed using a computer program Dietetyk 2011. The results were compared to recommendations for the healthy population of Poland (3) and recommendations for hemodialysis patients (4).

Laboratory measurements

Fasting blood samples were taken from a peripheral vein before and after dialysis. Blood was again collected after the hemodialysis session in order to determine urea nitrogen (BUN). As a part of the routine testing, the following measurements were performed: complete blood count, lipids, BUN, serum concentration of creatinine, sodium, potassium, calcium, phosphorus, intact parathyroid hormone (PTH), alkaline phosphatase (ALP) and C-reactive protein (CRP).

Statistical analysis

Standard descriptive statistics (mean, standard deviation, median) were used. Compliance distribution of variables with normal distribution was assessed by analyzing histograms. Comparisons between groups of variables with normal distribution were done using t-Student test or analysis of variance. If the distribution is non-normal, a U Mann-Whitney test was used. Correlations between variables were assessed using the Spearman method, p values < 0.05 were considered statistically significant. Calculations were performed using the software Statistica vs 10.0.

RESULTS

The laboratory and anthropometrical parameters

The results of the laboratory measurements are presented in table 2.

Tab. 2. The results of the laboratory measurements in study group

Parameters	Mean ± SD	Range	Recommendation (4, 5)
HB (g/l)	10.98 ± 0.95	8.6-12.8	11-12
BUN before HD (mg/dl)	65.37 ± 17.8	28.1 – 102.8	9.8-20.1
BUN after HD (mg/dl)	16.65 ± 6.72	4.9-34.8	9.8-20.1
Creatinine (mg/dl)	9.31 ± 2.68	3.96-15.96	0.6-1.1
Total cholesterol (mg/dl)	184.77 ± 57.48	106 -407	120-200
Triglycerides (mg/dl)	179.19 ± 119.11	40-617	< 150
LDL (mg/dl)	137.19 ± 96.61	25- > 350	60-135
HDL (mg/dl)	45.31 ± 16.99	21-99	> 40
Sodium (mEq/l)	135.47 ± 3.31	126-142	136-145
Potassium (mEq/l)	5.01 ± 0.78	3.6-6.7	3.5-5.1
Calcium (mg/dl)	8.38 ± 0.81	6.5-10.5	8.9-10
Phosphorus (mg/dl)	5.96 ± 2	2.7-12.4	2.3-4.7
Ca x P	49.93 ± 17.17	20.15-106.64	< 55
CRP (mg/dl)	14.35 ± 16.1	0.11-76	0-5
Kt/V	1.67 ± 0.23	1.28-2.22	> 1.2
PTH (pg/ml)	610.42 ± 997.34	6.7-5490	150-300
ALP (U/l)	124.6 ± 97.41	4-567	40-150
Albumin (g/l)	33.84 ± 3.26	26-39	35-50

Data are presented as means ± SD

In 15 patients (33.3%) the concentration of phosphorus was within the normal range, and in 30 (66.7%) it was elevated. In 12 patients (26.7%) the Ca-P index over 55 mg^2/dl^2 was observed. PTH level was decreased in 14 patients (31.11%), in 11 (24.44%) it was within the recommended range for hemodialysis patients, and 20 patients (44.44%) presented with elevated PTH levels. Also, elevated CRP (over 5 mg/dl) in 30 (66.67%) patients was observed. 24 (53.33%) patients presented low albumin concentration (below laboratory references range; < 35 g/l).

Figures 1 and 2 illustrate the concentration of selected parameters in the study group.

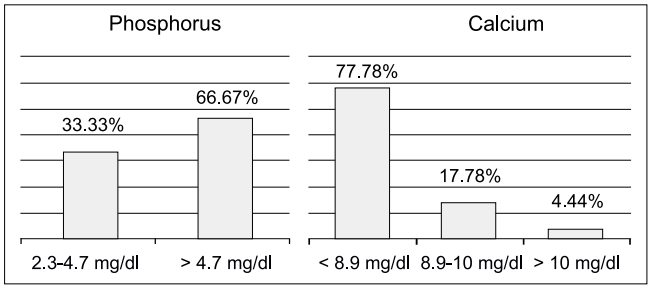

Fig. 1. Concentrations of phosphorus and calcium in the study group

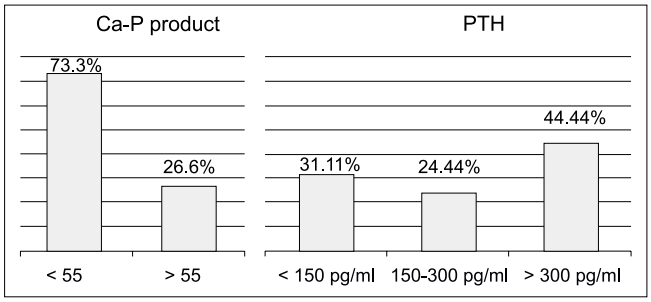

Fig. 2. The Ca-P product and PTH level in the study group

Mean BMI was 23.4 ± 4.7 in the study group (tab. 1), the negative correlation between BMI and intake of protein was noticed (R Spearman -0.3; $p < 0.05$).

