

## INFLUENCE OF ANGIOTENSIN CONVERTING ENZYME INHIBITORS AND CALCIUM CHANNEL BLOCKERS ON THE BLOOD CIRCULATION IN THE KIDNEY PARENCHYMA

Novychenko Svitlana\*, Zub Liliya, Kovalenko Svitlana, Roborchuk Stanislav  
Higher State Educational Establishment of Ukraine “Bukovinian State Medical University”  
Chernivtsi, Ukraine

\*[switlananovy70@gmail.com](mailto:switlananovy70@gmail.com)

### Abstract

Hemodynamic disturbances, occurring early or late as response to any pathological processes in the kidneys, are of great significance nowadays in the development of progressiveness of chronic kidneys disease (CKD). Dystrophic and scleral pathological processes that have more or less pronounced diffuse character, considered to acquire steady progression just due to stable hemodynamic changes. It is necessary to possess data concerning the state of the renal blood circulation to estimate the functional state of kidneys correctly. Kidney Doppler ultrasonography as relatively new ultrasound method of investigation of the organ bloodcirculation, occupied deserving place in cardiology, obstetrics and gynecology, vascular surgery and transplantology. Today the given method is not widely used in nephrology practice in spite of unique characteristics of this method – accuracy – 92%, sensitivity and specificity – 100%. In this connection the elaboration of the reliable diagnostic criteria of non-invasive estimation of the renal organ blood flow will enable to increase the accuracy of the ultrasound methods of investigation of kidneys, improvement of diagnostics, differential and early diagnostics of renal diseases, as well as dynamic control in the process of therapy. The purpose of this article was to make better diagnostics and dynamic control of the quality of treatment of patients suffering from chronic kidney disease with arterial hypertension presence by means of color duplex Doppler ultrasonography investigation of the renal organ blood flow.

**Keywords:** *color duplex Doppler ultrasonography, angiotensin converting enzyme inhibitors, calcium channel blockers, arterial hypertension, blood flow*

## Introduction

The problem of treating patients with chronic kidney disease (CKD), regardless of its development stage, remains extremely urgent and complicated. The majority of patients with arterial hypertension (AH), revealed for the first time, belongs to the outpatient network [1, 2]. The significance of ultrasound methods of investigation and expediency of their further research and improvement, taking into consideration noninvasiveness and accessibility of them to a wide circle of people, doesn't arouse doubts [3, 4]. In consequence of stable hemodynamic changes, dystrophic and sclerosing pathological processes, having diffuse nature, acquire steady progression [5, 6]. It is necessary to have data concerning the state of the renal circulation to assess accurately the functional state of the kidneys [7, 8].

Lesions of renal parenchyma may occur due to various nosological forms of kidney disease. Irrespective the etiological factor that led to the primary kidney affection, the further clinical course of the disease, its progression characterized by general regularities of the pathogenetic mechanisms and stages [9, 10]. In due course, in the absence of adequate treatment, impaired renal function occurs, which gradually progresses to the extreme manifestation - chronic renal failure (CRF). In addition to that, AH may first be a consequence, and then an important pathogenetic factor in the further progression of the disease [11, 12, 13].

At CKD, renin- aldosterone- angiotensin system (RAAS) activation is one of the leading components of the disease pathogenesis [14, 15]. Various hemodynamic and non-hemodynamic effects of RAAS, including an increase of the systemic and intraglomerular pressure, activation of the renal tissue growth, increased sodium reabsorption, and creation of conditions for proteinuria, may be considered as the main factors of the disease progression.

Effective antihypertensive therapy ensures the target- organs protection and in this way contributes to the reduction of the risk of the cardiovascular complications' rise and death. Like all antihypertensive agents, ACE inhibitors cause dilatation of the efferent artery, but unlike other classes of drugs lead to dilation of the afferent

artery, that significantly reduces blood pressure inside the glomerulus. Hydrostatic pressure decrease in glomeruli results in a significant hyperfiltration reduction and a decrease or absence of proteinuria [16, 17].

