Assessment Of Changes In Laboratory Indicators After Treatment In Patients Undergoing Hemodyalysis

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ABSTRACT

The article presents a comparative study of laboratory indicators in patients undergoing hemodialysis following complex treatment procedures. The results demonstrate that during renal replacement therapy, patients continue to experience deficiencies in hemoglobin, albumin, calcium, and vitamin D. Conversely, the study shows persistently elevated levels of leukocytes, urea, creatinine, parathyroid hormone, and fibroblast growth factor-23 in the blood serum. These findings emphasize the necessity of an individualized approach to addressing these issues for each patient.

Keywords: health care system, hemodialysis, chronic kidney disease

Introduction. It is known that chronic kidney disease (CKD) is defined as a disruption of the structure or function of the kidneys for a period of more than three months, regardless of the cause [2]. In practice, the classification of CKD recommended by the National Kidney Foundation of the United States (USA) in 2002 is used. According to it, 5 stages of this severe condition are distinguished [17].

Observations have shown that 25% of patients with CKD have limited knowledge about their health. This negatively affects people in low socio-economic situations and leads to unfavorable clinical outcomes [14].

One of the main strategies in combating CKD is to raise awareness and literacy of the population about the disease, as well as ensure timely referral to a nephrologist and initiation of treatment at early stages. The latter is very important, since CKD often progresses asymptomatically and only becomes clinically apparent after a significant portion of glomerular function is lost [7].

As this severe condition progresses from its early stages to end-stage renal disease (GFR <15 ml per 1.73m2 body surface), without timely renal replacement therapy (hemodialysis), patient treatment costs and mortality increase sharply, while life expectancy decreases significantly [12].

According to 2017 data, 3.9 million patients with CKD received hemodialysis, while approximately the same number who needed it did not receive renal replacement therapy for various reasons [1].

In patients undergoing hemodialysis, their survival is influenced not only by external factors but also by internal factors, namely a number of laboratory changes in the blood. One of the most widely discussed in recent years is fibroblast growth factor 23 (FGF-23), a protein consisting of 251 amino acids with a weight of 32 kDa, which is mainly synthesized and secreted by bone cells, primarily osteoblasts [21]. Unlike other proteins in this class, FGF-23 contains a signal peptide and has low affinity for heparin. It circulates throughout the body via the bloodstream and affects specific areas, including the kidneys.

FGF-23 signals are transmitted with high efficiency through four FGF receptors bound to the transmembrane Klotho protein as a co-receptor. Of these, FGF-2 is mainly expressed in the kidney's macula densa region, while FGF-3 is expressed in the proximal and distal tubules.

Conversely, the administration of 1,25-(OH) 2D to the body increases circulating FGF-23 levels in the blood [22].

The elevation of FGF-23 in the blood begins at CKD stage 2, before changes in calcium, phosphorus, and parathyroid hormone levels are observed [23]. When the disease reaches the terminal stage, its level often exceeds the normal range by 100 to 1000 times [24].

An increase in parathyroid hormone (PTH) in the blood parallel to the decrease in kidney function is often one of the early detectable changes [25]. Mortality from cardiovascular diseases is higher in patients with elevated serum PTH. According to statistical data provided by Hagström et al., in a study of 958 elderly individuals, a 1-SD increase in serum PTH increased the risk of death from cardiovascular diseases by 37-38% [25]. Several mechanisms can explain the relationship between PTH and mortality from cardiovascular diseases. Primarily, PTH directly participates in atherogenesis through vascular calcification and remodeling [26]. Additionally, PTH negatively affects the heart by causing left ventricular hypertrophy, calcification, and fibrosis [27].

Although some clinical observations suggest that FGF-23 is associated with an increase in C-reactive protein in CKD, there is insufficient data regarding its direct inducing effect on endothelial dysfunction [28].

In the available literature, data on FGF-23 levels during hemodialysis and the degree of its association with phosphorus are limited. Studying this protein allows for the assessment of its significance in this group of patients.

Purpose of the study: Assessment of changes in laboratory parameters before and after treatment in patients undergoing hemodialysis.

