# THE EFFECT OF CALCIUM CHANNEL BLOCKERS ON VASCULAR REMODELING AND INTRA-RENAL HEMODYNAMICS IN CHRONIC KIDNEY DISEASE

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**Key words**: *chronic kidney disease, glomerulosclerosis, calcium channel blockers, remodeling, dihydropyridine, lercanidipine, amlodipine, intima-media layer.*

## Relevance of the problem.

Chronic kidney disease is defined as damage or reduction of kidney function for 3 months or more. Chronic kidney disease is a pathological process that ends with the death of the patient as a complication of total kidney and some non-renal diseases. Therefore, at the moment, the main goal of experts in the field is to analyze the pathogenetic links of chronic kidney disease in depth and to slow down the process by correcting it in various ways, to prevent early disability, and to prolong the patient's life. [1,5,2]

Remodeling is a complex process, which is a structural and geometrical change as a result of vascular damage. Remodeling damaging factors toxic substances. Metabolic directly changes vascular structure and hemodynamic load. A change in the structure of the vessels leads to a violation of the function and blood supply of that organ. Therefore, to study the effect of calcium channel blockers (amlodipine and lercanidipine) on vascular remodeling in patients with chronic kidney disease. [3,4,6]

Currently, in the healthcare system, great importance is focused on choosing the drug of choice of hypotensive drugs for arterial blood pressure in chronic kidney disease and studying their effect on the thickness of large vessel walls, as well as evaluating their effect on vascular remodeling.[2, 6]

## The purpose of the study.

Comparative assessment of the effect of calcium channel blockers amlodipine and lercanidipine on functional status of kidneys, intrarenal hemodynamics and vascular system remodeling in patients with stage III of chronic kidney disease.

## Materials and research methods.

80 patients with SBK stage III a and b, who were treated at the Nephrology Department of the multidisciplinary clinic of the Tashkent Medical Academy, and then were under outpatient observation, took part in the study. The research period will be 30 days. Checkpoints will be the first, tenth, thirtieth day. All patients receive basic

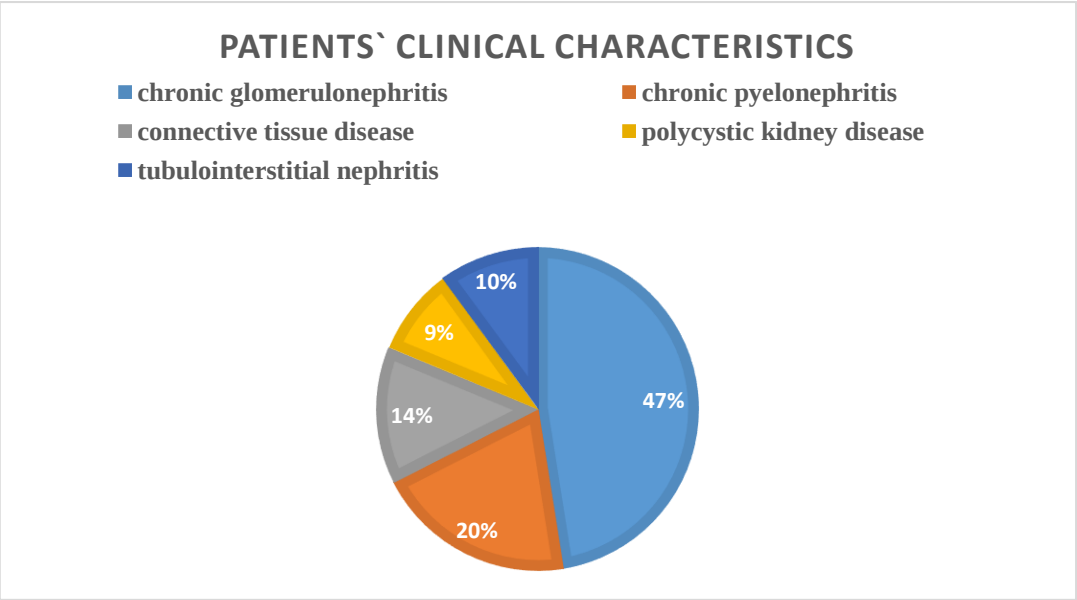
treatment according to approved national standards for SBK, including: diet, correction of water and electrolyte disturbances, treatment of arterial hypertension, acidosis. During the study, all patients received primary pathogenetic therapy, 41 of them aged 45.1 ± 8.0 years, men accounted for 19 (46.3%), women averaged 22 (53.6%) and 10 mg of amlodipine (group A) as antihypertensive therapy in addition to one patient with an average weight of 65.6 ± 2.7, and the remaining 39 patients with an average age of 44.8 ± 7.2 18 men (46.1%) and 21 women (53.8%) and patients with an average weight of 68.5±4.2 were given "lercanidipine" in a dose of 20 mg (group B). (listed in Table 1).

