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DISORDERS OF PHOSPHORUS-CALCIUM BALANCE IN PATIENTS ON CHRONIC HEMODIALYSIS - TIME-BASED DURATION RELATIONSHIP -

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Chronic renal failure (CRF) is a progressive, irreversible deterioration of kidney function that leads to complete loss of kidney function and the need for dialysis treatment. Bone disease is a chronic complication in the CRF and poses a significant problem in hemodialysis patients.

The aim of our study was to assess the influence of peritoneal dialysis treatment on biochemical parameters of mineral and bone metabolism in hemodialysis patients, and identify the most important parameters for the monitoring of this disorder.

The research involved 172 patients, mean age 58.69±12:54, divided into groups in respect to the length of dialysis treatment (group I - 5 years, group II - 5-10 years and group III - over 10 years).

Serum phosphorus in all the patients was increased, but the values increased with duration of dialysis (I: 1.77±0.58, II: 1.97±0.66, III: 1.92±0.82), with no statistical differences ($p>0.05$). Calcemia values were significantly increased (I vs. II. and I vs. III, $p<0.0001$), as well as the values of Ca x P (I vs. II., $p<0.001$, II vs. III., $p<0.01$), primarily on the account of the increased calcium value. The values of alkaline phosphatase (I: 105.12±65.60; II: 125.27±96.79, III: 172.43±163.99) were significantly higher in group III compared to other groups ($p <0.05$). Also, the values of PTH (I: 234.21±18.74; II: 273.09±247.98; III: 489.46±468.49) were significantly higher in group III compared to other groups ($p<0.001$). In the group of patients with duration of dialysis up to 5 years, the values of phosphorus were increased, the values of calcemia were decreased, with mild elevation of AF and PTH values, which best corresponds to the bone disease with rapid turnover. In the P group, there is a significant increase in calcemia in respect to phosphorus, alkaline phosphatase, and PTH.

The most reliable marker for clinical monitoring of bone disease in dialysis patients is PTH, which correlates well with the values of alkaline phosphatase and calcium. The values of calcium and phosphorus are highly variable and not the most reliable markers for bone disease monitoring. *Acta Medica Medianae 2011;50(1):32-37.*

Key words: *hemodialysis, duration, mineral and bone metabolism, PTH, calcium, phosphorus*

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Introduction

National Kidney Foundation - The American Kidney Foundation (NKF, 2002) defines the chronic renal failure as kidney damage lasting more than 3 months, caused by structural or functional disorders of the kidneys, with or without a fall in the volume of glomerular filtration rate (GFR), which is manifested by histological abnormalities or disorders in the characteristics of blood, urine or the appearance of kidney with a decrease in glomerular filtration rate (GFR) <60 ml/min/1.73m^2, which lasts more than 3 months, with or without renal failure (1,2).

Chronic renal failure (CRF) is a gradual, progressive and irreversible deterioration of kidney function, a toxic syndrome caused by decreased glomerular filtration due to the deterioration of functional nephrons. It is characterized by varying degrees of azotemia, but also by changes in volume and composition of body fluids and electrolyte imbalance, and many hormones.

Very early in the progression of CRF there occur disturbances in the metabolism of calcium (Ca) and phosphorus (P), i.e. parathyroid hormone (PTH) and vitamin D3, according to some authors, at glomerularae filtration rate (GFR) of 60ml/min/1,73m^2, that is, in the second stage of CRF. From stage to stage, this disorder is getting

worse, considerably affecting the patients on dialysis.

Complex causal relationships in the electrolyte-hormone imbalance can be explained by the decline in kidney tissue and leads to reduced synthesis of the active metabolite of vitamin D3 (1,25 (ON) 2D3), which leads to reduced absorption of Ca at the level of interstitial and hypocalcemia. Hypocalcemia leads to increased stimulation of parathyroid glands and develops the state of secondary hyper-parathyroidism, or there are changes in normal Ca-regulation of PTH secretion (impaired "set point" for Ca 2+). It also leads to phosphate retention in the kidney and hyperphosphataemia. If we add the effect of bone resistance to PTH, it can be concluded that this metabolic imbalance leads to significant disturbances in bone meta'-bolism, especially in patients on dialysis (3-6).

