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DISORDERS OF PHOSPHORUS-CALCIUM METABOLISM AND LIPID PEROXIDATION PROCESSES IN PATIENTS WITH END-STAGE CHRONIC FAILURE RECEIVING PROGRAM HEMODIALYSIS

Annotation: *In recent years, a steady increase in the number of patients treated with program hemodialysis has been registered worldwide. This trend is associated with a steady increase in the number of cases of chronic renal failure, including its terminal stage, as well as greater availability of hemodialysis. It is established that changes in key parameters of phosphorus-calcium metabolism increase the risk of bone and cardiovascular pathology, secondary hyperparathyroidism in dialysis patients. The article presents the results of statistical evaluation of phosphorus-calcium metabolism in patients undergoing treatment with program hemodialysis.*

Keywords: *phosphorus-calcium metabolism, hemodialysis, chronic renal failure.*

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Introduction. In recent years, a steady increase in the number of patients treated with program hemodialysis has been registered worldwide. This is due to the increase in the life expectancy of patients, greater availability of hemodialysis and the revision of many criteria governing the selection of patients for program hemodialysis [12]. One of the most frequent and difficult problems arising in the treatment of dialysis patients is the correction of phosphorus-calcium metabolism [1,3].

In chronic renal failure, all parts of phosphorus-calcium metabolism are disturbed. When the glomerular filtration rate (GFR) drops below 60 ml/min/1.73 m2, phosphorus filtration decreases and its serum concentration increases, which causes increased secretion of parathyroid hormone (PTH). Parathyroid hormone suppresses phosphorus reabsorption, thus normalizing its level in serum, but when the SCF falls below 30 ml/min/1.73 m2 this mechanism of maintaining normal serum concentration of phosphorus becomes insufficiently effective and develops persistent hyperphosphatemia, which stimulates increased secretion of PTH. In hyperphosphatemia, production and serum calcitriol content decrease. Calcitriol deficiency causes impaired calcium absorption in the small intestine and the development of hypocalcemia. In hypocalcemia, persistent for months, develops hyperplasia of the parathyroid glands (PGM), causing excessive production and secretion of PTH, which along with hyperphosphatemia is a manifestation of secondary hyperparathyroidism (SHPT). Hypocalcemia, vitamin D deficiency and hyperphosphatemia are the most important factors responsible for parathyroid hyperplasia [8]. An important stage in the diagnostic confirmation of secondary hyperparathyroidism is the establishment of the exact localization of pathologically altered (one or more) perithyroid glands - the so-called topical diagnosis [11].

Secondary hyperparathyroidism that develops in patients with chronic renal failure contributes to the development of cystic fibrosis osteodystrophy, characterized by a high rate of bone remodeling, decreased bone mineralization, formation of bone cysts, osteosclerosis and osteomalacia. The main

clinical symptoms of osteodystrophy are bone pain and muscle weakness. An important clinical consequence of osteodystrophy is a high incidence of pathologic fractures. It has been established that hyperparathyroidism plays an important role not only in the development of skeletal changes, but also in the pathogenesis of calcification of blood vessels and heart valves, left ventricular hypertrophy, immune system dysfunction, and anemia [3, 17]. It is empirically proved that in order to maintain the process of bone remodeling at a normal level in patients with CPN the PTH content in them should be 2-3 times higher than in healthy patients and should be 120-200 pg/ml [11].

Monitoring of parameters of phosphorus-calcium metabolism in dialysis patients includes determination of serum calcium and phosphorus, alkaline phosphatase, PTH. In patients treated with drugs affecting phosphorus-calcium metabolism, studies should be performed more frequently [3]. It is established that changes in some key parameters of phosphorus-calcium metabolism are risk factors for mortality in dialysis patients [4, 12]

Correction of hyperphosphatemia with a low-phosphorus diet and the use of phosphatebinders is increasingly recognized as an important therapeutic approach to prevent life-threatening complications in dialysis patients. According to the K/DOQI Clinical Practice Guidelines, phosphorus intake should be limited to 800-1000 mg/day (adjusted for protein intake) [2, 14]. If phosphorus and PTH levels cannot be controlled within the target range despite restriction of phosphate intake from food, phosphate binders should be prescribed [7, 16].