Table 1.

| | **Age** | **Male** | **Female** | **Weight** |
|---|---|---|---|---|
| **Amlodipin** | 8,0 | | | 6<br>5 |
| **Lerkanidipin** | 7,2 | | | |

38 (47.5%) patients with chronic glomerulonephritis, 16 (20%) patients with chronic pyelonephritis, 11 (13.7%) patients complicated by general chronic kidney disease III a and b stage patients with connective tissue diseases, 8 (10%) patients with tubulointerstitial nephritis, and the remaining 7 (8.7%) patients with polycystic kidney disease (Figure 1).Chronic renal failure level III was determined by calculating the KFT using the SKD-EPI formula, and the following examination methods were used: carotid and brachial artery duplex scanning examination; ultrasound examination of the kidneys and dopplerography of the intrarenal artery.

Pic 1




Results of evaluating the effect of calcium channel blockers on vascular remodeling in patients with stage III chronic kidney disease. To evaluate vascular

remodeling processes in patients with SBK, we performed vascular ultrasound examination in duplex scanning mode. Patients first underwent a duplex scan of the brachiocephalic artery. The thickness of the intima and media complex measured at the standard point of the common carotid artery was taken as the structural unit of vascular remodeling.

Table 2. Assessment of the effect of both groups on the carotid artery intima-media complex during treatment in patients with stage III chronic kidney disease.

| **Parameters** | **Amlodipin** | | **Lerkanidipin** | |
|---|---|---|---|---|
| | **Before treatment** | **Treatment`s 30th day** | **Before treatment** | **Treatment`s 30th day** |
| **The thickness of the intima-media complex** | 1,12±0,03 | 1,10±0,04 | 1,10±0,02 | 1,09±0,01 |

We compared the thickness of the intima and media complex in our two control groups. During our study, we monitored the thickness of the carotid artery intima-media complex in all our patients. There was no significant change in the thickness of the intima-media complex of the carotid artery during treatment in both groups of patients. In this case, the carotid artery intima-media complex changed from 1.12±0.03 to 1.10±0.02 in patients who received Amlodipine in group I. The thickness of the carotid artery intima-media complex changed from 1.10±0.02 to 1.09±0.01 in patients receiving Lercanidipine. The thickness of the carotid artery intima-media complex was determined before treatment of patients in our groups and on the 30th day of treatment. (Table 2). The thickness of the carotid artery intima and media complex during treatment was observed to change by 1.78% in the first group, and by 0.9% in the second group. Patients in our follow-up groups underwent a duplex scan to perform a test of coronary artery vasodilatation. Before treatment, umbilical artery diameter was found to be reliably lower in both our groups before treatment than in the control group. According to it, we can see that the diameter of the umbilical artery decreased by 14.80% ($r<0.001$) in our first group, and by 14.32% ($r<0.001$) in our second main group. The reason for this lies in the significant activation of systemic inflammatory reactions as a result of the accumulation of medium molecules in the development of endothelial dysfunction in patients with SBK. (See Table 3).