Diet assessment

The results of analysis of the diet are presented in table 3. The low protein intake was found in 28 patients (62.22%). Mean realization of recommendations for protein intake for hemodialysis patients was 79.26 ± 37.42%. The amount of calories from fat was 33.5 ± 9.3%. Seven patients (15.56%) presented a too – low intake of calories from fat and 19 patients a too – high intake. Saturated fatty acids (saturated FA) provide about 19 ± 11% of the daily energy. The consumption of saturated FA less than 7% was observed only in 3 patients (6.67%). Only 4 patients (8.89%) presented higher than 10% of the energy from PUFAs. Adequate intake of cholesterol – that is less than 200 mg/day – was maintained in 20 of the patients, or 44.44%. Carbohydrates in the study group were consumed at an average of 209.16 ± 124.75 g/day, which translated into the supplied amount of calories from this nutrient at an

average of 48.72 ± 14.06%. Adequate supply of energy from carbohydrates was found in 23 patients (51.11%). In 19 patients (42.22%) amount of carbohydrates was sufficient, and 3 persons (6.67%) provide too many calories coming from this macronutrient. Low fiber intake – up to 35 subjects (77.78%) was noticed.

Tab. 3. Results of diet analysis

Component	Mean ± SD	Min.-Max.	Recommendation (3, 4)
Energy (kcal/d)	1539.91 ± 801.97	308-4297	–
Energy (kcal/kg abm/d)	24.86 ± 13.66	6.6-64.62	35 kcal/kg bm/d
Protein (g/d)	59.32 ± 29.85	15.70-139.60	–
Protein (g/kg/abm/d)	0.95 ± 0.45	0.14-1.94	1.2 kcal/kg bm/d
Protein (g/kg/ibm/d)	1.02 ± 0.59	0.22-3.69	1.2 kcal/kg bm/d
Fat (g/d)	56.83 ± 33.80	16.41-185.4	–
% energy from fat (%)	33.53 ± 9.37	17.84-67.67	30% energy
% energy from saturated fatty acids	19.37 ± 11.45	3.49-63.67	< 7% energy
% energy from polyunsaturated fatty acids	5.15 ± 3.06	1.96-16.22	< 10% energy
Cholesterol (mg/day)	229.78 ± 152.29	28.5-694.52	< 200 mg/d
Carbohydrates (g/d)	209.16 ± 124.75	0.91-642.76	–
% energy from carbohydrates	48.72 ± 14.06	0.39-67.31	rest of energy (without fat and protein)
Fiber (g/d)	15.98 ± 11.46	0.37-60.2	20-30 g/d
Calcium (mg/d)	407.85 ± 330.16	34.6-1721.81	1000-1200 mg/d
Phosphorus (mg/d)	952.01 ± 530.24	231.9-2416.54	< 1000 mg/d

abm – actual body mass; bm – body mass; d – day; ibm – ideal body mass
Data are presented as means ± SD

Relationship between phosphate and calcium intake, laboratory parameters and adequacy of dialysis

Percentage of recommended calcium intake according to the age of the subjects was 37.84 ± 33.32%. Only 1 person (2.22%) consumed an adequate amount of calcium in their diet.

In 41 patients (91.11%), the supply of this component was below normal, and in 3 patients (6.67%) – above the norm. The recommendation of phosphate intake in hemodialysis patients was not fulfilled in 16 patients (35.56%). Figure 3 shows the amount of phosphate intake in the study group.

Kt/V negatively correlated with: phosphorus level (R Spearman = -0.56; $p < 0.05$) and Ca-P (R Spearman = -0.43; $p < 0.05$). BUN before dialysis session correlated positively with: phosphorus levels (Spearman R = 0.37; $p < 0.05$) and PTH (Spearman R = 0.31; $p < 0.05$). The BUN after dialysis session correlated only with the concentration of phosphorus (R Spearman = 0.38; $p < 0.05$). No correlation between the amount of energy consumed, and the value of Kt/V, BUN, calcium, phosphorus and PTH was noticed. The amount of protein in the diet positively correlated with the amount of, carbohydrates (Spearman R = 0.7; $p < 0.05$); phosphates (Spearman R = 0.89; $p < 0.05$) and calcium (Spearman R = 0.5; $p < 0.05$).

