COORDINATION OF INTERNAL HEMODYNAMIC DISORDERS IN PATIENTS WITH CHRONIC KIDNEY DISEASE OF DIABETIC GENESIS BY USING 2ND TYPE SODIUM-GLUCOSE COTRANSPORTER INHIBITORS

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Summary. *The article presents the results of the research on the alternative treatment of intrarenal hemodynamic disorders with the use of type 2 sodium-glucose cotransporter inhibitors in 103 patients with chronic kidney disease developed on the basis of diabetic nephropathy. Also, comparing the obtained results with the results of other authors' researches, the nephroprotective effect of the drug is once again based in detail.*

Key words: *diabetic nephropathy, glomerular filtration, maximum systolic, end diastolic, speed, resistance index.*

Regardless of the etiology, the standard high mortality rate of patients with chronic kidney disease (CKD) (70 deaths per 1000 patients) indicates the need for constant improvement in the detection of signs of the disease from the early stages of renal failure. [3]. Modern methods of diagnosing CKD currently include: determination of glomerular filtration rate (GFR), albuminuria/proteinuria, urinalysis, examination of electrolyte balance indicators, nephrobiopsy and ultrasound examination (USG) to determine structural changes and kidney size. [5,7,12]. However, these data are not clear, especially in the early stages of CKD, and do not allow for a sufficiently accurate characterization of the degree of kidney damage and nephrosclerosis. Moreover, biopsy is not always possible in this situation [2]. Therefore, it is necessary to search for other clinical and laboratory criteria for the diagnosis of CKD. In this regard, the study and analysis of intra-renal hemodynamic disorders is of particular importance [6]. One of the visual examination methods that allows characterizing the features of intrarenal hemodynamics is the examination of renal blood vessels with the help of ultrasound Dopplerography (UTDG), assessment of blood flow, and determination of the resistance index. [1,4,8,10].

Therefore, in our research on the study of the nephroprotective effect of Type 2 sodium-glucose cotransporter inhibitors by recommending its inhibitors, we considered it necessary to study, evaluate, analyze the gradients of intra-renal hemodynamics and investigate its new nephroprotective aspects in order to better assess the existing issue [9,11].

Purpose of the study.

Coordination of intra-renal hemodynamic disorders with the use of type 2 sodium-glucose cotransporter inhibitors in patients with diabetic progression of chronic kidney disease.

Research materials and methods.

103 patients with stage II and III A CKD, formed on the basis of nephropathies of diabetic etiology, who were hospitalized at the Republican Specialized Scientific and Practical Medical Center of Nephrology and Kidney Transplantation and subsequently under dispensary observation at this institution, were selected for the study. They were randomly divided into two groups. Group 1 (n-54) was satisfied only with traditional treatment, i.e., therapy in accordance with the standards of treatment of chronic kidney disease. In the 2nd group (n-47), in addition to traditional treatment, the drug empagliflozin (Empagliflozin 10 mg 1 tablet/day), belonging to the 2nd type of sodium-glucose cotransporter inhibitors, was prescribed for three months. All patients underwent Doppler ultrasonography of the renal vessels at the beginning of the study and after three months to determine

the resistance of the renal arteries and blood flow velocity in the vessels. This examination was performed on the "Sonoscape S20 Color Doppler Diagnostic" device in the admission department of the multidisciplinary clinic of the Tashkent Medical Academy. Through this examination, the blood flow velocity and vascular resistance in the main, arcuate, and interlobular vessels of the kidney were studied by spectral analysis. The study of intrarenal hemodynamics was carried out by spectral analysis of intrarenal hemodynamics using ultrasound Dopplerography. Right and left renal arteries are assessed at the entrance as follows:

- maximum systolic blood flow rate (V_s max);
- final diastolic velocity (Vd);

Intra-renal arteries:

- segmental – V max, Vd;
- Interstitial – V max, Vd;

To characterize renal vascular resistance, the resistance index (RI) was calculated based on the values of Vmax and Vd in specific arterial vessels. In the statistical analysis of the data, the average values of the indicators of the results of the examination of the vessels of the right and left kidneys were used. The obtained results were statistically analyzed.