Progressive bone abnormalities in patients with CRF is traditionally referred to as renal osteodystrophy (ROD). However, the American Kidney Foundation (National Kidney Foundation-NKF, 2007) approved a new recommendation on which the term ROD used to explain the change of the bone morphology in patients with CRF, based solely on the histological results obtained by bone biopsy. Clinical, biochemical and radio-logical abnormalities, which reflect the ROD, would be treated as elements of a broader clinical syndrome, a disorder of bone mineral metabolism in CKD (Chronic Kidney Disease-Mineral and Bone Disorder; CKD-MBD Syndrome). CKD-MBD syndrome is characterized by one of the following events:

- Abnormalities in the metabolism of Ca, P, PTH and vitamine D3
- Abnormalities of bone turnover, mineral-ization, volume, and bone growth
- Vascular calcification or calcification of other soft tissues (7).

Many authors believe that the bone biopsy is "gold" standard in the diagnosis and moni-toring of bone abnormalities (8), but bearing in mind invasiveness of a procedure, the American Kidney Foundation (National Kidney Foundation) recommends that a bone biopsy should be performed only in clinical-biochemically unclear cases (eg. in patients with high levels of PTH and low serum alkaline phosphatase) (9).

Clinical symptoms of bone and mineral metabolism occur quite late in the CRF. Some studies suggest that the clinical symptoms are present in less than 10% of patients and that histomorhological changes present in 35-90% of cases (10). Given that disturbance of mineral bone metabolism can be laboratory diagnosed before the onset of symptoms, it is important to monitor the levels, above all, of parathyroid hormone and alkaline phosphatase, Ca, P and vitamin D in order to timely apply an adequate therapy and avoid more difficult consequences.

It is certain that the extended, multi-year treatment of patients on hemodialysis can only worsen this problem, if not timely detected and properly treated. Given the chronic problems with the metabolism of calcium and phosphorus in patients on HD, we were interested to isolate the most important parameters which, during the time spent on HD, could influence bone disease in these patients.

Aim

The aim of this study was the assessment of the influence of peritoneal dialysis treatment on biochemical parameters of mineral and bone metabolism in hemodialysis patients as well as the allocation of the most important parameters to monitor this condition in these patients.

Methods

The study was conducted at the Department of Nephrology, Clinical Center Niš, January, 2009.

By type of clinical research, this study is among the epidemiological studies and behavioral studies, and according to the organization of clinical research, this is an observational-retrospective study, complying with the principles of evidence-based medicine.

The target group of this survey was the one involving patients on chronic hemodialysis, whose urine output decreased to 400 ml/24h. The study included 172 patients, 113 males and 59 females, mean age of 58.69 years.

Patients were divided into groups based on the length of peritoneal dialysis treatment:

I group - peritoneal dialysis treatment length less than 5 years;

II group - peritoneal dialysis treatment length from 5 to 10 years;

III group - peritoneal dialysis treatment length over 10 years.

In our patients we determined the following parameters: concentration of total serum calcium, serum phosphate, alkaline phosphatase, and aluminum in serum - all determined in the laboratory of the Clinic of Nephrology, Clinical Center Niš. Analyses were performed by routine biochemical methods in an automatic analyzer A25 Company Bio Systems. Determination of intact PTH was performed in the laboratory of the Centre for Nuclear Medicine, Clinical Center Niš, imunoradiometric analysis (IRMA) on LKB gamma counter.

The reference range was set according to the Recommendations of Good Practice of the American Initiative for successful outcome of dialysis (K / DOQI Clinical Practice Guidelines) for the PTH of 150-400 pg / ml, calcium from 2.10 - 2.60 mmol / 1, for phosphorus of 1.13-1.78 mmol/l and the product Ca x P <4:40 $mmol^2/l^2$, [11,12].

Statistical analysis was done with SSPS 16.0 statistical package (13). For age distribution, we used the arithmetic mean and standard deviation. To display the significance of differences between the studied characteristics of patients by age group, we used T-test and Pearson's linear correlation test.