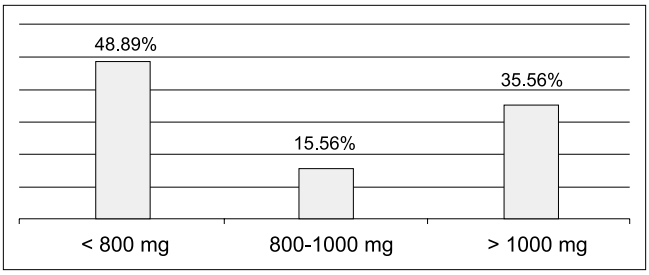

Fig. 3. The intake of phosphates in the study group

No correlation between the amount of calcium in the diet and the level of total calcium and phosphorus levels, or the value of the Ca-P, PTH or ALP was observed. However, the amount of phosphates in the diet correlated with: the amount of energy consumed with food, intake of protein, fat, cholesterol, saturated fat, fiber, calcium and PUFAs.

There was no correlation between intake of phosphates and: calcium levels, serum phosphorus, the value of the Ca-P and the concentration of PTH. Also, no correlation between the dose of sevelamer or cinacalcet and the concentration of calcium and phosphorus levels was observed.

DISCUSSION

The aim of the paper was to study the relationship between the diet and the occurrence of calcium-phosphorus disorders in patients with chronic kidney disease (CKD) treated with haemodialysis. Out of all disorders related to improper calcium-phosphorus management in haemodialysis patients, hyperphosphatemia entails the highest risk of death (approx. 12%) (6, 7). Increased phosphorus concentration in the present study was observed in 66.67% of the patients. According to the Report on the Renal Replacement Therapy in Poland (RRRTP) of 2007, hyperphosphatemia appeared in a lower rate of patients (among 48% with elevated phosphates, in 14% their concentration exceeded 7.5 mg/dl) (8). The average phosphorus concentration in the study population was comparable to the value in the study by Block et al. (6.2 mg/dl) (9). Block et al. proved that phosphate concentration exceeding 6.5 mg/dl causes a 27% increase of the mortality risk in comparison to patients with normal phosphorus levels. It needs to be added that serum phosphorus concentration > 6.5 mg/dl occurred in over 1/3 of the patients included in the study.

According to the RRRTP of 2007, calcium concentration below 8.4 mg/dl was observed in 34% of patients, in spite of receiving oral calcium preparations and

supplementation of vitamin D in its active form; what is more, the value has increased in comparison to the previous years. In our own study, calcium concentration below 8.4 mg/dl occurred in a larger group of patients, 55.56%, while in over three quarters of the patients the calcium levels were below the laboratory norm.

Hypercalcaemia results in an increase of the Ca-P, and its higher value contributes to a higher risk of death due to cardiovascular complications. In the study, only 4.44% of the patients exceeded the laboratory normal range while calcium concentration above 9.5 mg/dl was observed in 11.11% of them. The Report of 2007 mentions a similar rate of patients with the calcium concentration over 9.5 mg/dl (16%). From comparison of the data from previous reports, it is possible to conclude that the problem of hypercalcaemia has decreased year by year (in 2003, 33% of patients had calcium levels above 9.5 mg/dl). Both a lower rate of patients with hypercalcaemia, and a higher rate of patients with hyperphosphatemia may be related to the decrease of the doses of calcium preparations, and lowered calcium concentration, in the dialysis concentrate (8).

Another mortality risk factor is elevated Ca-P. In the study the rate of patients with an elevated calcium-phosphorus product, was 26.67%. When the value of Ca-P exceeds 72 mg^2/dl^2, insoluble tricalcium phosphate starts to precipitate and accumulate in the soft tissues – such a calcium concentration occurred in 8.89% of the study population.

Parathyroid hormone (PTH) is another death risk factor, independent of the calcium and phosphate concentrations. Block et al. proved that both PTH below 150 pg/dl, and above 300 pg/dl, results in an increased risk of death (9). In the studied group, 33.3% of the patients had the PTH level over 500 pg/dl. Similar results were obtained by Bunio et al. – 57% of the subjects had elevated PTH levels (10). According to the paper by Marco et al., a PTH level exceeding 476.1 pg/ml increases the death risk (even) by four (7).

Both the elevated levels of PTH and CRP are cardiovascular death risk factors. As much as 66.67% of the study population had CRP levels exceeding the normal range. In the study by Małgorzewicz, the results were slightly lower, as CRP over 5 mg/L was observed in 51.8% of the haemodialysis patients. CRP is both a marker, and a mediator, of cardiovascular diseases. Serum concentrations of CRP and PTH are considered as atherosclerosis risk factors in patients suffering from CKD (11-13).