Thus, today there is a rather clear conception about the mechanisms of renal circulatory disorders, but the emergence of the new scientific data about kidney disease progression, requires further study of this process, especially in the presence of hypertension in such patients.

## Methods

The problem of treating patients with chronic kidney disease (CKD), regardless of its development stage, remains extremely urgent and complicated.

The majority of patients with arterial hypertension (AH), revealed for the first time, belongs to the outpatient network [18, 19]. The significance of ultrasound methods of investigation and expediency of their further research and improvement, taking into consideration noninvasiveness and accessibility of them to a wide circle of people, doesn't arouse doubts [20, 21].

In consequence of stable hemodynamic changes, dystrophic and sclerosing pathological processes, having diffuse nature, acquire steady progression [22]. It is necessary to have data concerning the state of the renal circulation to assess accurately the functional state of the kidneys [23].

Lesions of renal parenchyma with the subsequent AP increase may occur due to various nosological forms of kidney disease. Irrespective the etiological factor that led to the primary kidney affection, the further clinical course of the disease, its progression characterized by general regularities of the pathogenetic mechanisms and stages. In due course, in the absence of adequate treatment, impaired renal function occurs, which gradually progresses to the extreme manifestation - chronic renal failure (CRF). In addition to that, AH may first be a consequence, and then an important pathogenetic factor in the further progression of the disease [24, 25].

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Thus, today there is a rather clear conception about the mechanisms of renal circulatory disorders, but the emergence of the new scientific data about kidney disease progression, requires further study of this process, especially in the presence of hypertension in such patients.

### Results

As a result of examination of healthy persons the mentioned below indices, used by us for comparison, were revealed (table 1.1.). As is obvious from table 1.1., a veritable difference between indices of the blood flow of the right and left kidneys in healthy individuals was not determined. No abnormalities were detected at renal sonography and duplex color scanning of healthy individuals. An improvement of effectiveness in the management of patients suffering from CKD with AH presence is one of the urgent tasks of the modern nephrology, stipulated by the high incidence of CKD and the growing proportion of patients with renoparenchymal hypertension, accompanied by complications and CKD progression with impaired renal functional capacity, disability of such patients and the impossibility of the existence without regular sessions of extrarenal cleansing of the body and, of course, a significant deterioration in the quality and life duration of patients.

Taking into account the results of our studies and identified numerous relationships of Doppler sonography indices of the renal blood circulation on the level of small vessels of the kidneys, namely a.interlobaris, with the main factors of CKD progression (GFR and diurnal proteinuria), as well as biochemical and immune markers, which are of great significance in CKD progression, the analysis of the dynamics of Doppler changes in the renal blood circulation, in our opinion, was to be expedient in the delayed period, namely in 6 months and in 1 year after the initial examination of patients.

Some patients (from 69 ) with AH during this period of time received lisinopril at a dose of 10 mg and amlodipine at a dose of 5 mg (39 patients) with the object to normalize AP and the remaining 35 patients received monotherapy with lisinopril 10 mg 1- 2 times a day (individually selected doses) and, if necessary, diuretics (Fig. 1). During one-year follow-up, the stage of CKD changed to CKD stage III in 11 patients from the group under observation. Each case was considered extremely carefully. Most of the patients did not follow the recommended treatment, diet and regimen, i.e. patients were not compliant. The treatment for the patients with CKD adjusted according to the clinical guidelines of the SE "Institute of Nephrology of the National Academy of Medical Sciences of Ukraine" from 2012. The treatment of nephrological pathology carried out in accordance with the existing principles of therapy of the detected nephrological diseases. Table 1.2 presents the results of a dynamic study of the renal blood flow against a background of the previously mentioned antihypertensive therapy. No changes occurred on a.renalis level in 6 months and in a year's time ( $p>0.05$ ) under the action of both drugs, even in patients with DN, who had a reliable decrease of the renal circulation indices during initial examination. That is to say, these indices neither worsen nor increased. Changes, which are shown in tables 1.2 and 1.3, occurred on the level of a.segmentalis and a.interlobaris. As it is obvious from table 1.2 the indices of the renal blood flow against a background of 6-month treatment with the use of antihypertensive pathogenetic therapy combination of lisinopril and amlodipine, veritably decreased in many cases at the level of a. segmentalis. In patients with CP, all indices did not differ from normal values of almost healthy