Results

Table 1. Gender and age distribution of the investigated patients

Gender	Number	%	Age
Men	113	65.70	58.66
Women	59	34.30	58.76
Σ	172	100	58.69±12.55

Table 2. Length of peritoneal dialysis treatment

Gender	Dialysis internship (Yrs)		
	up to 5	5-10	over 10
	Group I	Group II	Group III
Men	46 (67,65%)	43 (72,88%)	24 (53,33%)
Women	22 (32,35%)	16 (27,12%)	21 (46,67%)
Σ	68 (39,54%)	59 (34,20%)	45 (26,16%)

Table 4. Characteristics of patients by investigated groups

	Group I	Group II	Group III
Age	59.00±13.78	60.07±11.31	56.44±12.11
Range	116-81	26-82	27- 76
Dialysis length (yrs)	2.60±0.95	6.98±1.40	14.67±4.29
Range	1-4	5-9	10-28
Dialysis dosage	2.73±0.44	2.98±0.13	3.00 ± 0.00
Range	2-3	2-3	3-3
PTH	234.21±18.74	273.09±247.9	489.46±468.49
Range	23-1320	36-1249	9-1486
Phosphorus	1.77±0.58	1.97±0.66	1.92±0.82
Range	0.73-3.53	0.52-3.73	0.42-3.82
Calcium	2.21±0.31	2.50±0.33	2.53±0.32
Range	1.60-2.81	1.82-3.28	1.92-.40
AF	105.12±65.60	125.27±96.79	172.43±163.9
Range	33-226	2-545	39-666

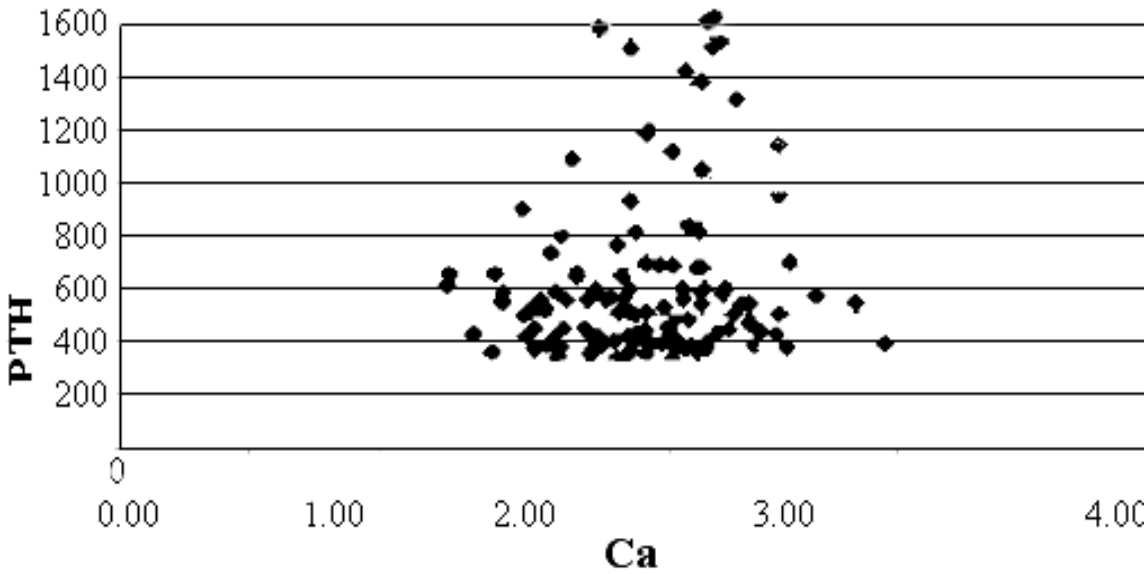

Figure 1. Correlation between serum calcium and PTH (rxy = 0904, p = 0.01)