Research materials and methods: The study involved 180 patients receiving hemodialysis in the terminal stage of chronic kidney disease in Samarkand region. Their average age was 50.4±5.52 years, comprising 112 men and 68 women. All patients were under complete observation, and their hemodialysis regimen was studied. The subjects underwent general blood and urine analyses and a series of biochemical tests (creatinine, albumin, vitamin D, parathyroid hormone, fibroblast growth factor-23).

Based on the changes detected in the observed patients, the following groups of medications were used during the treatment process, depending on the indications. Their dosage and duration were individually selected for each patient under medical supervision according to specific indications and are listed below:

1. Erythropoietin - for monitoring hemoglobin levels in patients undergoing continuous hemodialysis;
2. Vitamin D preparations - for patients diagnosed with renal osteodystrophy, osteoporosis, and hypoparathyroidism;
3. Folic acid - for the treatment of Vitamin B12 deficiency anemia;
4. B group vitamins - to replenish the amount of these vitamins lost during hemodialysis;
5. Sevelamer - to reduce hyperkalemia and hyperphosphatemia;
6. Calcium acetate - to ensure a positive calcium balance and reduce blood phosphorus levels by decreasing its absorption in the gastrointestinal tract;
7. Ascorbic acid - to prevent hypo- and avitaminosis C;
8. Heparin - as an anticoagulant;

Treatment was also carried out in collaboration with relevant specialists for cases of hypertension, coronary heart disease, chronic heart failure, bronchial asthma, chronic obstructive pulmonary disease, diabetes mellitus, gastric and duodenal ulcers, as well as a number of other chronic diseases.

Analysis of the research results. In our study, we comparatively examined the dynamics of laboratory indicators in patients receiving hemodialysis in the Samarkand region. The comparison was made relative to the period when the treatment began. The results obtained from the patients are presented in Table 1 below.

Table 1
Characteristics of laboratory parameters determined in patients undergoing hemodialysis in the sixth month of our observation.

Indicators		Patients who have begun hemodialysis	Patients undergoing hemodialysis for 3 months	Patients undergoing hemodialysis for 6 months	Patients undergoing hemodialysis for the first year	Patients receiving hemodialysis for 3 years	Patients undergoing hemodialysis for 5 years
Leukocytes, 10^9/l	Before treatment	6,80±2,4	7,2±2,3	7,3±2,5	7,1±2,2	7,4±2,8	8.2±2,6
	After treatment	7,0±2,3	7,3±2,5	7,5±2,4	7,4±2,4	7,6±3,1	8.4±2,4
Hemoglobin, g/l	Before treatment	120.5±10,1	116,3±1,7	114,1±11,4	18,0±9,8	108,0±10,4	102±11,2
	After treatment	107±11,5	105,4±11,2	105,1±11,4	102,0±11,6	100,0±11,5	94±10,6
Neutrophils, %	Before treatment	68,2±5,5	66,8±6,1	66,7±7,9	65,3±9,8	66,8±8,7	65,6±8,4
	After treatment	69,4±5,6	66,7±6,2	65,7±8,7	64,2±10,2	63,7±7,8	62,4±8,2
Lymphocytes, %	Before treatment	18,8±3,3	19,4±3,2	21,1±2,6	20.4±2,9	21,5±2,2	21,7±3,1
	After treatment	18,4±3,2	20,6±2,9	20,4±2,7	21±2,8	22,4±2,7	22,6±2,8
Serum albumin, g/l	Before treatment	36,8±3,4	36,6±4,1	36.4±3.6	35,6±3,7	35.4±3.5	34.8±3.0
	After treatment	37,2±3,8	36,5±4,2	35.4±3.4	34,2±3,6	34±3.4	32.4±2.5
Transferrin, g/l	Before treatment	62.5±1.4	68.7±1.3	78.2±1.5	76.3±1.7	70.3±2.0	68.4±2.4