Results and discussion.

The results obtained on the basis of Doppler ultrasound examination of renal arteries of various sizes, i.e., the dynamics of changes in the gradients of intrarenal hemodynamics in patients with chronic kidney disease of diabetic nephropathy genesis against the background of various treatment regimens, revealed the following picture. ***In the 1st group,*** consisting of patients limited to traditional treatment of the main renal arteries, Vs max was 55.3±3.27 cm/s at the beginning of the study and increased insignificantly to 59.4±3.74 cm/s at the end of the study. In the 2nd group, consisting of patients receiving empagliflozin in addition to traditional treatment, Vs max was 55.6±3.91 cm/s at the beginning of the study, and after three months it increased to 73.1±4.11 cm/s, which was also reflected in the results of statistical analysis. When comparing the results of patients in groups 1 and 2 at the end of the study, statistical analysis showed that the difference was insignificant ($p<0.05$). Vd in the 1st group at the beginning of the study was 16.4±2.19 cm/s, and at the end of the study unreliably increased to 17.5±2.23 cm/s. In the 2nd group, Vd was 16.1±1.88 cm/s at the beginning of the study, and after three months, a significant ($p<0.01$) increase to 25.3±1.95 cm/s was also observed in the results of the statistical analysis. At the end of the study, when comparing the main groups, the difference was less significant ($p<0.05$), which was confirmed by statistical analysis. Based on the values of Vmax and Vd, the resistance index in the 1st group at the beginning of the study was 0.70±0.01, and at the end of the study it decreased insignificantly to 0.68±0.01. In the 2nd group, a significant ($p<0.01$) decrease in RI to 0.65±0.01 at the end of treatment, which was 0.70±0.012 at the beginning of the study, was also confirmed by statistical analysis. At the end of the study, when comparing the main groups, it was noted that the difference between them changed insignificantly ($p<0.05$) (Table 1).

In the segmental renal arteries in the 1st group, Vs max was 39.5±1.52 cm/s. at the beginning of the study and an unreliable increase of 42.7±1.44 cm/s. at the end of the study. In the 2nd group, Vs max at the beginning of the study was 40.6±1.46 cm/s, and after three months it increased significantly ($p<0.01$) to 47.3±1.78 cm/s, which was also reflected in the statistical analysis. At the end of the study, when comparing the groups, the statistical analysis showed that the difference between them changed insignificantly ($p<0.05$). Vd in the 1st group at the beginning of the study was 12.3±1.1 cm/s, and at the end of the study it increased unreliably to 13.8±1.03 cm/s. In the 2nd group, Vd was 12.7±1.22 cm/s at the beginning of the study, and after three months, a less reliable ($p<0.05$) increase of 16.2±1.15 cm/s was also observed in the results of statistical analysis. At the end of the study, when comparing the groups, it was observed that the difference between them changed

insignificantly. The resistance index in group 1 was 0.69±0.01 at the beginning of the study and decreased insignificantly to 0.67±0.01 at the end of the study. In the 2nd group, a significant ($p<0.01$) decrease in RI to 0.64±0.01 at the end of treatment, which was 0.69±0.01 at the beginning of the study, was also reflected in the statistical analysis. At the end of the study, when comparing the groups, the difference between them also changed insignificantly ($p<0.05$), which was reflected in the statistical analysis conducted (Table 1).

Table 1

Picture of changes in patients against the background of various treatments of intrarenal hemodynamic disorders

Parameters	1-group (n-54)		2-group (n-47)	
	At the beginning of the study	At the end of the study	At the beginning of the study	At the end of the study
Major renal arteries				
V_s max, cm/c	55,3±3,27	59,4±3,74	55,6±3,91	73,1±4,11**^
V_d, cm/c	16,4±2,19	17,5±2,23	16,1±1,88	25,3±1,95**^
RI	0,70±0,01	0,68±0,01	0,70±0,012	0,65±0,01**^
Segmental renal artery				
V_s max, cm/c	39,5±1,52	42,7±1,44	40,6±1,46	47,3±1,78**^
V_d, cm/c	12,3±1,1	13,8±1,03	12,7±1,22	16,2±1,15*
RI	0,69±0,01	0,67±0,01	0,69±0,01	0,64±0,01**^
Interlobular renal artery				
V_s max, cm/c	23,8±0,88	26,1±0,87	24,9±0,99	28,6±0,98*
V_d, cm/c	7,8±0,67	9,7±0,63	8,5±0,68	11,0±0,54*
RI	0,67±0,01	0,65±0,01	0,67±0,01	0,63±0,01*^