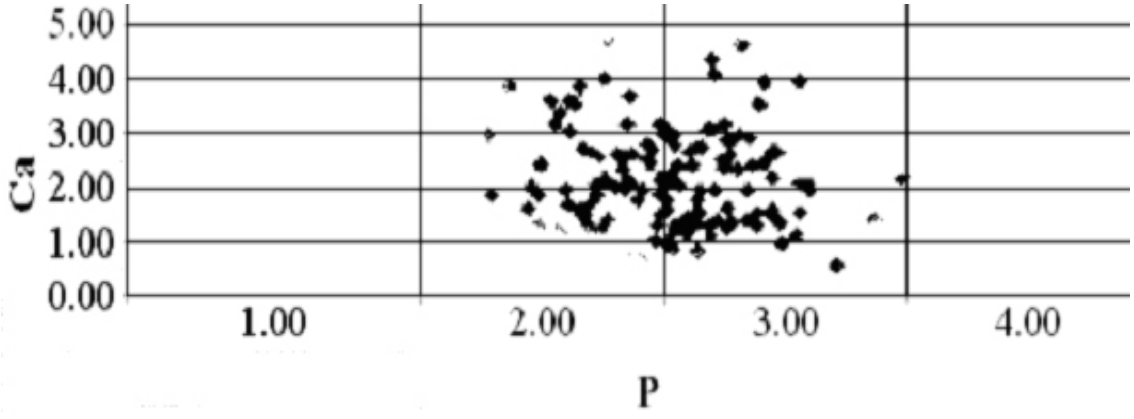

Figure 2. Correlation between serum calcium and phosphorus (rxy =- 0105, p = 0.01)

Table 3. Underlying disease in etiology of CRF

Gender	GN*	PN	Neph.	NAS	PKD	DN	Tr	Res.	Nfc	Tu	Cal.	U.E.	Σ
Men	11	4	2	2	7	8	3	5	11	1	3	57	114
Women	9	7	2	1	3	3	3	1	1	0	0	28	58
Σ	20	11	4	3	10	11	6	6	12	1	3	85	*172*

*GN-glomerulonephritis; PN-Pielonephritis; Nef.-nefritis; NAS-nephroangiosclerosis; PBB-policistic kidney disease; DN-diabetic nephropathy; Tr.-kidney transplantation; Res.- kidney resection (one and/or both); Nfc.-nefrectomy (partial and/or complete); Tu.- kidney tumor (one and/or both); Kalk.- kidney calculosis (one and/or both); N.E.- unknown etiology

Table 5. Distribution of parameters of mineral and bone metabolism by investigated groups

	Group I	Group II	Group III
PTH <150	43.75%	42.11%	29.27%
PTH 151-400	45.83%	36.84%	34.15%
PTH >401	10.42%	21.05%	36.58%
Ca <2.20	45.90%	20.00%	13.51%
Ca 2.21-2.60	29.41%	42.00%	45.95%
Ca >2.61	15.69%	38.00%	40.54%
P <1,12	11.76%	4.00%	18.92%
P 1,13-1.78	49.02%	40.00%	2432%
P >1,79	39.22%	56.00%	56.76%

Discussion

Abnormalities of mineral and bone metabolism are frequent in patients both with predialysis chronic renal insufficiency and patients on dialysis. An effective clinical approach to these patients includes the control of phosphate retention and prevention of hyperphosphataemia, maintaining the serum Ca concentrations in normal concentrations and prevention of proliferation of parathyroid gland and significant increase in PTH (14).

The present study included 172 patients, 113 male patients (65.70%) and 59 females, mean age 58.69±12:54 years (Table 1). This trend of age and sex distribution remains by the investigated groups (Tables 2 and 4).

The most common underlying disease in the group of examinees was chronic glomerulonephritis (20), the condition after nephrectomy (11) and chronic pyelonephritis (11). There were 11 diabetics in total. However, in most patients, 85 of them, primary renal disease is not known (Table 3).

The majority of patients have been dialysed less than 5 years, 39.54%, a slightly smaller percentage of 5 to 10 years - 34.20% of them. However, the number of patients (26.16%) on dialysis for more than 10 years is not negligible (Table 2).

The lowest dose of dialysis 2.73±0.44 is reported in patients during the first 5 years of dialysis; somewhat higher dose of 2.98±0.13 is applied in patients who are up to 10 years on peritoneal dialysis treatment; standard three hemodialyses for 4 hours a week are given to all patients with more than 10 years of dialysis treatment (Table 4).