	After treatment	63.4±1.7	75.6±1.2	85.5±1.1	82.0±1.9	71.3±2.1	74.5±2.0
Urea, μmol/l	Before treatment	12.2±1.5	12.6±1.9	14.3±1.8	14.1±1.8	16.6±2.5	16.4±3.2
	After treatment	26.4±1.2	21.8±0.9	24.7±1.0	24.5±1.3	26.6±1.4	26.8±1.2
Creatinine, μmol/l	Before treatment	247.8±30.4	228.4±32.5	236.2±32.2	241.1±30.2	279.4±30.9	244.3±31.2
	After treatment	447.7±32.3	322.4±31.4	326.2±31.1	340.1±31.8	379.2±36.9	345.2±33.9
Phosphate (mmol/l)	Before treatment	1.2±0.2***	2.0±0.1***	2.1±0.3***	1.8±0.1***	1.9±0.25***	2.1±0.2***
	After treatment	1.4±0.1	2.3±0.1***	2.7±0.1***	2.5±0.1***	2.5±0.1***	3.1±0.2***
Calcium Ca (mmol/l)	Before treatment	2.0±0.1	2.0±0.15	1.8±0.2	2.0±0.2	2.0±0.2	2.0±0.2
	After treatment	2.1±0.1	1.9±0.1	1.6±0.1	1.9±0.1	1.9±0.1	1,7±0.2

As shown in the table, the leukocyte count in blood serum of patients starting hemodialysis was 7.0±2.3*109. In patients receiving hemodialysis for 5 years, this count increased to 8.4±2.4*109, indicating that long-term planned renal replacement therapy leads to an increase in inflammatory processes in the body. The hemoglobin level at the start of dialysis was 107±11.5 g/l, and in patients who underwent this treatment for 3 months, 6 months, 1 year, 3 years, and 5 years, the levels were 105.4±11.2, 105.1±11.4, 102.0±11.6, 100.0±11.5, and 94±10.6 g/l, respectively. No statistically significant difference was observed when comparing these values. The neutrophil count in patients starting hemodialysis was 69.4±5.6%, but it was found to decrease in those who received this treatment for an extended period (62.4±8.2% in those who received hemodialysis for 5 years). Conversely, an increase in the number of neutrophils in the blood serum was noted. Albumin levels in patients undergoing hemodialysis were 37.2±3.8 g/l at the start, 36.5±4.2 g/l at 3 months, 35.4±3.4 g/l at 6 months, 34.2±3.6 g/l at 1 year, 34±3.4 g/l at 3 years, and 32.4±2.5 g/l at 5 years.

The level of transferrin in blood serum was 63.4±1.7 g/l in patients starting hemodialysis, 75.6±1.2 g/l in patients receiving hemodialysis for 3 months, 85.5±1.1 g/l in patients receiving hemodialysis for 6 months, and 82.0±1.9, 71.3±2.1, and 74.5±2.0 g/l in patients receiving hemodialysis for 1 year, 3 years, and 5 years, respectively. When comparing the obtained results, no significant difference was found (r>0.05). Albumin levels in patients starting hemodialysis were 37.2±3.8 g/l, at 3 months 36.5±4.2 g/l, at 6 months 35.4±3.4 g/l, at 1 year 34.2±3.6 g/l, at 3 years 34±3.4 g/l, and at 5 years 32.4±2.5 g/l. The level of transferrin in blood serum was 63.4±1.7 g/l in patients starting hemodialysis, 75.6±1.2 g/l in patients receiving hemodialysis for 3 months, 85.5±1.1 g/l in patients receiving hemodialysis for 6 months, and 82.0±1.9, 71.3±2.1, and 74.5±2.0 g/l in patients receiving hemodialysis for 1 year, 3 years, and 5 years, respectively. When comparing the obtained results, no significant difference was found (r>0.05). Urea levels were also 26.4±1.2, 21.8±0.9, 24.7±1.0, 24.5±1.3, 26.6±1.4, and 26.8±1.2 μmol/l between the groups, respectively, and no significant difference was observed (r>0.05). Creatinine levels also did not differ significantly between the groups (r>0.05). The level of phosphorus in blood serum was 1.4±0.1 mmol/l in patients starting hemodialysis, 2.3±0.1 mmol/l in patients undergoing hemodialysis for 3 months, and 2.7±0.1, 2.5±0.1, 2.5±0.1, and 3.1±0.2 mmol/l in patients undergoing renal replacement therapy for 6 months, 1 year, 3 years, and 5 years, respectively. When comparing these indicators between the groups, a highly significant difference (r<0.001) was noted compared to the initial indicators. No significant difference was found between the groups in serum calcium indicators (r>0.05).