individuals ( $p < 0.05$ ), except index Vd. In patients with CKD, Vd ( $p < 0.05$ ) and IR ( $p < 0.05$ ) values probably decreased but did not differ from the normal values. And at the level of a.interlobaris in patients with CP, all indicators of the renal blood flow were on the level of normal values. It should be noted that on a.interlobaris level indices of the renal blood flow of the group of patients with CKD were uncertainly reduced compared to normal ones ( $p > 0.05$ ). And in DN group of patients with hypertension, the indices were torpedo and did not respond to 6-month therapy of the combined use of lisinopril at a dose of 10 mg and amlodipine at a dose of 5 mg once a day.

Patients, who were taking lisinopril as monotherapy for renal hypertension, did not show significant changes in the renal blood flow during the 6-month treatment period ( $p > 0.05$ ).

Table 1.3 shows the results of Doppler sonography examination after 1 year with the use of pathogenetic antihypertensive therapy of lisinopril at a dose of 10 mg in combination of amlodipine at a dose of 5 mg 1 time a day and monotherapy with lisinopril. Thus, the results of the study of the renal blood flow in patients who used lisinopril and amlodipine in combination for 1 year, showed a probable decrease in the values of all indices under study at both levels of investigation (a. segmentalis and a. interlobaris) ( $p < 0, 05$ ) in groups of patients with CP and CKD ( changes were uncertain only in Vs and Vvol ( $p > 0.05$ ) in patients with CKD at a.interlobaris level), but the resistance index was close to normal). Only indices of the renal blood flow in patients with DN did not change ( $p > 0.05$ ).

In patients, who were taking lisinopril for one year, practically all indicators of the renal blood flow at both levels (a. Segmentalis and a. Interlobaris) of the study did not differ from the norm only in the group of CP patients with hypertension ( $p < 0.05$ ). In patients with CKD and hypertension, indices of the renal blood flow changed only at the level of a. segmentalis ( $p < 0.05$ ), but they were still far from the normal values. Doppler sonography indices in the group of patients with DN and AH did not undergo significant changes ( $p > 0.05$ ).

Therefore, under the influence of the combined use of lisinopril and amlodipine as a pathogenetic treatment, Doppler indices underwent changes within 6 month period mainly at the level of a.

segmentalis, and in a year's time most of the indices of the renal blood flow were normal or close to normal values, except the corresponding indices in patients with DN.

In our opinion, taking into account the results of our previous studies, the mechanisms of the blood pressure increase are diverse in DN patients and, perhaps, in the most patients with DN, participated in our study, other significant changes (hyperglycemia, hyperlipidemia) and/or other factors were not sufficiently compensated that lead to irreversible changes in the vessels of the kidneys, and require further study with the object of possible correction of the revealed changes.

Probably improvement of the renal blood flow indices under 1-year influence of the combined use of antihypertensive drugs of the pathogenetic action lisinopril and amlodipine, indicates a significant improvement in the blood flow of the small renal vessels, that provides slowing down of CKD progression and, in the light of the aforesaid correlation of the Doppler sonography indices, studied by us, with the main factors of CKD progression (GFR, diurnal proteinuria) and the main biochemical and immune markers of CKD progression, it is expedient to prefer the combined use of lisinopril and amlodipine in such patients.

Thus, the analysis of studies, carried out in patients with CKD I and II stage with the presence of AH II stage showed the great importance of Doppler sonography indices, studied by us, to determine the prognosis of CKD progression in patients with CP, CGN and DN with the presence of AH stage II. In our opinion, color duplex Doppler examination of the renal circulation will be of great importance in timely diagnostics and dynamic quality control of the treatment of patients with chronic kidney disease with arterial hypertension, provide timely conduction of medicinal-preventive measures to slow down the rates of chronic renal disease progression.