Examined parameters of bone metabolism showed the following characteristics in our respondents (Tables 4 and 5).

Phosphorus, as the most important parameter of mineral bone metabolism control was increased in all our patients, with rising of values along with the duration of dialysis (Group I: 1.77±0.58; II: 1.97±0.66, III: 1.92±0.82); statistical differences were not found among the four groups ($p>0.05$).

Calcemia values were also on the rise with duration of dialysis, but, unlike phosphorus, statistically significantly higher (I:II 2.21±0.31/ 2.50±0.33, $p<0.0001$; I:III 2.21±0.31/2.53±0.32, $p<0.0001$), so that the proportion increased as well as the value of products CaxP after 5 years of dialysis (group II patients, $p=0.002$). The increase in product CaxP was maintained (III, $p=0.01$) and, above all, on the account of the increased value of calcemia.

Similar results to the values of calcemia were obtained for alkaline phosphatase (group: 105.12±65.60; II: 125.27±96.79, III: 172.43± 163.99), with significantly higher values of AF for group III ($p<0.05$).

Although PTH showed the rising trend during the time spent on dialysis treatment (PTH for the first group: 234.21±18.74; II: 273.09±247.98; III: 489.46±468.49;) higher values of PTH were found only for group III patients ($p<0001$).

In respect to the analyzed groups, patients in group I had higher values of phosphorus and lower values of calcemia and moderately elevated serum PTH and AF in 63% of cases, which best suits the bone disease with rapid turnover (Table 5). Although all our patients were treated with trusses calcium phosphate-based, a satisfactory control of phosphorus during their stay on HD was not achieved. The reasons may be numerous, but most are inadequate intake of phosphorus through diet and irregular intake of phosphorus trusses.

In our study, after five years of dialysis, we observed a significant increase in calcemia in relation to phosphorus, alkaline phosphatase, and PTH (Table 5). These findings support further deterioration of bone diseases, development of mixed forms and adynamic bone disease. These disorders require a more complex approach to treatment and monitoring of bone disease on hemodialysis, and often, in addition to severe bone deformities, results in deterioration of cardiovascular morbidity and mortality in these patients (15-18).

Some studies suggest that bone-specific AF (BAF) shows a very large statistically significant correlation between the PTH in monitoring the progression of bone disease, whereas this correlation is not always present in the Ca-P-AF and AF. It is also stated that there is a statistically significant correlation between AF and total PTH, but to a lesser extent (19,20).

In our study, PTH showed a good correlation with alkaline phosphatase (r_{xy}=0961, p=0.01) and calcium (r_{xy}=0904, p=0.01) (Figure 1), but not with the product CaxP (r_{xy}=0245, p=0.01). Alkaline phosphatase is also well-correlated with calcium (r_{xy}=0.776, p=0.01) but not with the product CaxP (r_{xy}=0256, p=0.01). However, the correlation of serum calcium and phosphorus was statistically insignificant (r_{xy}=-0.105, p=0.01) (Figure 2), on the basis of which it follows that the most reliable marker for clinical monitoring of bone disease is PTH, which correlates well with the alkaline phosphatase and calcemia, while the values of calcium and phosphorus, especially phosphorus, varied.

Bearing in mind that mineral bone metabolism disorder leads to a significant deterio-ration in quality of life, morbidity and mortality, primarily by cardiovascular system, the Recommendations for Good Clinical Practice of the American Initiative for the Successful Outcome of Dialysis (K/DOQI Clinical Practice Guidelines) require that in patients on dialysis every three months the levels of PTH and AF be determined, as well as monthly levels of Ca and P in patients on therapy and more frequently, (21) to allow for adequate control, slow the progression and improve quality of life of patients on dialysis.

Conclusion

In our study we have shown that the duration of hemodialysis is correlated with significant metabolism disorders of calcium and phosphorus in hemodialysis patients. During the first 5 years of hemodialysis in the patients examined we noticed elevated values of serum phosphorus and low values of calcemia and moderately elevated serum PTH and AF in 63% of our patients, which corresponds to the bone disease with rapid turnover.