Table 3. Results of duplex scanning of the brachial artery in patients in our groups.

| Indicators | The first control group Amlodipine | | The second control group Lercanidipine | |
|---|---|---|---|---|
| | Before treatment | Treatment`s 30th day | Before treatment | Treatment`s 30th day |
| Diameter 0, mm | | | | |
| Diameter in 5 seconds after the test, mm | | | | |
| 5 seconds % | | | | |
| Diameter test 5 seconds, mm | 3,67±0,13 | 4,35±0,07 | 3,64±0,13 | 3,96±0,061* |
| 60 seconds % | 4,56±0,76 | 9,57±0,21 | 3,12±0,51 | 8,4±0,29* |

*Note: * - differences are significant compared to the values on the day before treatment (*r <0.05.)*

At the 30th day of treatment, brachial artery duplex scan results, when tested for vasodilation, showed (Table 4) that brachial artery diameter showed positive changes during treatment in both groups. According to it, the diameter of the brachial artery increased to 3.97±0.07 ($p<0.05$) before the vasodilatation test after the treatment in our first group, while the diameter of the brachial artery increased to 4.25±0.07 ($P<0.001$) after 5 seconds of the test. ), and in 60 seconds after the test, it increased to 4.35±0.07($P<0.05$). In our group 1, we can see that the brachial artery diameter increased by 13.1% before the test, 16.1% at 5 seconds after the test, and 18.53% at 60 seconds after the test compared to the pre-treatment value.

Vasodilatation test was performed in our second main group. According to it, after the treatment, the diameter of the brachial artery increased to 3.65±0.08 ($r<0.01$) before the test, and to 3.70±0.06 ($r<0.001$) 5 seconds after the test. At 60 seconds after screening, the brachial artery diameter was 3.96 ± 0.061 ($r < 0.01$) and a positive improvement was achieved. In our 2 groups, we can see that the brachial artery diameter increased by 3.39% before the test, 2.49% at 5 seconds after the test, and 8.79% at 60 seconds after the test compared to the pre-treatment value.

We compared treatment efficacy and brachial artery diameter change scores between the two groups (see Figure 2). If we analyze the picture of the changes in the brachial artery diameter during the treatment in our groups, the brachial artery diameter before the treatment in group 1 was 1.13 ($r<0.001$) times compared to the value before the vasodilatation test, and the value 5 seconds after the test was 1.16 ($r < 0.001$) times. and on the 30th day of treatment, the mean difference increased and reached a 1.18 ($r < 0.001$) fold increase. However, the changes in brachial artery diameter during

treatment in our group 2 patients were unreliable. In our group of patients, the brachial artery diameter was 1.03 times the pre-test value after treatment and 1.02 times the pre-treatment value at 5 seconds post-test, but 1.08 times the pre-treatment value at 30 days of treatment ($r < 0.01$ ) was observed to double. Based on the results obtained as a result of the above study, we can say that during 30 days of hypotensive treatment, vascular remodeling was more evident in patients of our group 1 than in patients of our group 2. Because of this, we can say that lercanidpine has a higher vasodilator property than amlodipine. The intima-media complex of the sleep ray did not change significantly during the treatment in both groups.

