The State of Renal Functional Reserve During the Predialysis Stages of Chronic Kidney Disease

Barnoev Khabib[1,*], Sabirov Maksud[2], Munavvarov Burhonjon[2]

[1]Department of Nephrology, Multidiscipline Clinic of Tashkent Medical Academy, Tashkent, Uzbekistan
[2]Department of Therapeutic Subjects №2, Tashkent State Dental Institute, City Tashkent, Uzbekistann

Abstract   The article presents the results of a study to assess the functional reserve of the kidneys in a comparative study of antiaggregant therapy with pentoxifylline and alltrombosepin in 60 patients with a relatively early stage of chronic kidney disease. Studies have shown that long-term administration of alltrombosepin to patients has resulted in better maintenance of renal functional reserves. Therefore, pentoxifylline, which is widely used as an antiaggregant drug in chronic kidney disease can be easily matched by alltrombosepin, which is produced in our country from local raw materials - fact that was also confirmed during our research.

Keywords   Chronic kidney disease, Renal functional reserve, Glomerular filtration rate, Antiaggregant, Alltrombosepin, Pentoxifylline

1. Introduction

Despite the beginning of the new century, the problems of the transition and treatment of chronic kidney disease have not been adequately addressed [3,8,20]. The disease is characterized by severe and irreversible damage to many pathogenic joints. One of the most important of these is the disruption and disproportion of hemostasis. According to the National Kidney Foundation, all patients with chronic kidney disease should be included in the high-risk group for the development of cardiovascular disease, in which traditional factors do not play a significant role [12,13,17,21]. Hemostasis is an important pathogenetic link in the development of cardiovascular diseases in chronic kidney disease [4,7,12].

Ball filtration rate (BFR) evaluates the simultaneous function of kidneys, which is influenced by several factors and even when there are reliable markers, true filtration is still maintained at the norm because it does not lose up to 50% of the nephrons. Functional reserve of the kidneys is a response to physiological or pathological stimulation of the renal working capacity by increasing the rate of ball filtration [5,11,15,19].

At present, various anti-aggregant drugs are used in the treatment of chronic kidney disease in the world community. Of these, pentoxifylline is widely used in nephrological patients, has a high response rate and is included in the

standard of treatment [6,10,18]. At the same time, the drug alltrombosepin, which is derived from local raw materials and has undergone a number of laboratory and clinical trials, is used in cardiology as an antiplatelet agent. The main essence of our research is to improve the state of hemostasis and blood rheology in patients with relatively early stage of chronic kidney disease, as well as to reduce the aggregation of trace elements. Thus, in the treatment of chronic kidney disease, blood rheology-enhancing and antiplatelet agents are important. Therefore, we have conducted research to monitor and evaluate the effect of antiplatelet drugs pentoxifylline and alltrombosepin on the functional reserve of the kidneys in chronic kidney disease.

2. The Purpose of the Study

Evaluation of the effect of antiplatelet therapy on the functional reserve of the kidneys in patients with stage II and III renal disease on the basis of comparative observations in groups with the addition of pentoxifylline and alltrombosepin.

3. Research Material and Methods

For the study, 60 patients with chronic kidney disease, treated in the nephrology department of the Multidisciplinary Clinic of the Tashkent Medical Academy, developed as a result of nephropathy of various genesis (creatinine glomerular filtration rate (GFR) 30-89 ml/min/m2) were selected. Groups of 1 (n-30) and 2 (n-30) were selected from 60 patients who could be tested for RFR, ie those without

massive tumors, severe and moderate symptomatic arterial hypertension, in short, whose body was able to withstand protein loading. Group 1 consists of CKD (chronic kidney desease) patients who have started taking pentoxifylline. The second group consisted of patients receiving alltrombosepine 200 mg/day (1 capsule of the drug in a dose of 100 mg, prescribed 1 capsule 2 times a day for 3 months).

On the first day RFR of all patients was calculated by protein loading through parenteral administration of amino acid solution (Akumin-Nephro 1000 ml). RFR was calculated using the following formula [1]:

$$RFR = (GFR2 - GFR1)/GFR1) \times 100\%,$$

- GFR1 is the starting dose of GFR.
- GFR2 - the amount of GFR after protein transfer.