### Discussion

In this article the authors present the results of a dynamic study of the renal blood flow against a background of the previously mentioned antihypertensive therapy.

It should be noted that no significant changes occurred ( $p > 0.05$ ) under the action of both



antihypertensive drugs on a.renalis level in 6 months and after year's time, even in the group of DN patients, who had a reliable decrease in the renal blood flow during initial examination.

That is to say, these indices neither deteriorated nor increased.

Changes occurred at the level of a. segmentalis and a.interlobaris. Indices of the renal blood flow against a background of 6-month treatment with the use of lisinopril and amlodipine as antihypertensive pathogenetic management probably decreased in many cases at level a. segmentalis. In patients with CP, all indices did not differ from the normal values of practically healthy individuals ( $p < 0.05$ ), except Vd index. In patients with CKD, Vd ( $p < 0.05$ ) and IR ( $p < 0.05$ ) values probably decreased and did not differ from the normal values. And at a.interlobaris level, all indices of the renal blood flow were at the level of normal values in patients with CP. It should be noted that at the level of a.interlobaris indices of the renal blood flow of the group with CKD were uncertainly reduced compared to the normal values ( $p > 0.05$ ). And in the group of DN patients with AH, the indices were torpedo and did not respond to 6-month combined therapy with lisinopril and amlodipine.

Patients who were taking lisinopril as monotherapy for renal arterial hypertension did not show significant changes in the renal blood flow during 6-month treatment period ( $p > 0.05$ ).

The results of Doppler examination after 1 year with the use of pathogenetic antihypertensive therapy of the combined use of lisinopril at a dose of 10 mg and amlodipine at a dose of 5 mg once a day, showed a veritable decrease in the values of all indices studied by us at both levels of investigation (a. Segmentalis and a. Interlobaris) ( $p < 0.05$ ) in the groups of patients with CP and CKD (in patients with CKD at the level of a.interlobaris only changes in Vs and Vvol ( $p > 0.05$ ) were uncertain, but the resistance index was close to the normal value). Only indices of the renal circulation in patients with DN practically did not change ( $p > 0.05$ ).

In patients, who were taking lisinopril during one year of examination, almost all indices of the renal circulation changed and did not differ from the normal value at both levels (a.segmentalis and a. Interlobaris) of investigation, except in the group of CP patients with hypertension ( $p < 0, 05$ ). In patients

with CKD and AH presence, indices of the renal blood flow veritably changed only at the level of a. segmentalis ( $p < 0.05$ ), but they were still far from normal values. Doppler indices of the group of patients with DN and AH did not undergo veritable changes ( $p > 0.05$ ).

Therefore, under the action of the combined use of lisinopril and amlodipine as a pathogenetic therapy, Doppler indices underwent significant changes within 6 months, mainly at the level of a. segmentalis, and during a year's time of examination against a background of taking this drug, the most indices of the renal blood flow were normal or close to the normal value, except the corresponding indices in patients with DN.

In our opinion, taking into account the results of our previous studies, the mechanisms of AP increase are diverse in DN patients and, perhaps, in most DN patients, participated in our study, other significant changes (hyperglycemia, hyperlipidemia) were not sufficiently compensated and/or other factors that lead to irreversible changes in the vessels of the kidneys and require further study with the object of possible correction of the identified changes.

Probable improvement in the renal blood flow under a year's time influence of the pathogenetic effect of the combined use of lisinopril at a dose of 10 mg and amlodipine at a dose of 5 mg per day, indicates a significant improvement in the blood flow of the small renal vessels, which slows down the progression of CKD and in the light of the above correlations of Doppler indices, studied by us, with the main factors of CKD progression (GFR, diurnal proteinuria) and the main biochemical and immune markers of CKD progression, it is expedient to prefer the combined use of lisinopril at a dose of 10 mg and amlodipine at a dose of 5 mg once a day in such patients.