Pic2

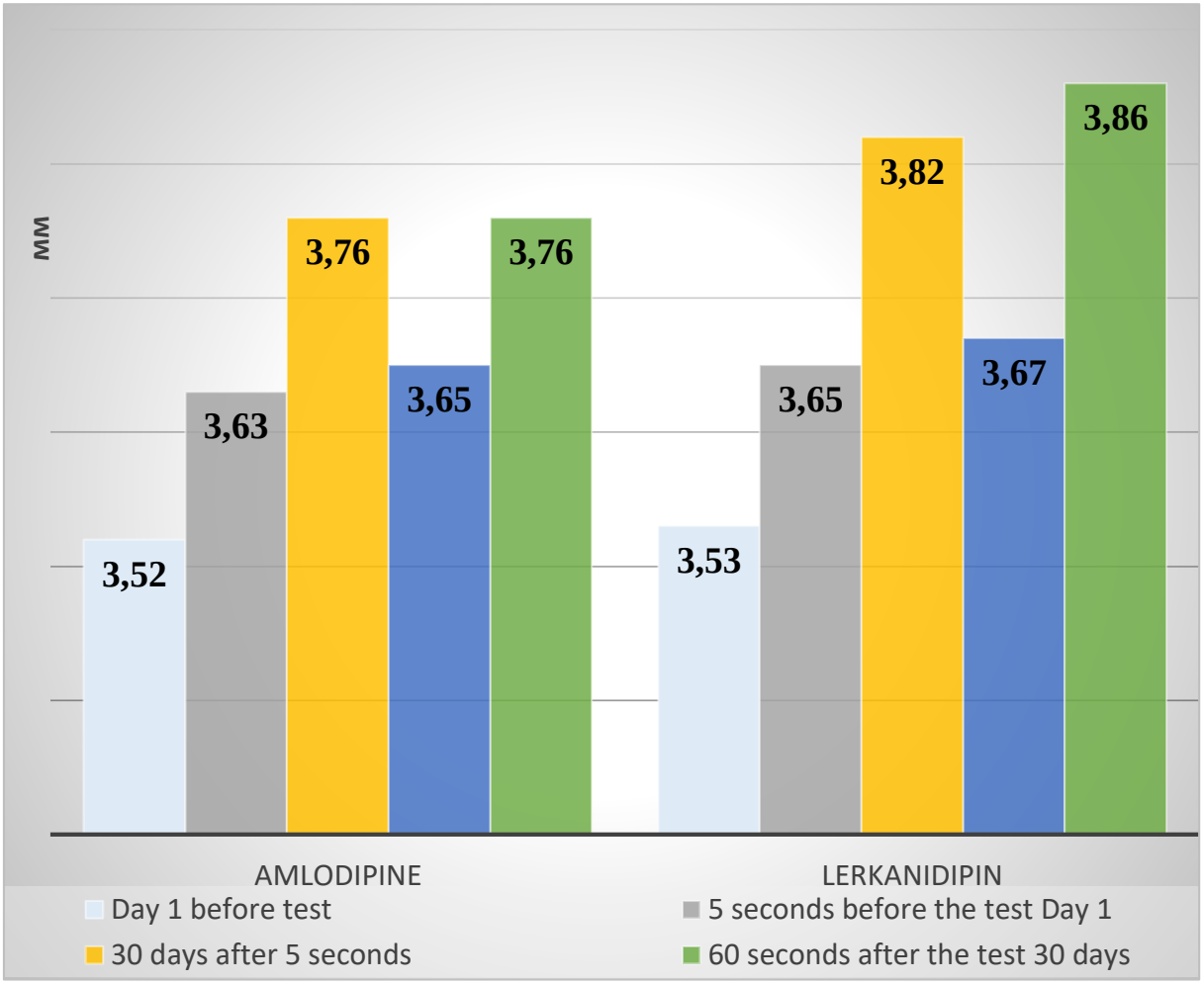



**Table 4. Indicators of changes in blood circulation velocity and peripheral resistance in the main artery of the kidney before treatment and during treatment in the first group of patients (M±m). Blood circulation indicators.**

| | 1 day before treatment | 10 days of treatment | 30 days of treatment |
|---|---|---|---|
| Vs, sm/s | 63,3±0,89 | 65,09±0,56 | 70.13±0,86 |
| Vd, sm/s | 20,07±0,25* | 24,09±0,26* | 28,87±0,17* |
| S/D | 2,82±0,07* | 2,82±0,01* | 2,71±0,08* |
| RI | 0,76±0,006 | 0,65±0,02 * | 0,61±0,02** |
| PI | 1,30±0,019** | 1,20±0,017** | 1,15±0,03** |

Note: the indicators are significant compared to the pre-treatment indicator * - r<0.05** - r<0.01* compared to the initial day. Analyzing the table, the maximum systolic speed (Vs) in the patients of the second control group was 56.67±0.89 cm/s on the first day of treatment. On the 30th day of treatment, it was 68.09±0.56 cm/s (12.15%), and on the 90th day, this indicator improved by 1.37 times compared to the first day, but the result was lower by 1.13% compared to the first group. We also observed changes in the ratio of maximum systolic and minimum diastolic speeds during treatment. This indicator was 2.82±0.57 (r<0.05) on the 1st day of treatment and improved during treatment. 10 days of treatment reached 2.82±0.01 (r<0.05), by 30 days of treatment the S/D was 2.71±0.08 (r<0.05), and during treatment compared to the first day of treatment, 90 days of treatment day, the result was improved to 6.02%.

