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CORRECTION OF CLINICAL AND FUNCTIONAL CHANGES IN THE KIDNEYS WITH INFLUENCE ON THE STRUCTURAL AND FUNCTIONAL STATE OF THE VESSELS AND, ON THIS BASIS, ASSESSMENT OF THE DEVELOPMENT OF CHRONIC KIDNEY DISEASE

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ABSTRACT

The article reflects the results of studies conducted in 101 patients in the conservative stage of chronic kidney disease to assess structural and functional changes in blood vessels and improve the clinical and functional state of the kidneys with the use of hypotensive and angioprotective drugs, as well as to assess the progression of renal failure. In this case, the level of exacerbation of chronic kidney disease based on various treatment regimens is substantiated by accurate statistical calculations. At the same time, opinions and considerations are presented on various areas of future prospective research that should be carried out for the further improvement of the industry.

Key words: chronic kidney disease, vascular, creatinine, glomerular filtration, exacerbation.

INTRODUCTION

Chronic kidney disease (CKD) is currently a global problem in modern medicine. A large part of the world's population, approximately 13%, suffers from this disease, and their number increases by 5-8% annually [5, 9]. Due to the presence of a long latent period of the disease, most patients with kidney disease are unaware of the impairment of kidney function, which is the main reason for the progressive increase in the frequency of the disease. For example, in the USA, out of 37 million people with CKD, only one in ten is aware of having CKD [5, 11].

Coordination of the structural and functional state of blood vessels in chronic kidney disease and its prevention and slowing down of dysfunction is one of the priority tasks of modern clinical nephrology [7]. The fact that CKD is a risk factor for cardiovascular diseases and, conversely, a multitude of irrefutable factors contributing to the progression of renal failure in cardiovascular pathologies is the basis for systematic monitoring of the state of blood vessels [1, 2, 4]. Also, the fact that in recent years the age of patients with CKD is increasing and, conversely, the age of patients with CVD is increasing determines the need to strengthen our approach to the problem [1, 4, 9].

It is known that nephropathies of any genesis are based on impaired blood circulation in the glomerular apparatus, microthromboses, renal parenchymal ischemia, and, as a consequence, glomerular nephroangiosclerosis. Therefore, the role of drugs affecting blood vessels in the treatment of CKD is invaluable. Among them, hypotensive agents have a reliable effect on blood vessels. Among antihypertensive drugs, the most angioprotective effect on blood vessels is exhibited by ACE inhibitors acting on RAAT [8, 10]. By the end of the last century, a number of undeniable side effects (cough, angioneurotic edema) on this group of drugs, widely used in several areas of clinical medicine, limited their prospects. By this time, new angiotensin II receptor blockers appeared, replacing them in this case. In the 21st century, the introduction of new generations of drugs of this group into practice requires research to reveal new aspects of their effect on blood vessels.

Research objective.

Analysis of renal functional changes with vascular impairment in chronic kidney disease and assessment of the progression of renal failure in patients depending on it.

Research materials and methods.

101 patients with stage II and III A CKD, who received inpatient treatment at the Republican Specialized Scientific and Practical Medical Center of Nephrology and Kidney Transplantation and were subsequently under dispensary observation at this institution, were selected for the study. All patients included in the study, depending on the degree of arterial hypertension, individually took the necessary dose of azilsartan for hypotensive purposes (40-80 mg/day). They were divided into the 1st group (n-53) who received only azilsartan in addition to traditional treatment, and the 2nd group (n-48) who received azilsartan and ethylmetalhydroxypyridine succinate in addition to traditional treatment. Group 2 was prescribed ethylmetalhydroxypyridine succinate (EMGS) at a dose of 250-500 mg/day by injection during inpatient treatment and 125-250 mg/day per os during

outpatient observation. The study groups were observed for 6 months. In all patients at the beginning of treatment and at the end of the study, markers of kidney damage (proteinuria, erythrocyturia, cylindruria, albuminuria, albumin/creatinine ratio), indicators of renal function (urea and creatinine) were examined, and GFR was calculated based on the level of creatinine in the blood. The results were statistically analyzed. Also, at the end of the study, the criteria for the dependence of the degree of exacerbation of renal failure on treatment methods in patients were calculated using an online computer program https://medstatistic.ru/calculators/calchi.html.