Therefore, the carried out analysis of investigations in patients with CKD stage I and II with the presence of AH stage II have shown the great importance of Doppler indices, studied by us, to determine the prognosis of CKD progression in patients with CP, CKD and DN with the presence of grade II hypertension. In our opinion, color duplex Doppler examination of the renal organ circulation will be of great importance in timely diagnostics and dynamic quality control of treatment of patients with chronic kidney disease with hypertension

presence, ensure timely conduction of medicinal-preventive measures to slow down the progression of the kidney chronic disease. It has been determined that the combined use of lisinopril at a dose of 10 mg and amlodipine at a dose of 5 mg per day in the complex therapy of CKD stage I-II patients with AH stage II during a year contributes to the probable improvement of the renal blood flow indices (Vs, Vd, Vvol, TAMX, IR) ( $p < 0.05$ ) of the small renal vessels (at the level of a.interlobaris).

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Table 1.1.

Quantitative description of the blood circulation of the renal vessels in healthy persons under examination  
(n, M±m)

Levels of investigation	Dopplerometric parameters	Healthy persons (n=20)	
		Right kidney	Left kidney
1	2	3	4
a. renalis	Vs (cm/sec) Vd (cm/sec) TAMX (m/sec) Vvol (ml/min) IR	67,30 ± 2,62 29,12 ± 2,78 0,39 ± 0,09 108,60 ± 2,54 0,58 ± 0,03	64,23 ± 2,52 28,19 ± 2,47 0,38 ± 0,06 109,72 ± 2,65 0,57 ± 0,09
a. segmentalis	Vs (cm/sec) Vd (cm/sec) TAMX (m/sec) Vvol (ml/min) IR	47,33 ± 3,12 24,72 ± 2,18 0,29 ± 0,09 98,80 ± 2,55 0,56 ± 0,04	45,22 ± 2,97 25,62 ± 3,18 0,29 ± 0,08 98,62 ± 2,46 0,56 ± 0,03
a.interlobaris	Vs (cm/sec) Vd (cm/sec) TAMX (m/sec) Vvol (ml/min) IR	35,66 ± 2,52 18,12 ± 2,08 0,22 ± 0,07 92,86 ± 2,34 0,55 ± 0,03	34,38 ± 2,47 16,69 ± 2,11 0,21 ± 0,06 90,87 ± 2,45 0,54 ± 0,02



Table 1.2

Quantitative description of the circulation in the renal vessels after 6 months of treatment (n, M±m)