GFR, urea and creatinine in whey, and total protein and proteinuria, which are directly related to the dynamics of protein intake and are directly related to the calculation of RFR, were not excluded. Doppler examination of the renal arteries was also performed. GFR was calculated using the formula CKD-EPI (2009) modified in 2011 for the amount of creatine in whey (using an on-line calculator at http://nefrosovet.ru/). In it, the indicators of resistance (RI) and pulse (PI) index, calculated from the main gradients that determine the level of vascular resistance, were studied in the main and segmental renal arteries. Ninety days after treatment in groups 1 and 2, the same test and analysis were re-examined. The obtained results were statistically analyzed.

4. Results

In the analysis conducted to assess the functional reserve of the kidneys in group 1 patients, the results were as follows. According to this, on the first day of treatment, the amount of creatinine before protein loading was 169.4 ± 12.41 μmol/l, and after protein loading, creatinine decreased to 164.1 ± 10.72 μmol/l. At 90 days of treatment, creatinine before protein loading was 156.6 ± 7.05 μmol/l, and after protein loading, creatinine decreased to 151.4 ± 7.22 μmol/l.

Urea in the blood was 11.1 ± 0.47 mmol/l before protein loading on the first day, but decreased to 10.4 ± 0.34 mmol/l after protein loading. By 90th day of treatment, the value of urea was 9.0 ± 1.55 mmol/l before the protein load and the urea after the protein load was 8.9 ± 0.46 mmol/l.

GFR was 42.1 ± 2.42 ml/min before protein loading at the beginning of treatment and increased to 44.9 ± 2.21 ml/min after protein loading. By 90th day of treatment, GFR was 44.9 ± 1.55 ml/min before protein loading and 47.8 ± 1.32 ml/min after protein loading.

Thus, when patients were given a protein load, the oncotic pressure of plasma increased due to an increase in total protein in the blood. As a result, an increase in GFR was observed as a result of the addition of reserve glomerulus to the activity, and a consequent decrease in products such as urea and creatinine in the blood.

Proteinuria at the beginning of treatment was 1.9 ± 0.78 before protein loading; after protein loading, it increased to 1.94 ± 0.64. By the 90th day of treatment, however, proteinuria was 0.86 ± 0.282 prior to protein loading; an increase of 0.90 ± 0.218 was observed after protein loading. This condition is due to the tension of the damaged nephrons during protein loading.

Total protein was 61.8 ± 1.72 g/l before protein loading at the beginning of the study, but increased to 62.4 ± 1.33 g/l after protein loading. By the 90th day of treatment, total protein was 63.0 ± 1.43 g/l before protein loading and increased to 64.6 ± 1.35 g/l after protein loading.

Indicators determining the level of renal vascular resistance, resistance and pulse indices were studied in the main and segmental renal arteries. According to it, the resistance index in the main renal artery was 0.70 ± 0.018 before the protein load at the beginning of treatment, and it decreased to 0.68 ± 0.015 after the protein load. After 90 days of treatment, this figure showed a value of 0.65 ± 0.021 before protein loading and decreased to 0.62 ± 0.016 after protein loading. The pulse index was 1.60 ± 0.23 before protein loading at the beginning of treatment and it was seen to decrease to 1.54 ± 0.32 after protein loading. After 90 days of treatment, this value was 1.49 ± 0.24 before the protein load and decreased to 1.45 ± 0.21 after the protein load.

In the segmental renal arteries, the resistance index was 0.69 ± 0.018 before protein loading at the beginning of treatment and decreased to 0.68 ± 0.020 after protein loading. After 90 days of treatment, this figure showed a value of 0.64 ± 0.014 before protein loading and decreased to 0.62 ± 0.016 after protein loading. The pulse index was 1.21 ± 0.019 before the protein load at the beginning of treatment and was seen to decrease to 1.20 ± 0.021 after the protein load. After 90 days of treatment, this value was 1.16 ± 0.012 before protein loading and decreased to 1.14 ± 0.017 afterwards. Resistance and pulse indices are related to blood viscosity and vascular resistance. When patients were given a protein load, the oncotic pressure of plasma increased due to an increase in albumin and total protein in the blood. As a result, due to the relative improvement of hemodynamics resulting from the increase in total circulating blood volume caused by the return of tissue plasma into the blood vessel, a positive shift in these indicators was observed. However, this shift is based on the fact that the reliable improvement in patients receiving pentoxifylline for three months is due to a decrease in the aggregation of trace elements and the vasodilator properties of the drug.

In group 1 patients receiving pentoxifylline as an antiplatelet therapy, RFR based on blood creatinine clearance was 6.7% before treatment and increased by 7.1% after 90 days of treatment.