Results and Discussion.

Our prospective research conducted over six months revealed the following results. In the first group, consisting of patients who received only azilsartan in addition to traditional treatment, proteinuria was 2.24±0.18 g/l at the beginning of the study and decreased to 1.72±0.19 g/l at the end of the study, showing a less significant reduction ($p<0.05$). In the second group, comprising patients who received azilsartan and ethylmethylhydroxypyridine succinate in addition to traditional treatment, proteinuria was initially 2.23±0.18 g/l and significantly decreased to 1.13±0.19 g/l by the end of the study ($p<0.001$). Statistical analysis of the results showed that all indicators in the study groups changed significantly ($p<0.001$) compared to the control group. At the end of the study, the more substantial decrease in proteinuria in the second group compared to the first group, although less statistically significant ($p<0.05$), was of considerable clinical importance (Table 1).

Erythrocyturia in the first group was 7.3±0.52 cells per field of view at the beginning of the study and decreased to 5.9±0.45 cells by the end, although this reduction was less significant ($p<0.05$). In the second group, erythrocyturia was initially 7.3±0.61 cells and significantly decreased to 4.7±0.49 cells by the end of the study ($p<0.01$). Statistical analysis of the results demonstrated that all indicators in the study groups changed significantly ($p<0.001$) compared to the control group. However, at the end of the study, the change in erythrocyturia in the second group was not statistically significant compared to the first group (Table 1).

At the beginning of the study, cylindruria in Group 1 was 5.8±0.14 per field of view, and by the end of the study, it decreased to 5.3±0.13, although with lower statistical significance ($p<0.05$). In Group 2, at the beginning of the study, 5.7±0.14 were detected, and by the end of the study, a significant ($p<0.001$) decrease to 4.6±0.25 was observed. Statistical analysis of the results showed that all indicators in the study groups changed significantly ($p<0.001$) compared to the control group. At the end of the study, cylindruria decreased more in Group 2

compared to Group 1, although with lower statistical significance (), which is attributed to the effectiveness of the complex treatment (Table 1).

Table 1

Laboratory changes in glomerular injury markers

Parameters	Control group (n=20)	Group 1 (n=53) Azilsartan		Group 2 (n=48) Azilsartan+EMGS	
		Study start	Study end	Study start	Study end
Proteinuria	0±0,0	2,24±0,18***	1,72±0,19***^	2,23±0,24***	1,13±0,19***^^^ #
Erythrocyturia	1,4±0,42	7,3±0,52***	5,9±0,45***^	7,3±0,61***	4,7±0,49***^^
Cylindruria	0,1±0,01	5,8±0,14***	5,3±0,13***^	5,7±0,14***	4,6±0,25*** ^^^ #
Albuminuria, mg/day	4,6±0,55	51,3±2,97***	42,9±2,19***^	50,9±2,96***	35,8±2,17***^^#
A/C mg/mmol	0,59±0,07	4,82±0,09***	4,53±0,08***^	4,91±0,09***	4,42±0,08***^^

Note: * - values are significant compared to the control group indicators (*- p<0.05, **- p<0.01, ***- p<0.001); ^ - differences are significant compared to the values at the beginning of the study (^ - p<0.05, ^^ - p<0.01, ^^^ - p<0.001), values at the end of the study are significant compared to the indicators of differences between groups 1 and 2 (# - p<0.05, ## - p<0.01, ### - p<0.001).