With further duration of dialysis, the values of calcemia significantly grow in relation to phosphorus, PTH and AF, which speaks in favor of development of other mixed forms of bone disease, and in some patients of development of adynamic bone disease.

By the investigation of biochemical markers of bone-mineral metabolism we have shown that PTH is the most reliable marker for clinical monitoring of bone disease, which correlates well with the alkaline phosphatase and calcemia, while the values of calcium and phosphorus, especially phosphorus vastly varied and were not reliable indicators of bone metabolism in hemo-dialysis patients.

Increased calcium and phosphorus product along with dialysis treatment leads to increased risk of intravascular calcifications and subsequent increase in cardiovascular morbidity and mortality in these patients.

References

1. Natural Kidney Fondation. Evaluation, Classification and Stratification. Am J Kidney Dis 2002;39:SI-S226.
2. Kostić S, Paunović G, Avramović M, Veličković R, Kostić I, Stojanović M. Chronic renal failure today. Acta Medica Medianae 2004; 43(3): 45-9.
3. Ilić S. Interna madicina. Niš: Prosveta; 2004.
4. D'Haese PC, Spasovski G, Sikole A, Hutchison A, Freemont T, Sulkova S, et al. A multicenter study on the effects of lanthanum carbonate (Fosrenol™) and calcium carbonate on renal bone disease in dialysis patients. Kidney International 2003; 63, S73-S8. [CrossRef]
5. Locatelli F, D'Amilo M, Ezneševski H. The epidemiology of and stage disease in Baluts countries. Nephrol Dial Transplant 2001;16:42-1338. [CrossRef]
6. Brandi L. 1alpha(OH)D3 One-alpha-hydroxy-chole-calciferol-an active vitamin D analog. Clinical studies on prophylaxis and treatment of secondary hyperparathyroidism in uremic patients on chronic dialysis. Dan Med Bull 2008;55(4):186-210. [PubMed]
7. Tsukamoto Y. Disorders of bone and mineral metabolism in CKD: CKD-MBD as a new entity. Clin Calcium 2007; 17(5):660-4. [PubMed]
8. Gal-Moscovici A, Popovtzer MM. New worldwide trends in presentation of renal osteodystrophy and its relationship to parathyroid hormone levels. Clin Nephrol 2005; 63(4):284-9. [PubMed]
9. Moe S, Drueke T, Cunningham J, Goodman W, Martin K, Olgaard K, et al. Definition, evaluation, and classification of renal osteodystrophy: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2006; 69:1945-53. [CrossRef] [PubMed]
10. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al. Harrison's Principles of Internal Medicine. 17th ed. USA: Publisher: McGraw-Hill Professional; 2008.
11. Committee on Examination of the Evolving Science for Dietary Supplements. Food and Nutrition Board, Institute of Medicine. "Evolution of Evidence for Selected Nutrient and Disease Relationships". Washington, D.C.: National Academy Press; 2002.
12. Wei M, Taskapan H, Esbaei K, Jassal SV, Bargman JM, Oreopoulos DG. K/DOQI guideline requirements for calcium, phosphate, calcium phosphate product, and parathyroid hormone control in dialysis patients: can we achieve them? Int Urol Nephrol 2006; 38(3-4):739-43. [PubMed]
13. SPSS: Data Analysis with Comprehensive Statistics Software "computer program". Version 16.0. SPSS Inc; 2004.
14. Spasovski G, Bervoets A, Geert J, Behets S, Ivanovski N, Sikole A, et al. Spectrum of renal bone disease in end-stage renal failure patients not yet on dialysis. Nephrol Dial Transplant 2003;18:1159-66. [CrossRef]