Note: ** - differences are significant compared to the indicators at the beginning of the study. (*- p<0,05, **- p<0,01, ***- p<0,001); ^ - the differences are significant compared to the indicators of groups 1 and 2. (^ - p<0,05, ^^ - p<0,01, ^^^ - p<0,001).*

In the interlobular renal arteries in the 1st group, Vs max was 23.8±0.88 cm/s at the beginning of the study and increased unreliably to 26.1±0.87 cm/s after treatment. In the 2nd group, Vs max was 24.9±0.99 cm/s at the beginning of the study, and after three months it increased to 28.6±0.98 cm/s less reliably ($p<0.05$), which was also reflected in the statistical analysis. At the end of the study,

when comparing the groups, it was observed that the difference between them changed insignificantly. Vd in the 1st group at the beginning of the study was 7.8±0.67 cm/s, and at the end of the study it increased insignificantly to 9.7±0.63 cm/s. In the 2nd group, Vd was 8.5±0.68 cm/s at the beginning of the study and increased by 11.0±0.54 cm/s less reliably ($p<0.05$) after three months. When comparing the results after treatment between the groups, it was noted that the difference between them changed insignificantly. The resistance index in group 1 was 0.67±0.01 at the beginning of the study and decreased insignificantly to 0.65±0.01 at the end of the study. In the 2nd group, a low-significance ($p<0.05$) decrease in RI to 0.63±0.01 at the end of treatment, which was 0.67±0.01 at the beginning of the study, was also reflected in the statistical analysis. At the end of the study, the statistical analysis showed that the difference between the groups did not change reliably when compared with each other (Fig. 1).