Levels of investigation	Dopplerometric parameters	Examined persons (n=88)			
		Healthy (n=20)	Patients with CKD I-II stages with AH (n=68)		
			CP with AH	DN with AH	CGN with AH
			(n=11)	(n=12)	(n=11)
LISINOPRIL+ AMLODIPINE					
a. segmentalis	Vs (cm/sec)	56,38 ± 3,32	50,25 ± 2,22 <sup>^</sup>	43,01 ± 2,11*	44,76 ± 2,55*
	Vd (cm/sec)	24,22 ± 2,28	19,13 ± 2,23* <sup>^</sup>	14,95 ± 2,17*	19,35 ± 2,21
	TAMX (m/sec)	0,29 ± 0,06	0,26 ± 0,05 <sup>^</sup>	0,19 ± 0,03*	0,20 ± 0,02*
	Vvol (ml/min)	98,71 ± 2,35	94,74 ± 2,15 <sup>^</sup>	88,22 ± 2,34*	92,10 ± 2,32
	IR	0,55 ± 0,05	0,57 ± 0,03	0,63 ± 0,04*	0,56 ± 0,03
a.interlobaris	Vs (cm/sec)	34,87 ± 2,12	31,19 ± 2,17 <sup>^</sup>	23,51 ± 2,12*	26,21 ± 2,21*
	Vd (cm/sec)	17,42 ± 2,26	15,11 ± 2,16 <sup>^</sup>	9,12 ± 2,14*	12,33 ± 2,06* <sup>^</sup>
	TAMX (m/sec)	0,21 ± 0,06	0,19 ± 0,04 <sup>^</sup>	0,13 ± 0,06*	0,16 ± 0,05
	Vvol (ml/min)	91,35 ± 2,39	89,22 ± 2,15 <sup>^</sup>	81,44 ± 2,12*	85,17 ± 2,11*
	IR	0,54 ± 0,02	0,55 ± 0,02 <sup>^</sup>	0,72 ± 0,03*	0,68 ± 0,05*
			(n=12)	(n=12)	(n=11)
LISINOPRIL					
a. segmentalis	Vs (cm/sec)	56,38 ± 3,32	48,21 ± 2,12* <sup>^</sup>	42,10 ± 2,11*	44,66 ± 2,43*
	Vd (cm/sec)	24,22 ± 2,28	19,05 ± 2,10*	14,56 ± 2,34*	18,02 ± 2,17*
	TAMX (m/sec)	0,29 ± 0,06	0,25 ± 0,06*	0,23 ± 0,03*	0,24 ± 0,04*
	Vvol (ml/min)	98,71 ± 2,35	94,54 ± 2,11	88,92 ± 2,44*	92,36 ± 2,32*
	IR	0,55 ± 0,05	0,60 ± 0,03 <sup>^</sup>	0,74 ± 0,05*	0,65 ± 0,02* <sup>^</sup>
a.interlobaris	Vs (cm/sec)	34,87 ± 2,12	30,88 ± 2,19 <sup>^</sup>	22,55 ± 2,16*	26,25 ± 2,28*
	Vd (cm/sec)	17,42 ± 2,26	14,10 ± 2,14* <sup>^</sup>	8,83 ± 2,32*	8,77 ± 2,06*
	TAMX (m/sec)	0,21 ± 0,06	0,19 ± 0,04*	0,14 ± 0,06*	0,16 ± 0,03*
	Vvol (ml/min)	91,35 ± 2,39	86,58 ± 2,27* <sup>^</sup>	80,55 ± 2,16*	82,77 ± 2,22*
	IR	0,54 ± 0,02	0,55 ± 0,02* <sup>^</sup>	0,72 ± 0,02*	0,71 ± 0,05*

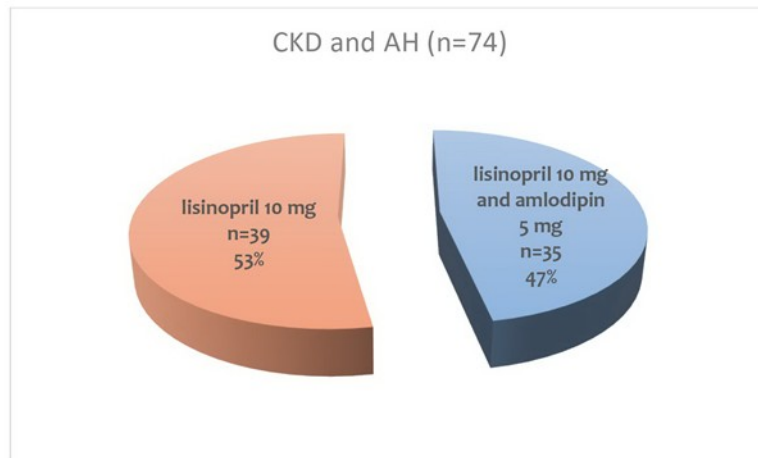
Notes: \* - p&lt;0,05 in comparison with the group of healthy persons

<sup>^</sup> - p<0,05 in comparison with DN patients

Table 1.3

Quantitative description of the circulation of the renal vessels after a year's time treatment (n, M±m)