In our second group, the indicators of changes in blood circulation speed and peripheral resistance in the main renal artery before treatment and during treatment are M±m. Along with the improvement of our above indicators, it was observed that vascular resistance also decreased. Compared to the vascular resistance index on the first day of treatment, we observed a 1.17-fold (22.36%) decrease on the 10th day of treatment, and a 1.24-fold (28.9%) decrease on the 30th day of treatment. The pulse index was also observed to decrease by 1.13 times (11.54%) on the 30th day of treatment compared to the 1st day of treatment. We could see the difference in the tone when comparing the dynamics of Vs indicators of patients in both control groups after 30 days of treatment. Renal peak systolic velocity (Vs) was observed to improve during treatment in both groups. Comparative evaluation of these indicators.

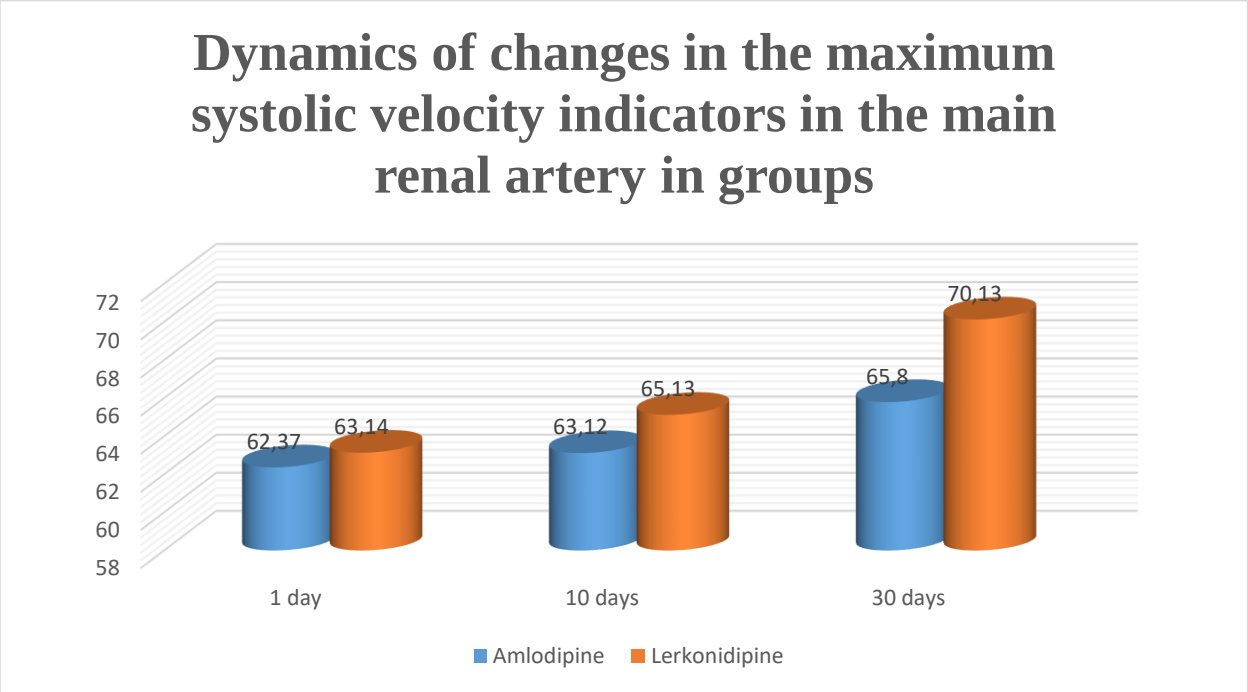



*Fig. 3. Comment: indicators are significant compared to the indicator before treatment *- $p < 0.05$*