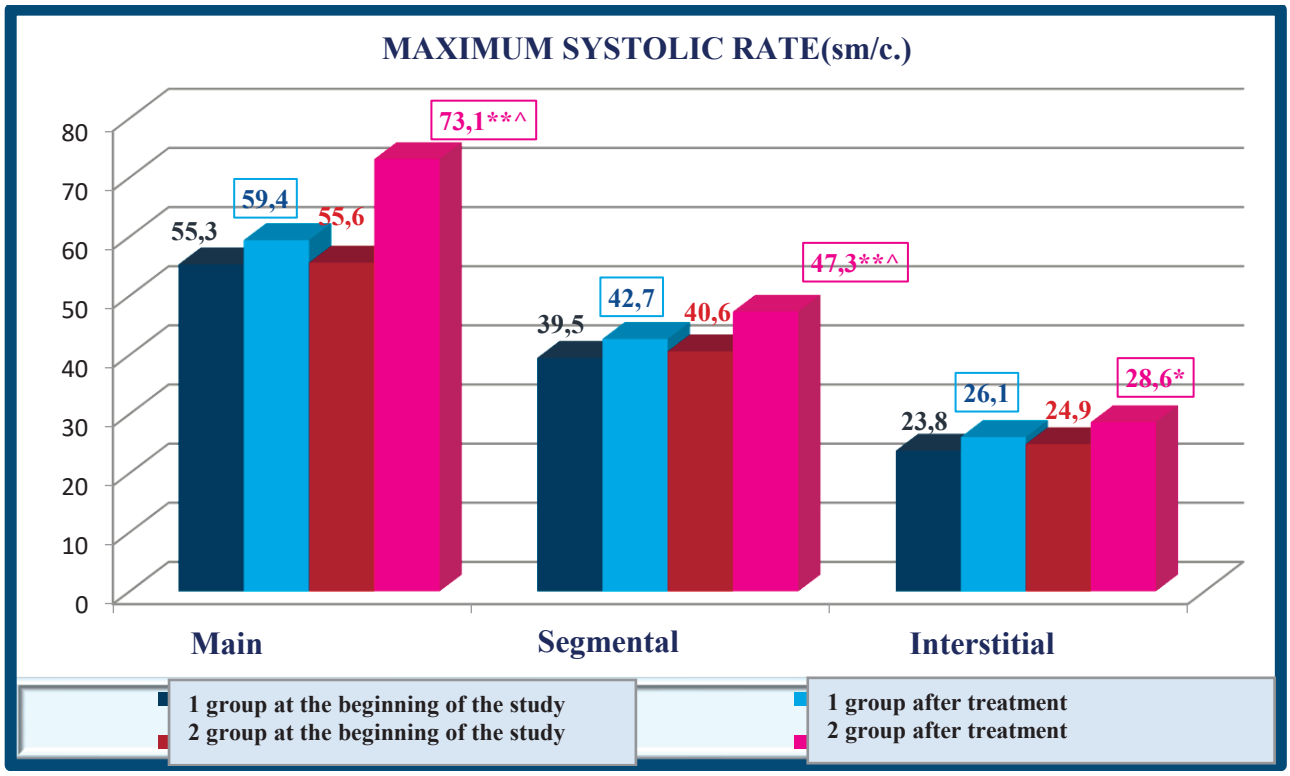

Fig 1. Dynamics of changes in the maximum systolic rate in the studied groups against the background of various treatment regimens.

Doppler ultrasound gradients of renal arteries of different sizes reflected a specific picture in the study groups based on different treatment regimens. It manifested itself in accordance with the effectiveness of various treatment recommendations and the degree of sclerosis of the renal vessels in patients with CKD. If we look at the diagram formed on the basis of the values of these gradients, then in the 2nd group, where empagliflozin was prescribed in addition to traditional treatment, compared to the beginning of treatment, the maximum systolic velocity in the main and segmental arteries increased reliably ($p>0.01$), while in the interlobular arteries it increased less reliably ($p>0.05$), which indicates an improvement in blood flow in the intrarenal vessels. In the 1st group, which was satisfied only with traditional treatment, although this indicator increased to a certain extent in the numbers after treatment, statistical analysis proved that the values in the renal vessels of all sizes changed insignificantly. Also, at the end of the study, when comparing the differences between the groups, the change in the maximum systolic velocity in the main and segmental renal

arteries was less reliable (p>0.05), which is explained by the nephroprotective effectiveness of the proposed drug (Fig. 1). In the literature, according to a study conducted by T. A. Maryanova et al. (2023) in 233 pregnant women with CKD, it is recognized that measuring the maximum systolic velocity of the interlobar arteries in this contingent provides relatively more information.

In patients of the 2nd group, the final diastolic rate increased reliably (p>0.01) only in the main renal artery compared to the beginning of treatment, and less reliably (p>0.05) in the segmental and interlobular arteries, which indicates an improvement in blood flow in the kidneys and intrarenal vessels. In the 1st group, although Vd indicators increased by certain arithmetic values after treatment, statistical analysis revealed unreliable changes in the results of renal arteries of all diameters. At the same time, at the end of the study, when comparing the differences between the groups, it was observed that the final diastolic velocity changed only in the main renal artery, although to a low degree of reliability (p>0.05), and in the intrarenal arteries this difference changed insignificantly (Fig. 2). Consequently, the effect of the drug on the final diastolic rate is less pronounced.