Albuminuria in the 1st group, consisting of patients who received only azilsartan in addition to traditional treatment, was 51.3±2.97 mg/day at the beginning of the study and decreased to 42.9±2.19 mg/day at the end of the study with low statistical significance (p<0.05). In the 2nd group, consisting of patients who received azilsartan and EMGS in addition to traditional treatment, albuminuria was detected at 50.9±2.96 mg/day at the beginning of the study and significantly decreased (p<0.01) to 35.8±2.17 mg/day at the end of the study. Statistical analysis of the results showed that all indicators in the study groups changed significantly (p<0.001) compared to the control group. At the end of the study, the decrease in albuminuria in the 2nd group, although less statistically significant (p<0.05) compared to the 1st group, has important clinical significance (Table 1). In this case, the significant decrease in albuminuria in patients of the 2nd group and a more positive change in values, although less statistically significant than in the 1st group, is attributed to the effectiveness of the complex treatment (Figure 1).

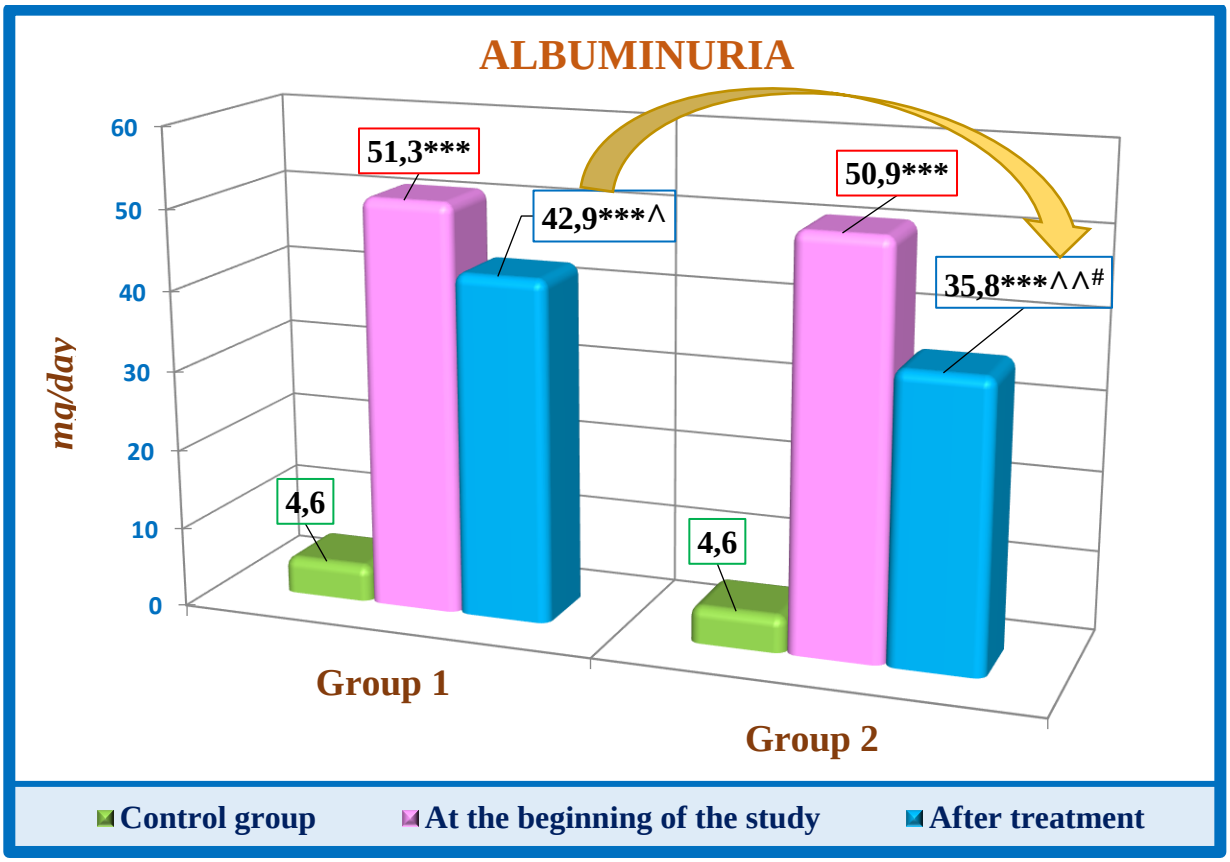

Figure 1. Changes in markers of glomerular damage in chronic kidney disease in response to various treatment regimens