Another factor which increases mortality among patients with CKD is a low albumin level, which may indicate protein-energy malnutrition. In the present study, over half (53.33%) of the patients had albumin concentrations below the normal range. In other studies, the rate of patients with low albumin levels is two times smaller (Rakowicz et al. – 23.33%, Małgorzewicz – 25.3%) (11, 14).

Diet assessment

In the presented study, we observed that the energetic value of daily food intake was too low (the average adherence to the norm for the current body mass was 71.04%) and the protein supply in the diet was insufficient (the average adherence to the norm for the current body mass was 79.3%). Similarly, an insufficient energy level in the haemodialysis patients' diets was observed previously (15-20). However, the same studies do not agree as to the adherence to the protein supply norm. Insufficient protein and calorie supply in the diet of haemodialysed patients is associated with the risk of malnutrition. Furthermore, the studies showed that better nutritional status of the patients results in higher chances of survival, in comparison to malnourished patients (11, 15-22).

It is alarming that both the amount of energy from saturated fatty acids, and the supply of cholesterol, exceeded the norms. As far as the amount of fibre is concerned, its average intake was 15.98 g. In the studies by Kardasz et al., Małgorzewicz et al., Lou et al. and Heleniak, similar relationships were observed (11, 15, 16, 23). The insufficient amount of fibre may be related to the reduction of the amount of fruit, vegetables and wholemeal products in the diet (11, 15, 17, 24).

The recommendations for phosphate intake were fulfilled in 64.4% of the patients, and the average intake was 952.01 mg. In the studies by Gajewska et al. and Kardasz et al., the obtained values of phosphate intake were slightly lower (24, 25). However, there are also studies which indicate that the average phosphate intake by the patients was exceeded (Lou et al. observed an average phosphate intake of 1067 mg, and Rzeszotarski et al. – 1186 mg) (6, 16). Phosphate intake within the normal range could be a result of an insufficient protein intake. It is assumed that 1 g of protein provides 13-15 mg of phosphates. The diet of the studied patients did not ensure an adequate caloric intake. If the patients consumed food of higher caloric value, they would take in more phosphates – the study showed a strong relationship between the caloric value of the diet and phosphate intake (25-28). The diet of the studied patients was characterized by a very low calcium supply. The norms for calcium intake were fulfilled, on average, in 37.8% of those studied. Low intake of this mineral element may result from the need to reduce phosphate intake. However, if the calcium supply is much lower than phosphate supply (even if recommendations for phosphate intake are not exceeded), calcium absorption decreases (29, 30). The insufficiencies of energy, protein, fiber and calcium, with a simultaneous excess of fats, saturated fatty acids, and cholesterol, may contribute to a higher risk of death. Furthermore, the study by Wyskida et al. showed that only 29.8% of patients strictly observe the recommendations for calcium and phosphate intake, 39.3% does it partially, and 30.9% does not adhere to the rules at all (31). It seems important to use best efforts to make the patients' diet comply with the recommendations. A step taken in this direction is the introduction of education programs for patients with CKD at various stages of the disease.

Relationship between diet and calcium-phosphorus management disorders

According to the assumed hypothesis, it could be expected that the amount of calcium and phosphates in the diet would correspond to the calcium and phosphorus level in serum, Ca-P and PTH concentration. However, the study did not reveal such a correlation.

In the study by Lynch et al., no relationship was found between the reduction of phosphate intake and lowered death risk (32). On the other hand, Noori et al. concluded that both higher phosphate intake, and higher phosphate/protein rate, results in a higher risk of death (27).

As far as hyperphosphatemia itself is concerned, it must also be remembered that phosphorus is one of the elements which are not eliminated sufficiently by hemodialysis techniques (one hemodialysis session removes 500-600 mg of phosphorus). The additional use of phosphate-binding drugs enables the binding of only about 200-300 mg of phosphorus. Therefore, the reduction of phosphate intake in diet is one of the elements of treating hyperphosphatemia (33, 34).

Our study confirmed the relationship between dialysis adequacy (Kt/V), and serum phosphorus concentration, and Ca-P. It shows that adequate dialysis procedure, and dietary intake, reduces the intensity of impairment in calcium-phosphorus management.

CONCLUSIONS

1. Adequate dialysis improves calcium and phosphorus disorders.
2. Dietary restrictions have a marginal effect on serum phosphorus levels in patients on hemodialysis.
3. Significant reduction of phosphate in the diet may be a risk factor for low calorie and protein intake, which in turn can lead to malnutrition.

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