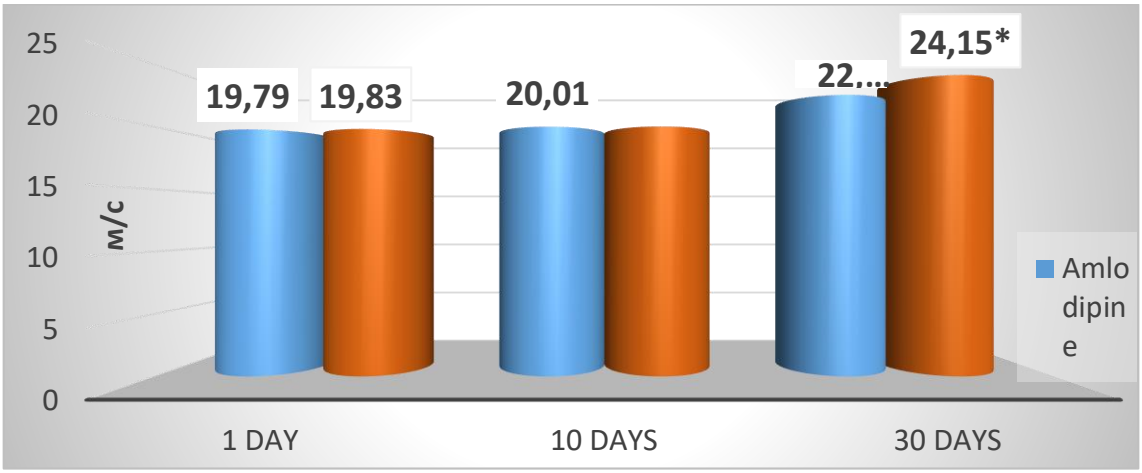
Analyzing the graph comparing the maximum systolic velocity values in our control groups, Vs in both our groups were close to each other on the first day of treatment. Over the course of treatment, both of our groups showed a positive change in this score, and at 10 days of treatment, our first control group achieved a 4.19% better result than our second baseline group, and at 30 days of treatment, a 1.13% reduction in the difference between our first and second control group Vs was achieved.

Another important indicator for us is the minimum diastolic speed Vd. This indicator was also observed to be significantly accelerated by treatment in both control groups, as in Vs. The results of our comparative study of changes in both control groups during 30 days of treatment are presented. Based on the results shown in the chart above, we can see that the changes in both our control groups were positive. In our first group, we observed a 1.28-fold (28.5%) improvement in Vd compared to the first day at 30 days of treatment, and in our second main group, a 1.20-fold (20.0%) improvement. During the 30 days of treatment, our first group achieved 8.5% better results than the second group. However, after continuing the antiaggregant treatment, by the 90th day of the treatment, the rate of Vd increased by 1.47 times or 47.23% compared to the pre-treatment indicator in our first group. In our second group, this indicator improved by 1.44 times or 43.84% by 30 days of treatment. The difference in Vd between our first group and our second primary control group at 30 days of treatment was 3.39%.

In patients of both our control groups, during the antiaggregant treatment, improvement of blood flow rate in blood vessels was observed. At the same time,