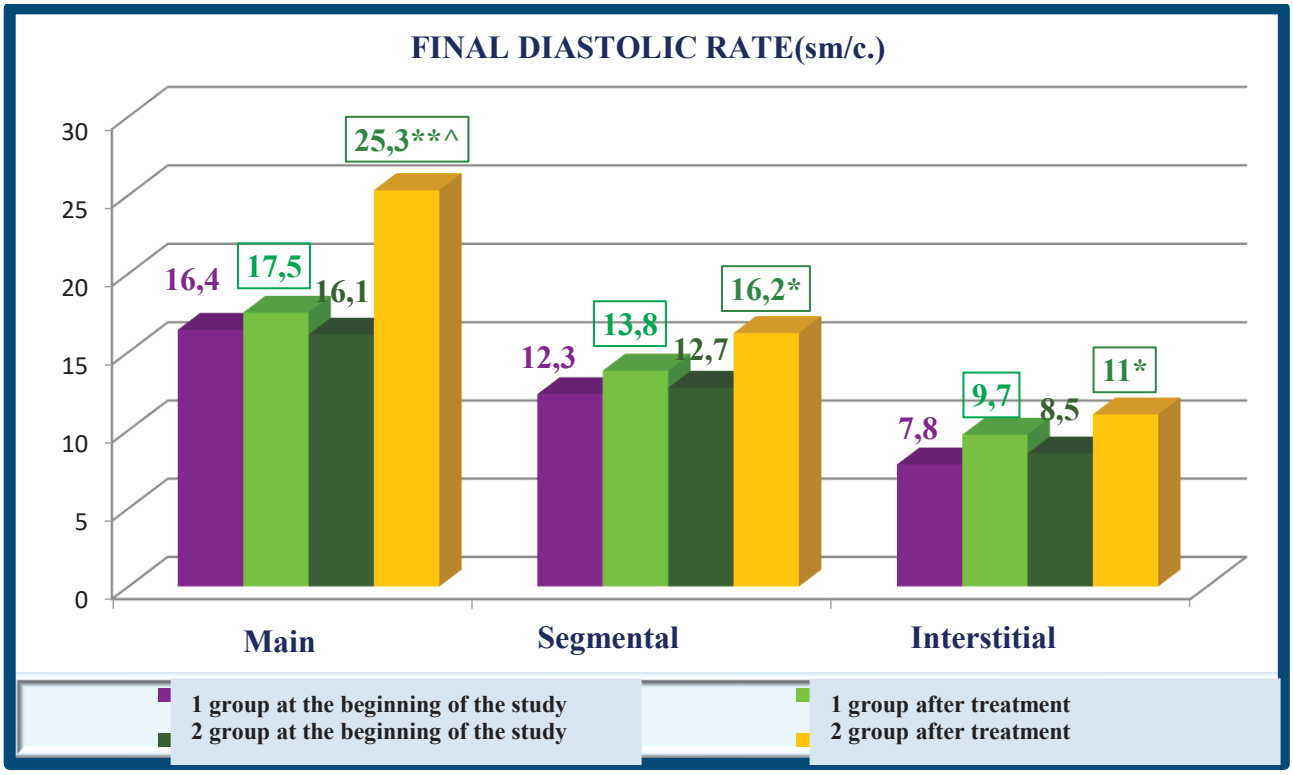

Fig 2. Dynamics of changes in terminal diastolic velocity in the studied groups against the background of various treatment regimens.

In patients of the 2nd group, the resistance index decreased significantly (p>0.01) in the main and segmental renal arteries and less reliably (p>0.05) in the interlobular arteries compared to the beginning of treatment, which indicates a decrease in renal and intrarenal vascular resistance against the background of treatment. In the 1st group, a certain decrease in RI after treatment is also visible in the diagram images, but the conducted statistical analysis shows unreliable changes in RI results of vessels of all sizes. Also, when comparing the results of the main groups at the end of treatment, when comparing the differences between the groups, it was noted that RI in the main and segmental renal arteries changed to a less reliable (p>0.05) level, and in the interlobular vessels, this difference changed insignificantly (Fig. 3).