During the observation period, the leukocyte count in the blood serum of patients who started hemodialysis was 6.80±2.4*109. In patients receiving hemodialysis for 1 year and 5 years, the count was 7.1±2.2*109 and 8.2±2.6*109, respectively. The hemoglobin level at the start of dialysis was 120.5±10.1 g/l, and in those who underwent this treatment for 3 months, 6 months, 1 year, 3 years, and 5 years, the levels were 66.8±6.1, 66.7±7.9, 65.3±9.8, 66.8±8.7, and 65.6±8.4, respectively. When compared, no significant difference was found between these values (p>0.05). Albumin levels in patients undergoing hemodialysis were 36.8±3.4 g/l at the start, 36.6±4.1 g/l at 3 months, 36.4±3.6 g/l at 6 months, 35.6±3.7 g/l at 1 year, 35.4±3.5 g/l at 3 years, and 34.8±3.0 g/l at 5 years (p>0.05). When comparing the transferrin levels in blood serum, no significant difference was noted (p>0.05). Urea levels were 12.2±1.5, 12.6±1.9, 14.3±1.8, 14.1±1.8, 16.6±2.5 and 16.4±3.2 μmol/l between the groups, respectively, and a highly significant difference was observed (p<0.001). Creatinine levels also showed a highly significant difference between the groups during the observation period (p<0.001). The phosphorus level in blood serum was 1.2±0.2 mmol/l in patients starting hemodialysis, 2.0±0.1 mmol/l in patients undergoing hemodialysis for 3 months, and 2.1±0.3, 1.8±0.1, 1.9±0.25 and 2.1±0.2 mmol/l in patients undergoing renal replacement therapy for 6 months, 1 year, 3 years and 5 years, respectively. When comparing these indicators between the groups, a highly significant difference (p<0.001) was revealed compared to the initial values. Despite positive changes in calcium levels in blood serum (2.0±0.1, 2.0±0.15, 1.8±0.2, 2.0±0.2, 2.0±0.2 and 2.0±0.2 mmol/l, respectively), no significant difference was observed between the groups compared to the baseline values (p>0.05). Figure 1 below shows the indicators of vitamin D in patients.