The albumin/creatinine ratio in the 1st group was 4.82±0.09 mg/mmol at the beginning of the study and decreased slightly to 4.53±0.08 mg/mmol at the end of the study, which was statistically insignificant ($p<0.05$). In the 2nd group, the A/C ratio was 4.91±0.09 mg/mmol at the beginning of the study and decreased significantly ($p<0.01$) to 4.42±0.08 mg/mmol by the end of the study. Statistical analysis of the results showed that all indicators in the study groups changed significantly ($p<0.001$) compared to the control group. However, at the end of the study, the change in the A/C ratio in the 2nd group compared to the 1st group was not statistically significant (Table 1). In this case, under the influence of complex treatment, a positive shift in the A/C ratio was observed in patients of the 2nd group. Although statistical analysis revealed insignificant changes in the values, the more pronounced decrease in the A/C ratio in the 2nd group compared to the 1st group is of sufficient clinical importance (Figure 2).

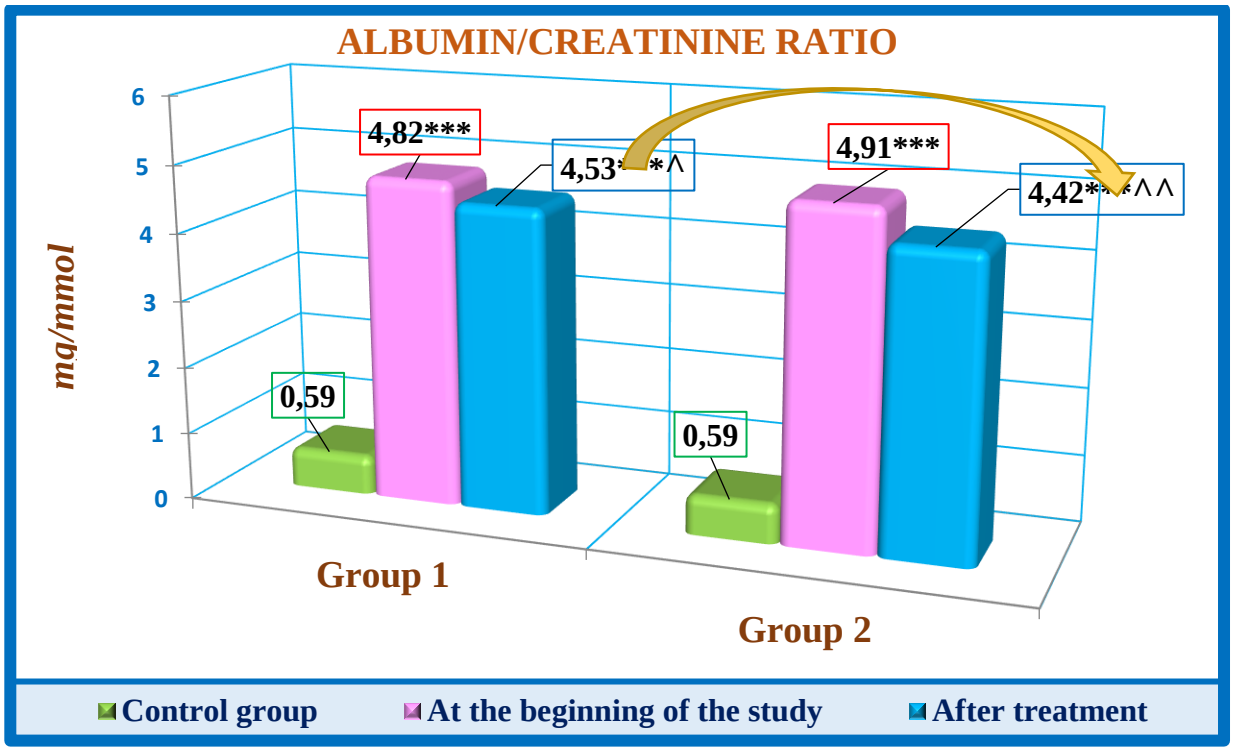

Figure 2. Changes in markers of glomerular damage in chronic kidney disease in response to various treatment regimens