Levels of investigation	Dopplerometric parameters	Examined persons (n=88)			
		Healthy (n=20)	Patients with CKD I-III st. with AH (n=68)		
			CP with AH (n=22)	DN with AH (n=25)	CGN with AH (n=21)
			(n=10)	(n=11)	(n=11)
LISINOPRIL + AMLODIPINE					
a. segmentalis	Vs (cm/sec)	56,38 ± 3,32	52,15 ± 2,21 <sup>^</sup>	43,92 ± 2,15*	50,55 ± 2,15
	Vd (cm/sec)	24,22 ± 2,28	21,34 ± 2,42 <sup>^</sup>	14,99 ± 2,27*	21,33 ± 2,22 <sup>^</sup>
	TAMX (m/sec)	0,29 ± 0,06	0,27 ± 0,05 <sup>^</sup>	0,19 ± 0,04*	0,25 ± 0,02 <sup>^</sup>
	Vvol (ml/min)	98,71 ± 2,35	96,55 ± 2,25 <sup>^</sup>	88,79 ± 2,13*	94,15 ± 2,33 <sup>^</sup>
	IR	0,55 ± 0,05	0,56 ± 0,02	0,63 ± 0,05*	0,56 ± 0,04
a.interlobaris	Vs (cm/sec)	34,87 ± 2,12	32,29 ± 2,16 <sup>^</sup>	22,53 ± 2,42*	29,11 ± 2,01*
	Vd (cm/sec)	17,42 ± 2,26	16,01 ± 2,27 <sup>^</sup>	9,33 ± 2,24*	16,05 ± 2,13 <sup>^</sup>
	TAMX (m/sec)	0,21 ± 0,06	0,20 ± 0,05 <sup>^</sup>	0,14 ± 0,05*	0,19 ± 0,03 <sup>^</sup>
	Vvol (ml/min)	91,35 ± 2,39	91,37 ± 2,05 <sup>^</sup>	82,04 ± 2,44*	89,10 ± 22,32
	IR	0,54 ± 0,02	0,55 ± 0,03 <sup>^</sup>	0,70 ± 0,02*	0,57 ± 0,05 <sup>^</sup>
			(n=12)	(n=12)	(n=12)
LISINOPRIL					
a. segmentalis	Vs (cm/sec)	56,38 ± 3,32	48,55 ± 2,34*	42,66 ± 2,38*	45,66 ± 2,13*
	Vd (cm/sec)	24,22 ± 2,28	22,78 ± 2,00 <sup>^</sup>	14,89 ± 2,77*	18,79 ± 2,12*
	TAMX (m/sec)	0,29 ± 0,06	0,26 ± 0,03	0,23 ± 0,04*	0,24 ± 0,05*
	Vvol (ml/min)	98,71 ± 2,35	94,77 ± 2,54 <sup>^</sup>	89,11 ± 2,04*	92,77 ± 2,22*
	IR	0,55 ± 0,05	0,56 ± 0,03 <sup>^</sup>	0,72 ± 0,04*	0,63 ± 0,02 <sup>^</sup> *
a.interlobaris	Vs (cm/sec)	34,87 ± 2,12	30,99 ± 2,10 <sup>^</sup>	23,35 ± 2,18*	26,67 ± 2,20*
	Vd (cm/sec)	17,42 ± 2,26	14,11 ± 2,74 <sup>^</sup>	9,13 ± 2,44*	10,48 ± 2,17*
	TAMX (m/sec)	0,21 ± 0,06	0,19 ± 0,07	0,14 ± 0,05*	0,16 ± 0,02*
	Vvol (ml/min)	91,35 ± 2,39	86,55 ± 2,17 <sup>^</sup> *	81,62 ± 2,11*	83,26 ± 2,25*
	IR	0,54 ± 0,02	0,55 ± 0,04 <sup>^</sup>	0,70 ± 0,01*	0,69 ± 0,04*
Notes: * - p<0,05 in comparison with the group of healthy persons; ^ - p<0,05 in comparison with DN patients					



**Fig. 1.** Design of antihypertensive therapy of CKD with AH II degree