Calcium carbonate and calcium acetate are most commonly used [8, 15]. However, long-term administration of phosphate-binding preparations based on calcium salts can cause hypercalcemia, which is 3.5 times more frequent with calcium carbonate than with calcium acetate [6, 13].

Calcium-based phosphate binders effectively reduce serum phosphorus concentration and can be used as initial phosphate-binding therapy. However, the total dose of elemental calcium used to bind dietary phosphorus should not exceed 1.5 g/day [1, 14]. Calcium-based phosphate binders should not be used in dialysis patients with hypercalcemia (corrected total serum calcium above 2.54 mmol/l) and when plasma PTH levels are below 150 pg/mL (16.5 pmol/L) on 2 consecutive measurements [8, 10]. In such patients, calcium-free phosphatebinders should be preferred [5, 14].

In some patients receiving long-term hemodialysis treatment, in some cases, it is not possible to achieve optimal correction of phosphorus-calcium metabolism, which can lead to the progression of secondary hyperparathyroidism, its transition to tertiary hyperparathyroidism. In such cases, the question of parathyroidectomy is considered. Indications for parathyroidectomy may occur when the level of parathormone more than 800 pg/mL, severe osteodystrophy, osteomalacia, hypercalcemia and hyperphosphatemia, resistant to treatment. The method of choice is subtotal parathyroidectomy or total parathyroidectomy with autotransplantation of parathyroid tissue [3, 19].

According to the clinical guidelines of NKF-KDOQITM (National Kidney Foundation Kidney Foundation Kidney Disease Quality Improvement Initiative in the United States), the main goal of therapy is to achieve target levels of the main indicators of phosphorus-calcium metabolism: PTH level - 150-300 pg/mL, adjusted total calcium (Ca) - 2.1-2.37 mmol/L, phosphorus (P) - 1.13-1.78 mmol/L and calcium-phosphorus product (Ca × P) - < 4.44 mmol2/L2 [9].

Adequate control of the four major biochemical parameters of bone and mineral metabolism remains one of the most difficult tasks, which can be achieved only in less than 6% of patients receiving dialysis [9, 14].

Numerous clinical studies have shown that the risk of death is significantly lower among patients who have achieved target values for PTH, Ca and P levels [9, 15].

Purpose of work: to study indices of phosphorus-calcium metabolism in patients treated with program hemodialysis depending on sex, duration of dialysis therapy, concomitant diseases.

Materials and methods of research. To study phosphorus-calcium metabolism, the following parameters in blood plasma were investigated: the level of total calcium (Ca), serum phosphorus (P), parathyroid hormone (PTH), and the calcium-phosphorus product (Ca×P) was calculated.

Statistical processing of the data was carried out using standard application program packages Excel (Microsoft, 2007), STATISTICA 7 after checking for normality of their distribution.

Results of the study and their discussion. A retrospective analysis of 46 case histories of patients undergoing treatment with program hemodialysis was performed. 19 men - 41.3%, mean age 49.2±9.42 years, 27 women - 58.7%, mean age 51.15±5.5 years. According to the duration of program hemodialysis treatment there was the following distribution: up to 1 year on dialysis - 36.96% (n=17) of patients, from 1 year to 5 years - 43.48% (n=20) of patients, more than 5 years - 19.56% (n=9) of patients. All patients underwent bicarbonate hemodialysis 3 times a week with a session duration of at least 4 hours. Calcium concentration in dialysis solution was 1.75 mmol/l. In the structure of diseases that led to chronic renal failure, chronic glomerulonephritis prevailed in 47.83% (n=22) of cases, diabetic nephrosclerosis took the second place in 15.22% (n=7) of cases, chronic pyelonephritis occurred in 10.87% (n=5) of cases, polycystic kidney disease in 8.7% (n=4) of cases, kidney damage due to arterial hypertension in 6.52% (n=3) of cases, other kidney damage in 10.86% (n=5) of cases. It should be noted that according to the Russian Register of renal replacement therapy, diabetic nephrosclerosis was only in the third place in the structure of causes of chronic renal failure in the population of patients treated with program hemodialysis as of 31.12.2011 [1]. This trend additionally confirms the pandemic of diabetes mellitus [10]. So according to Smirnova M.S. the main causes of terminal CKD development in the Russian Federation and in the Belgorod region agree on nosologies. The leading cause is chronic glomerulonephritis, the second place is shared by polycystic kidney disease and pyelonephritis, in our region is noted and diabetic nephropathy. In particular, kidney diseases arising against the background of diabetes mellitus are the most common cause of terminal CKD in the United States and Canada and account for more than a third of the frequency of new cases of CKD. For other nosologies the picture is approximately the same [10].