These changes in kidney damage markers are certainly reflected in the functional state of the kidneys. Accordingly, in the 1st group of patients who received only azilsartan in addition to traditional treatment, urea levels at the beginning of the study were 9.44±0.27 mmol/l, and at the end of the study, they decreased insignificantly to 9.38±0.29 mmol/l. In the 2nd group, consisting of patients who received azilsartan and EMGS in addition to traditional treatment, urea levels, which were 9.45±0.18 mmol/l at the beginning of the study, significantly decreased to 8.6±0.22 mmol/l at the end of the study ($p<0.001$). Statistical analysis of the results showed that all indicators in the study groups changed significantly ($p<0.01$, $p<0.001$) compared to the control group. At the end of the study, a less significant ($p<0.05$) decrease in urea was observed in the 2nd group compared to the 1st group (Table 2).

Creatinine levels in the 1st group at the beginning of the study were 131.2±3.2 µmol/l, and at the end of the study, they decreased insignificantly to 129.6±3.98 µmol/l. In the 2nd group, creatinine levels, which were 132.1±3.98 µmol/l at the beginning of the study, decreased significantly ($p<0.01$) to 117.4±3.37 µmol/l at the end of the study. Statistical analysis of the results showed that all indicators in the study groups changed significantly ($p<0.001$) compared to the control group. At the end of the study, the decrease in creatinine levels in the 2nd group, although less significant ($p<0.05$) compared to the 1st group, was of considerable clinical importance (Table 2).

Table 2

Laboratory profile of renal functional changes

Parameters	Control group (n=20)	Group 1 (n=53) Azilsartan		Group 2 (n=48) Azilsartan+EMGS	
		At the beginning of the study	At the end of the study	At the beginning of the study	At the end of the study
Urea	5,42±1,08	9,44±0,27***	9,38±0,29***	9,45±0,18***	8,6±0,22**^^^#
Creatinine	71,6±4,26	131,2±3,2***	129,6±3,98***	132,1±3,98***	117,4±3,37***^^#
eGFR	97,8 ±4,24	59,6±3,21***	61,4 ±2,73***	60,3 ±2,73***	69,7±1,91***^^ #

Note: * - values are significant compared to the control group indicators (*- p<0.05, **- p<0.01, ***- p<0.001); ^ - differences are significant compared to the values at the beginning of the study (^ - p<0.05, ^^ - p<0.01, ^^^ - p<0.001), values at the end of the study are significant compared to the indicators of differences between groups 1 and 2 ($^{\#}$ - p<0.05, $^{\#\#}$ - p<0.01, $^{\#\#\#}$ - p<0.001).

The estimated GFR (eGFR), calculated based on serum creatinine, in Group 1 at the beginning of the study was 59.6±3.21 ml/min, and at the end of the study it increased insignificantly to 61.4±2.73 ml/min. In Group 2, the eGFR, which was 60.3±2.73 ml/min at the beginning of the study, increased significantly (p<0.01) to 69.7±1.91 ml/min at the end of the study. Statistical analysis of the results showed that all values in the study groups changed significantly (p<0.001) compared to the control group. At the end of the study, the increase in the eGFR index in Group 2, although less significant (p<0.05) compared to Group 1, is important for the functional state of the kidneys (Table 2).

If we analyze the results of kidney function tests reflected in the diagram, we observe that in the 2nd group, consisting of patients receiving azilsartan and EMGS in addition to traditional treatment, there was a significant decrease in creatinine levels at the end of the study compared to the beginning. A similar positive trend was also observed in the GFR gradient, which can be attributed to the effectiveness of the complex treatment. Moreover, after treatment, this group showed a slight, albeit less significant, decrease in creatinine levels compared to the 1st group, as well as a somewhat more pronounced increase in GFR values. These findings are of great importance in clinical nephrology practice (Figure 3).