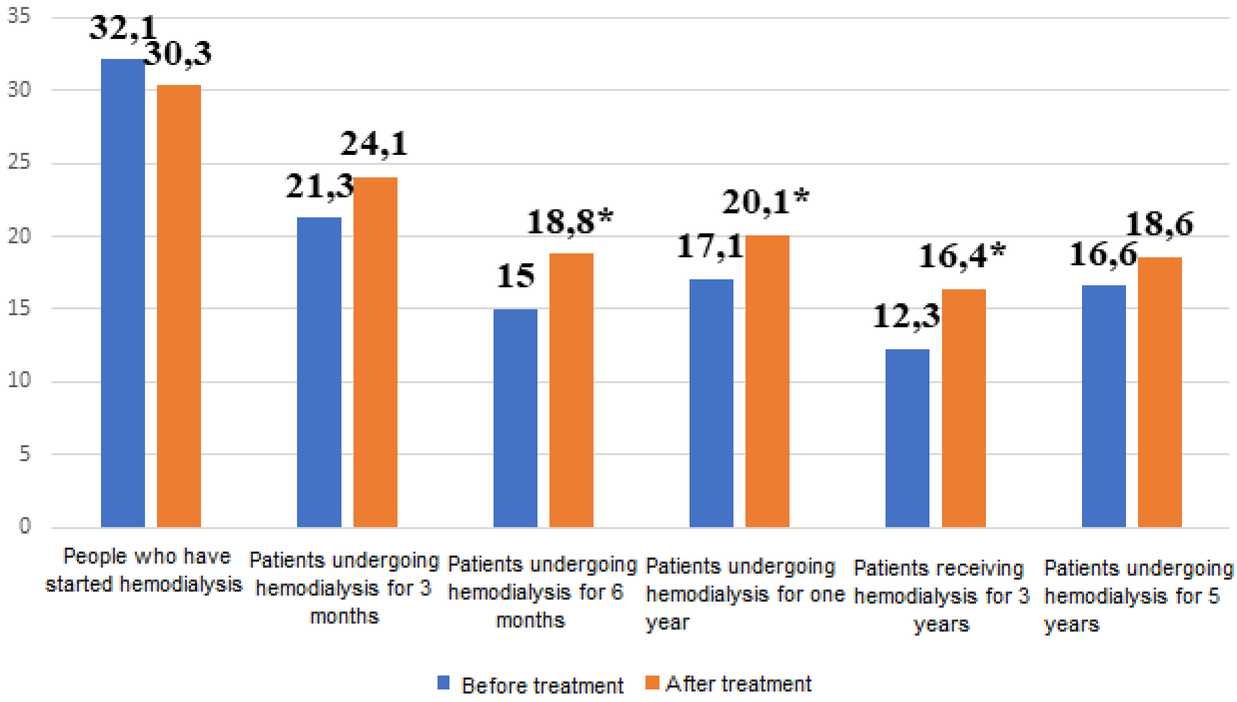

Figure 1. Comparative analysis of vitamin D indicators over time in patients undergoing hemodialysis.

The level of vitamin D decreased from 32.1±1.3 ng/ml to 30.3±1.4 ng/ml in the group of patients who started hemodialysis, but no significant difference ($p>0.05$) was found. In patients receiving hemodialysis for 3 months, no significant difference was observed, with levels of 21.3±0.6 ng/ml before treatment and 24.1±1.3 ng/ml after treatment ($p>0.05$). In patients receiving renal replacement therapy for 6 months, a significant difference ($p<0.05$) was revealed, with levels equal to 15.0±0.7 and 18.8±1.4 ng/ml, respectively, before and after treatment. In patients undergoing hemodialysis for 1 year, levels increased from 17.1±0.7 to 20.1±1.3 ng/ml after treatment, and a significant difference was found ($p<0.05$). In patients receiving hemodialysis for 3 years, levels were 12.3±0.6 ng/ml before treatment and 18.4±1.2 ng/ml after treatment, with a significant difference ($p<0.05$) between them. In patients who underwent 5 years of hemodialysis, levels were 16.6±0.7 and 18.6±1.0 ng/ml before and after treatment, respectively ($p>0.05$).

Along with the aforementioned, we also conducted a comparative study of parathyroid hormone parameters in our observed patients during the hemodialysis process, and the obtained results are presented in Figure 2.