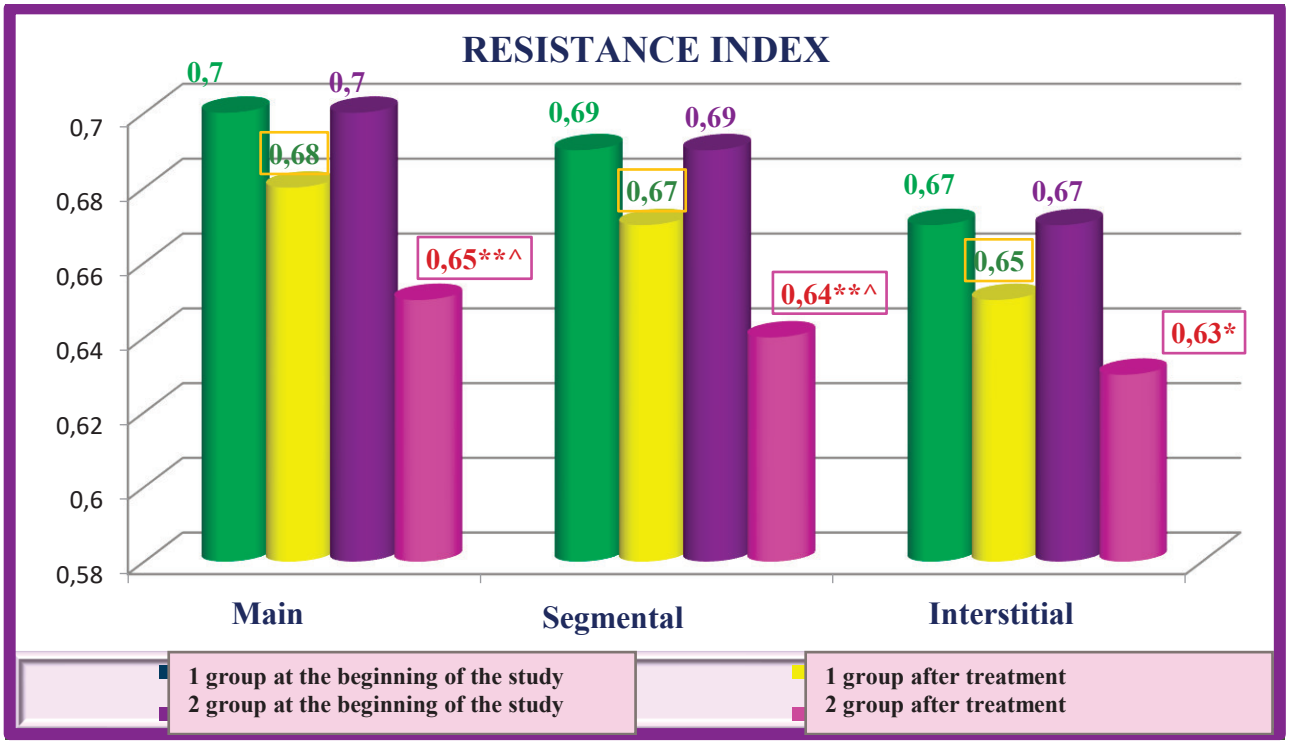

Fig 3. Dynamics of changes in the resistance index in the studied groups against the background of various treatment regimens.

In general, it is recognized in the literature that in renal failure, RI becomes more pronounced by the III stage of the disease, and therefore, the main attention should be paid not to the rate of blood flow in the renal vessels, but to the assessment of RI values. It was also established that there is a correlation between an increase in the resistance index values in the blood flow of the renal and renal arteries and a decrease in GFR in patients.

Conclusion. Thus, in our studies, observing the effect of the drug empagliflozin on intrarenal hemodynamics in the study groups consisting of chronic kidney diseases formed on the basis of diabetic nephropathies, an effective increase in the Vmax and Vd gradients and a decrease in RI after treatment were especially pronounced in the main and segmental arteries. This process is also important for the manifestation of the drug's nephroprotective effect. In fact, if hyperglycemia is one of the main pathogenetic links that exacerbates diabetic nephropathy, then an increase in glucose reabsorption in the renal tubules is a mechanism that negatively affects the process. In this case, it is advisable to achieve this effect by alternating treatment with the use of 2nd type sodium-glucose cotransporter inhibitors in these patients. In the literature, it is recognized that the use of empagliflozin in patients with diabetes mellitus not only reduces blood glucose to the target level, but also leads to a decrease in the frequency of cardiovascular complications, a slowdown in diabetic kidney damage (reduction of albuminuria, improvement of glomerular filtration).

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