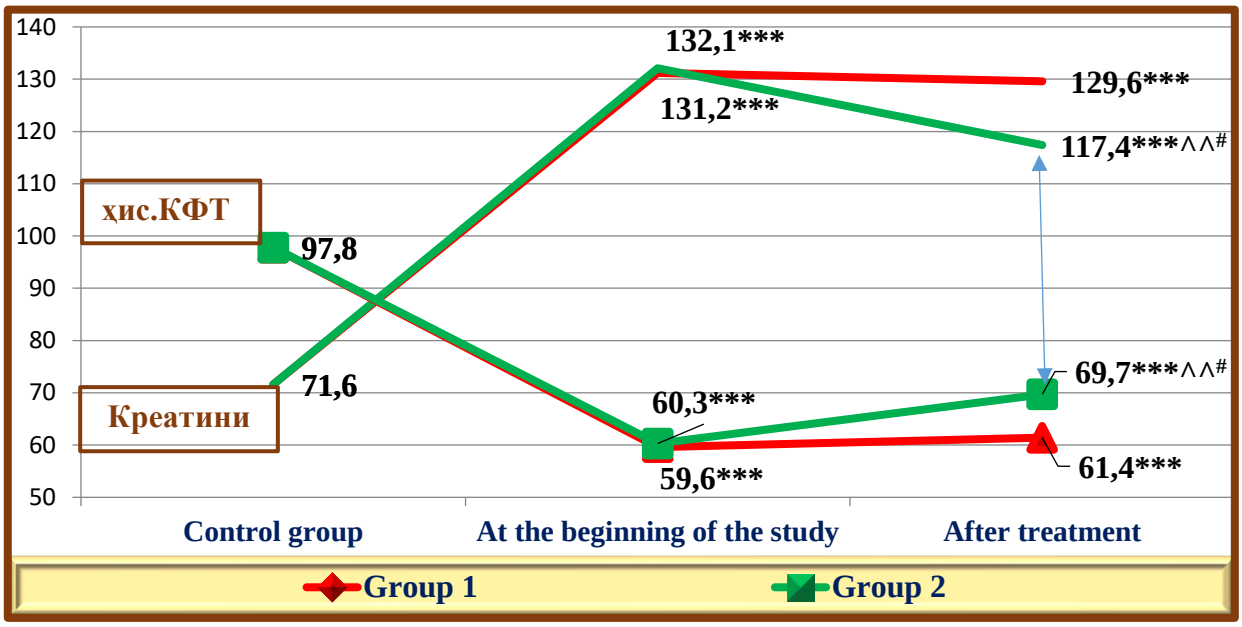

Figure 3. Changes in renal function indicators in chronic kidney disease based on various treatment regimens

It is known that glomerulosclerosis is the main criterion for the progression of CKD. In this context, influencing the blood vessels to any degree is one of the primary tasks of clinical medicine. In fact, it would not be incorrect to refer to glomerulosclerosis as "glomeruloangiosclerosis." Therefore, since our research focused on combating glomeruloangiosclerosis, it is necessary to analyze the progression of CKD.