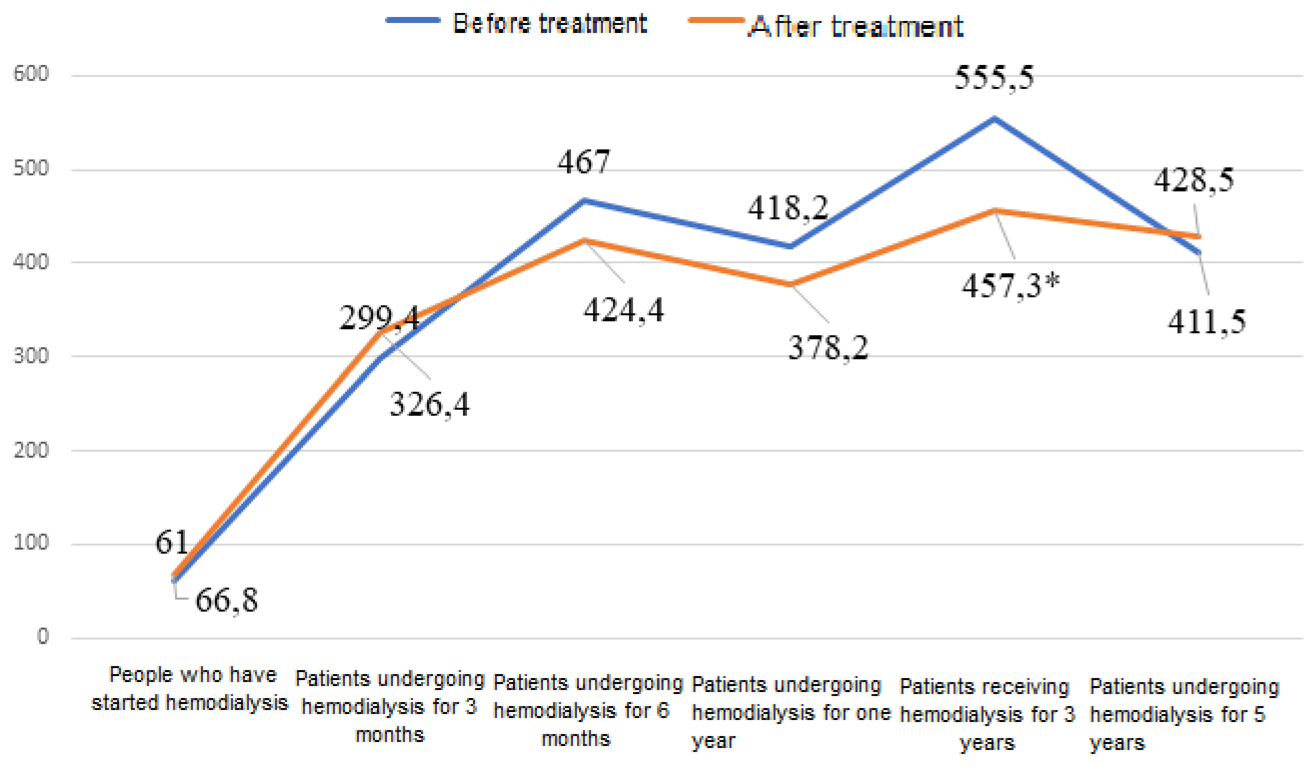

Figure 2. Comparative analysis of parathyroid hormone levels in patients undergoing hemodialysis over time.

As shown in the figure, the initial levels of parathyroid hormone in the groups were 61.0±2.7 ng/ml, 299.4±16.2 ng/ml, 467.0±25.5 ng/ml, 418.2±22.2 ng/ml, 555.5±26.0 ng/ml, and 411.5±23.1 ng/ml, respectively. The results revealed that the parathyroid hormone level in the blood of patients undergoing hemodialysis for five years increased by 6.74 times, with a highly significant difference ($p<0.001$) observed when compared. Hormone levels were found to stabilize somewhat by the sixth month of hemodialysis treatments. After the treatment, the parathyroid hormone levels in the groups were 66.8±5.7 ng/ml, 326.4±17.3 ng/ml, 424.0±26.4 ng/ml, 378.2±20.4 ng/ml, 457.3±25.4 ng/ml, and 428.5±29.4 ng/ml, respectively. When compared, a significant difference ($p<0.05$) was noted only in patients receiving hemodialysis for three years.

In our observations, PTH indicators confirmed a corresponding increase in its levels with an increase in the duration of dialysis. It was established that the indicators in patients undergoing renal replacement therapy for 5 years were 6.74 times ($p<0.001$) higher than the initial hormone level. However, by the sixth month of hemodialysis treatments, it was found that the hormonal indicators had relatively stabilized. In contrast to the above, by the 3rd year of replacement therapy, PTH indicators showed a significant difference.

The conducted analysis demonstrates the importance of determining PTH during long-term hemodialysis in chronic kidney disease and the necessity for its dynamic monitoring.

Recent studies have shown that fibroblast growth factor 23 plays an important role in regulating phosphorus-calcium metabolism and vitamin D metabolism. Taking this into account, we examined its indicators at different stages of hemodialysis in our observation, which is presented in Figure 3.