Among the comorbidities diagnosed in patients on hemodialysis, arterial hypertension predominated 39.13% (n=18) of cases and secondary hyperparathyroidism 21.74% (n=10) of cases, other comorbidities occurred in less than 10% of cases.

Analysis of blood biochemical study data showed that blood phosphorus level in men was 1.69±0.11 mmol/l and in women - 1.71±0.16 mmol/l. While the target values of phosphorus for dialysis patients are 1.13-1.78 mmol/l. Compared to the target values, 34.78% (n=16) of the observed patients had significantly elevated phosphorus levels. Blood calcium level in men was - 2.39±0.14 mmol/l and in women - 2.41±0.18 mmol/l. While the target values of calcium for dialysis patients are 2.1-2.37 mmol/l. Compared to the target values, 47.83% (n=22) of the observed patients had significantly elevated phosphorus levels. To correct phosphorus-calcium metabolism in such patients, calcium-free phosphatebinders should be preferred. Calcium-phosphorus product (Ca×P) was - 4.16±0.10 mmol/L in men and 4.22±0.16 mmol/L in women, with target values for dialysis patients below 4.44 mmol/L. The parathyroid hormone level in men was 317.9±78.7 mmol/L and in women 322±84.3 mmol/L, with target values for dialysis patients of 150-300 mmol/L. It should be noted that parathyroid hormone level was significantly elevated in 39.13% (n=18) of patients, compared to the target values, while secondary hyperparathyroidism was diagnosed only in 21.74% (n=10) of patients. This trend shows that 17.39%(n=8) of patients have high risk of developing secondary hyperparathyroidism.

To correct phosphorus-calcium metabolism, all patients were prescribed hypophosphatemic diet. 76.1% (n=35) of the total number of patients were prescribed phosphate-binding drugs. Of these, 52.18% (n=24) of patients took calcium-containing preparations, and 23.92% (n=11) took calcium-free preparations. To correct the level of parathyroid hormone, patients were prescribed calcimimetics, the dose of the drug and the frequency of administration were determined individually.

Conclusion. The study revealed that the main causes of chronic renal failure were chronic glomerulonephritis in 47.83% of cases and diabetic nephrosclerosis in 15.22% of cases. Among comorbidities, arterial hypertension prevailed in 39.13% of cases and secondary hyperparathyroidism in 21.74% of cases.

Analysis of blood biochemical study data showed that correction of phosphorus-calcium metabolism regardless of the duration of treatment with program hemodialysis is quite effective. It turned out that calcium-phosphorus product and blood phosphorus level were within the target values, there was a moderate increase in calcium level. But the level of parathyroid hormone in men and women exceeded the target values (317.9±78.7 mmol/l and 322±84.3 mmol/l, respectively), which is a risk of secondary hyperparathyroidism development in this group of patients.

In patients on program hemodialysis it is necessary to regularly monitor the basic parameters of phosphorus-calcium metabolism (level of calcium, phosphorus, as well as calcium-phosphorus product) in order to prevent bone and cardiovascular pathology, as well as to monitor the level of parathyroid hormone, in order to prevent secondary hyperparathyroidism.

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