DYNAMICS OF CHRONIC KIDNEY DISEASE PROGRESSION IN PATIENTS DURING THE STUDY

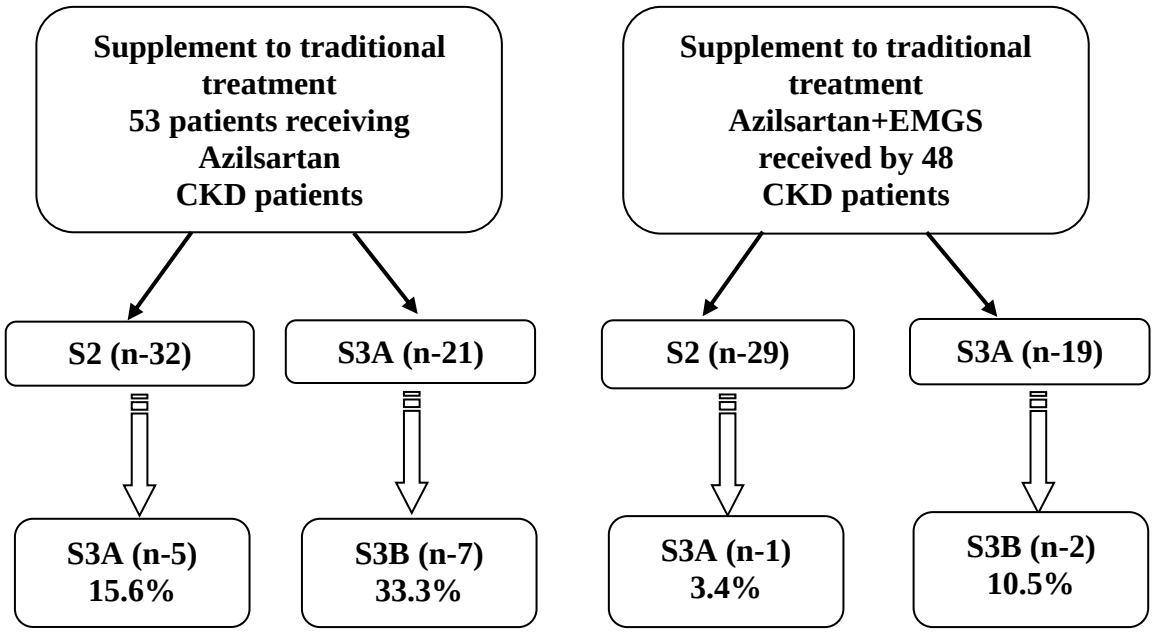

Figure 4. Dynamics of chronic kidney disease progression during the study

The composition of CKD patients in group 1, who received only azilsartan in addition to traditional treatment, consisted of 32 patients with stage S2 and 21 patients with stage S3A. After six months of observation and treatment, 5 (15.6%) patients in this group progressed from stage S2 to stage S3A, and 7 (33.3%) progressed from stage S3A to stage S3B. Overall, 12 (22.6%) patients in this group experienced worsening of renal failure. In the 2nd group, where azilsartan and EMGS were recommended in addition to traditional treatment, the composition of CKD patients consisted of 29 patients with stage S2 and 19 patients with stage S3A. At the end of the study, 1 (3.4%) patient in this group progressed from stage S2 to stage S3A, and 2 (10.5%) progressed from stage S3A to stage S3B. In total, 3 patients in this group experienced worsening of renal failure. It should be noted that as CKD progresses from stage to stage and becomes more severe, its rate of progression also increases. This process occurs regardless of the treatment method recommended to the patient (Fig. 4).

Table 3

Progression of Chronic Kidney Disease
Analysis results according to the criteria for assessing the influence and correlation of various treatment methods

Study groups	Number of patients	Number of patients with CKD not progressing to the next stage	Number of patients with CKD progressing to the next stage	χ^2-index	Reliability
Group that received azilsartan in addition to traditional treatment	n-53	41	12	5.352	p=0.02 The correlation is moderate
Group receiving azilsartan + EMGS in addition to traditional treatment	n-48	45	3		

* The criteria for dependence on treatment methods https://medstatistic.ru/calculators/calchi.html were calculated using an online computer program.

Statistical analysis of the results obtained on the progression of CKD revealed the value of the χ^2-index depending on various treatment regimens. According to it, the χ^2-index was equal to 5.352 (p=0.02), which showed a moderate correlation between various treatment methods and the exacerbation that occurred based on them, according to Pearson's numerical coefficient (Table 3, Figure 5).