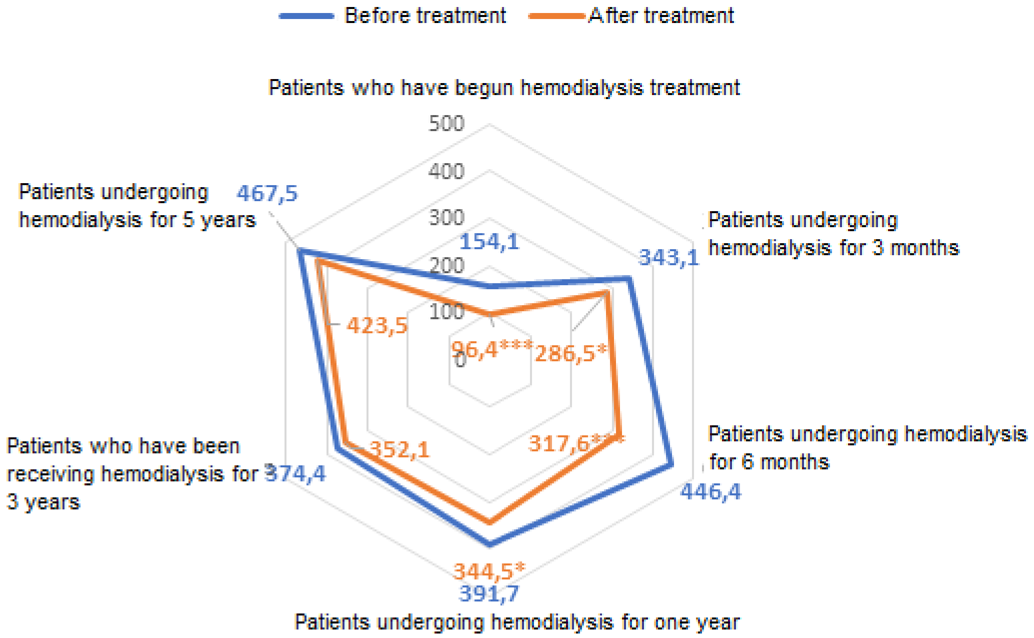

Figure 3. Fibroblast-23 levels in the blood of patients during various periods of hemodialysis.

As shown in the figure, the fibroblast 23 level in blood serum was 154.1±12.9 ng/ml in the early period of hemodialysis and decreased to 96.4±10.3 ng/ml after six months of treatment. When comparing these values, a highly significant difference ($p<0.001$) was observed. In patients receiving hemodialysis for three months, a significant difference was noted, with levels of 343.1±12.6 ng/ml before treatment and 286.5±16.7 ng/ml after treatment ($p<0.05$). In patients receiving renal replacement therapy for 6 months, a highly significant difference ($p<0.001$) was found, with levels of 446.4±12.8 and 317.6±13.8 ng/ml before and after treatment, respectively. In patients undergoing hemodialysis for one year, the level significantly decreased ($p<0.05$) from 391.7±14.6 to 344.5±16.2 ng/ml after treatment. In patients receiving hemodialysis for 3 years, the levels before and after treatment were 374.4±14.2 ng/ml and 352.1±18.7 ng/ml, respectively, with no significant difference ($p>0.05$) between them. In patients who underwent 5 years of hemodialysis, the levels before and after treatment were 467.5±16.2 and 423.5±18.4 ng/ml, respectively ($p>0.05$).

Conclusion. The results obtained confirmed the necessity of implementing complex treatment regimens for patients from the onset of renal replacement therapy. In patients who underwent long-term hemodialysis, the effectiveness of conservative treatment was found to be low due to irreversible changes in internal organs. The analysis of vitamin D-related findings showed that patients receiving renal replacement therapy exhibited various changes depending on the duration of treatment. In its initial stages, during the first three months and the last five years, the indicators did not differ significantly before and after treatment. These results confirm the limited effect of vitamin D on patients' bodies during these periods. In the remaining periods, significant positive changes were observed ($p<0.05$). This can be attributed to the positive effect of vitamin D on metabolism in the patient's body during these periods. Our results indicate that the problem of vitamin D deficiency persists during renal replacement therapy in the patients under our observation, and an individual approach to addressing this deficiency is necessary for each patient.

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In the early and relatively short periods of hemodialysis (3-6 months), a significant and reliable decrease in the serum levels of fibroblast growth factor 23 (FGF-23) was observed. Especially in the period up to 6 months, this decrease was of high statistical significance ($p<0.001$). The level of FGF-23 also significantly decreased in patients receiving hemodialysis for up to one year. However, with an increase in the duration of hemodialysis (3-5 years), no significant difference was found in FGF-23 levels before and after treatment. This indicates the possibility of FGF-23 level stabilization or a decrease in treatment effectiveness during long-term hemodialysis.

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