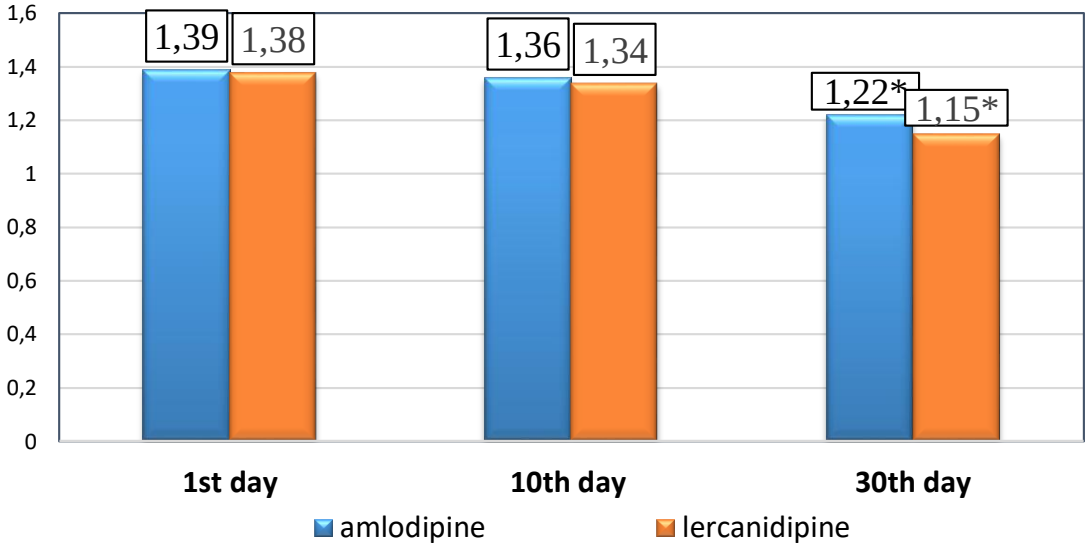
studying the peripheral resistance of renal vessels, i.e. RI and PI, is of great importance in the study of intrarenal hemodynamics in our groups. RI and PI in the basin of the main renal artery of patients in both our groups before treatment, 10 and 30 days after treatment were compared. According to it, in the patients of our first controlled group, RI-0.75±0.007 (r<0.001) before treatment was RI-0.62±0.006 (r<0.001) on the 10th day of treatment, 17.3% on the 10th day compared to the 1st day of treatment. we can see improvement. On the 30th day of treatment, the RI decreased to 0.60±0.02 (r<0.01), and on the 30th day, compared to the 1st day of treatment, this indicator was improved by 1.25 times, i.e. by 20.0%. At the same time, in our second main control group, in the basin of the main renal artery, RI-0.76±0.006 (r<0.001) before treatment, 30 days after treatment RI-0.65±0.02 (r<0.01), 30 days after treatment and RI-0.61±0.02 (p<0.01) indicators changed to a positive side. In our group, compared to day 1 of treatment, RI decreased by 1.16 times, i.e. 14.47% on day 30, and by 1.24 times, i.e. 19.73%, on day 10 of treatment. The difference between the first group and the second group during the 10-day treatment was 2.83%, and by the 30th day of treatment, the difference was reduced to 0.27%.

Fig. 4. Dynamics of changes in the basin of the main renal artery in our IR groups




In the basin of the main renal artery, along with monitoring other dopplerographic indicators, the dynamics of the pulse index PI indicator was also observed. The pulse index was observed on the 1st day, 30th and 90th day of treatment as above. According to it, in our first controlled group, PI was 1.29±0.015 (r<0.01) before treatment, 1.21±0.015 (r<0.01) on the 10th day of treatment, and on the 30th day of treatment, this indicator was 1 ,17±0.01 (r <0.01) positive change was observed.

Figure 5. Dynamics of RI changes in the air of the main renal artery in groups.




During the 30-day treatment, in our group, compared to the 1st day of treatment, there was an improvement of 6.2% on the 10th day, and on the 30th day of the treatment, it was 1.10 times, that is, up to 9.3%. In our second main control group, PI-1.30±0.019 (r<0.01) before treatment, the average value of the pulse index at the 10-day follow-up examination was PI-1.20±0.017 (r<0.01), and on the 30th day of treatment, this indicator continued to change to the positive side and amounted to PI-1.15±0.03 (r<0.01). During antiaggregant treatment with traditional treatment for 10 days, 1.08 times i.e. 7.69% improvement in pulse index on day 1, and 1.13 times i.e. 11.53% improvement in results on day 30 of treatment was achieved.

**Summary.**

The thickness of the intima-media complex in the carotid artery in both groups of patients with SBK was unreliably changed. It was found that the maximum systolic pressure, the minimum diastolic pressure of the renal artery increased reliably in patients receiving Lercanidipine compared to patients receiving Amlodipine, as well as vascular resistance (IR) and pulsatility index (PI) decreased reliably. Correspondingly, the results also changed positively in the remaining renal artery basins. Patients receiving lercanidipine showed reliably positive changes compared to patients receiving amlodipine.

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