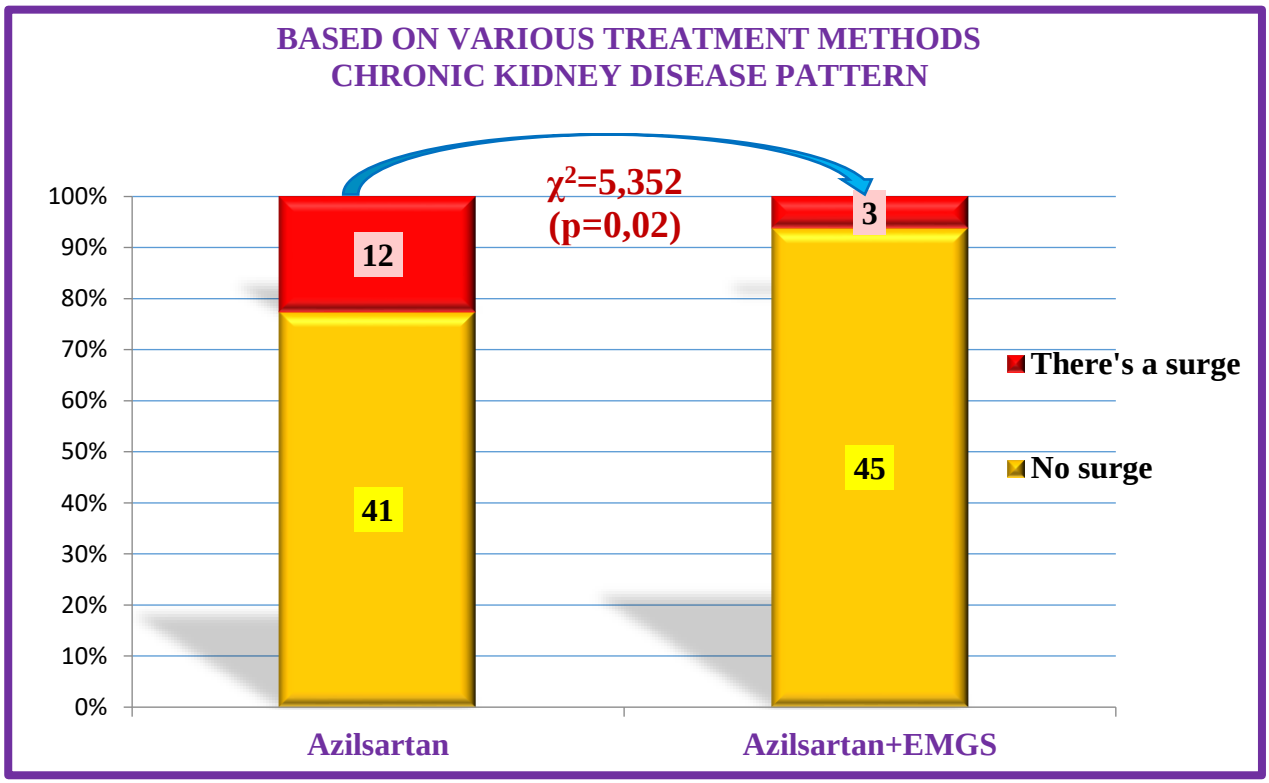

Figure 5. Illustration of the influence and relationship of various treatment methods on the progression of chronic kidney disease

Conclusion.

Thus, nephroangiopathy is considered one of the main pathogenetic mechanisms in the progression of renal failure. This is also reflected in our research. In this case, kidney damage markers, indicators of renal dysfunction, and the progression of CKD presented a distinctive pattern in specific study groups. This pattern emerged as a result of various treatment regimens. It can be observed that in patients receiving azilsartan and EMGS in addition to traditional treatment, the kidney damage markers and parameters determining renal function shifted in a positive direction, and the progression of renal failure in these study groups slowed down. At the same time, it is of particular clinical significance that the acceleration of chronic renal failure progression from stage to stage, as it deepens, occurs independently of the treatment measures being implemented. Therefore, in patients with CKD, any influence on blood vessels (hypotensive, angioprotective) has a positive effect on their structural and functional state and leads to a slowdown in the progression of renal failure.

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