15. Jesri A, Braitman LE, Pressman GS. Severe mitral annular calcification predicts chronic kidney disease. Int J Cardiol 2008;128(2):193-6. [CrossRef] [PubMed]
16. Spasovski G. New aspects of treatment of renal bone disease in dialysis patients. Contributions, Sec Biol Med Sci 2007; 28(1):205–13.
17. Jonjic N, Djordjevic V, Djordjevic N, Ljubenovic S. Effect of the hemodialysis duration, age and gender on the emergence of the renal osteodystrophy symptoms. Acta Medica Medianae 2008;47(4):19-24.
18. Goodman GW. Medical management of secondary hyperparathyroidism in chronic renal failure. Nephrol Dial Transplant 2003;18: 2-8. [CrossRef]
19. Jorge C, Gil C, Possante M, Silva E, Andrade R, Santos N, et al. Bone alkaline phosphatase besides intact parathyroid hormone in hemodialysis patients—any advantage? Nephron Clin Pract 2005; 101(3): cl22-7.
20. Cavalier E, Delanaye P, Collette J, Krzesinski JM, Chapelle JP. Evaluation of different bone markers in hemodialyzed patients. Clin Chim Acta 2006;371(1-2):107-11. [CrossRef] [PubMed]
21. Arenas MD, Alvarez-Ude F, Gil MT, Soriano A, Egea JJ, Millan I, et al. Application of NKF-K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease: changes of clinical practices and their effects on outcomes and quality standards in three haemodialysis units. Nephrol Dial Transplant. 2006; 21(6):1663-8. [CrossRef] [PubMed]

POREMEĆAJI FOSFO-KALCEMIČNOG BILANSA KOD BOLESNIKA NA HRONIČNOJ HEMODIJALIZI – UTICAJ DUŽINE DIJALIZIRANJA

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Hronična bubrežna insuficijencija (HBI) je progresivno, ireverzibilno oštećenje bubrežne funkcije koje dovodi do potpunog gubitka bubrežne funkcije i neophodnosti lečenja dijalizom. Koštana bolest je hronična komplikacija u sklopu HBI i predstavlja značajan problem kod bolesnika na hemodijalizi.

Cilj našeg istraživanja bio je procena uticaja dužine dijaliznog staža na biohemijske parametre mineralno-koštanog metabolizma kod bolesnika na hemodijalizi, kao i izdvajanje najvažnijih parametara za praćenje ovog poremećaja.

Istraživanje je obuhvatilo 172 bolesnika, prosečne starosti 58.69±12.54 godina, podeljenih u grupe u odnosu na dužinu dijaliznog lečenja (I grupa - do 5 godina, II - 5-10 godina i III - preko 10 godina).

Koncentracija serumskog fosfora je kod svih ispitivanih bolesnika bila povećana, s tim da su vrednosti rasle sa dužinom boravka na dijalizi (I: 1.77±0.58; II: 1.97±0.66; III: 1.92±0.82), ali bez statističke razlike ($p>0.05$). Vrednosti kalcemije značajno su rasle (I vs. II, i I vs. III, $p<0.0001$), kao i vrednosti proizvoda Ca x P (I vs. II, $p<0.001$; II vs. III, $p<0.01$) pre svega, na račun povišenih vrednosti kalcijuma. Vrednosti alkalne fosfataze (I: 105.12±65.60; II: 125.27±96.79, III: 172.43±163.99) značajno su više u III grupi u odnosu na ostale ($p<0.05$). Takođe, vrednosti PTH (I: 234.21±18.74; II: 273.09±247.98; III: 489.46±468.49) značajno su više u III u odnosu na ostale grupe ($p<0.001$). U grupi bolesnika sa dijalizom do 5 godina povišene su vrednosti fosfora, snižene vrednosti kalcemije i umereno povišene vrednosti AF i PTH, što najviše odgovara koštanoj bolesti sa brzim prometom. U II grupi je značajniji porast kalcemije u odnosu na fosfor, alkalnu fosfatazu i PTH.

Najpouzdaniji marker za kliničko praćenje koštane bolesti kod bolesnika na dijalizi je parathormon, koji dobro korelira sa vrednostima alkalne fosfataze i kalicijuma. Vrednosti kalcijuma i fosfora jako variraju i nisu najpouzdaniji marker za praćenje koštane bolesti. *Acta Medica Medianae 2011;50(1):32-37.*

Ključne reči: *hemodijaliza, trajanje, mineralno-koštani metabolizam, PTH, kalcijum, fosfor*