We now present the results in the analyzes performed to assess the functional reserve of the kidneys in group 2 patients receiving the drug alltrombosepin as an antiaggregant treatment. According to it, on the first day of treatment, the amount of creatinine before protein loading was 166.5 ± 10.87 μmol, while after protein loading

creatinine decreased to 160.6 ± 11.43 μmol. By the 90th day of treatment, the creatinine level before protein loading was 158.9 ± 7.09 μmol, while after protein loading, creatinine decreased to 153.4 ± 6.31 μmol.

Urea in the blood was 11.3 ± 0.45 mmol/l before protein loading on the first day, but decreased to 10.4 ± 0.34 mmol/l after protein loading. By the 90th day of treatment, the urea value was 9.0 ± 1.52 mmol/l before protein loading and after loading went down to 8.8 ± 0.52 mmol/l.

GFR was 42.1 ± 2.16 ml/min before protein loading at the beginning of treatment and increased to 44.8 ± 2.32 ml/min after protein loading. By the 90th day of treatment, GFR was 44.8 ± 1.28 ml/min before protein loading and 47.9 ± 2.08 ml/min after protein loading.

Thus, the oncotic pressure of plasma increased due to an increase in total protein when patients were given a protein load. As a result, kidney function indicators, such as GFR, urea, and creatinine, have changed for the better as a result of the addition of reserve glomerulus to the activity.

Proteinuria was 2.3 ± 0.63 before protein loading at the beginning of treatment; after protein loading, it increased to 2.32 ± 0.64. By the 90th day of treatment, however, proteinuria was 1.72 ± 0.72 before protein loading; increased by 1.73 ± 0.311 after protein loading. This condition is due to the tension of the damaged nephrons during protein loading.

Total protein was 62.3 ± 1.68 g/l before protein loading at the beginning of the study, but increased to 63.2 ± 1.24 g/l after protein loading. By the 90th day of treatment, total protein was 64.1 ± 1.39 g/l before protein loading and increased to 65.2 ± 1.33 g/l after protein loading.

According to the results of renal vascular dopplerography, the resistance index in the main renal artery was 0.69 ± 0.022 before protein loading at the beginning of treatment and decreased to 0.68 ± 0.012 after protein loading. After 90 days of treatment, this figure showed a value of 0.64 ± 0.019 before protein loading and decreased to 0.62 ± 0.016 after protein loading. The pulse index was 1.59 ± 0.28 before the protein load at the beginning of treatment and was seen to decrease to 1.52 ± 0.22 after the protein load. After 90 days

of treatment, this value was 1.46 ± 0.16 before protein loading and decreased to 1.43 ± 0.19 after protein loading.

In the segmental renal arteries, the resistance index was 0.69 ± 0.022 before protein loading at the beginning of treatment and decreased to 0.68 ± 0.012 after protein loading. After 90 days of treatment, this figure showed a value of 0.64 ± 0.019 before protein loading and decreased to 0.62 ± 0.016 after protein loading. The pulse index was 1.20 ± 0.024 before protein loading at the beginning of treatment and it was seen to decrease to 1.19 ± 0.018 after protein loading. After 90 days of treatment, this value was 1.15 ± 0.016 before protein loading and decreased to 1.14 ± 0.017 after protein loading. It is known that resistance and pulse index are related to blood viscosity and vascular resistance. When patients were given a protein load, the oncotic pressure of plasma increased due to an increase in total protein in the blood. As a result, due to the relative improvement of hemodynamics resulting from the increase in total circulating blood volume caused by the return of tissue plasma into the blood vessel, a positive shift in these indicators was observed. However, we interpret this shift as a significant improvement in patients receiving alltrombosepin for three months due to a steady decrease in the aggregation of shaped elements over months.

In group 2 patients receiving alltrombosepin as an antiplatelet therapy, RFR based on blood creatinine clearance was 6.6% before treatment and increased up to 7.2% after 90 days of treatment.

Looking at the results, we observed that the changes were close to each other when we followed the dynamics of the indicators assessing the functional status of the kidneys in both research groups. Although no significant positive shift was observed in both groups when calculating RFR according to creatinine clearance, it is also important that RFR persists for some time against the background of treatment with antiplatelet agents [9,21]. The dynamics of RFR in the background of treatment with antiplatelets is illustrated in Figure 1 on the basis of horizontal and vertical diagrams:
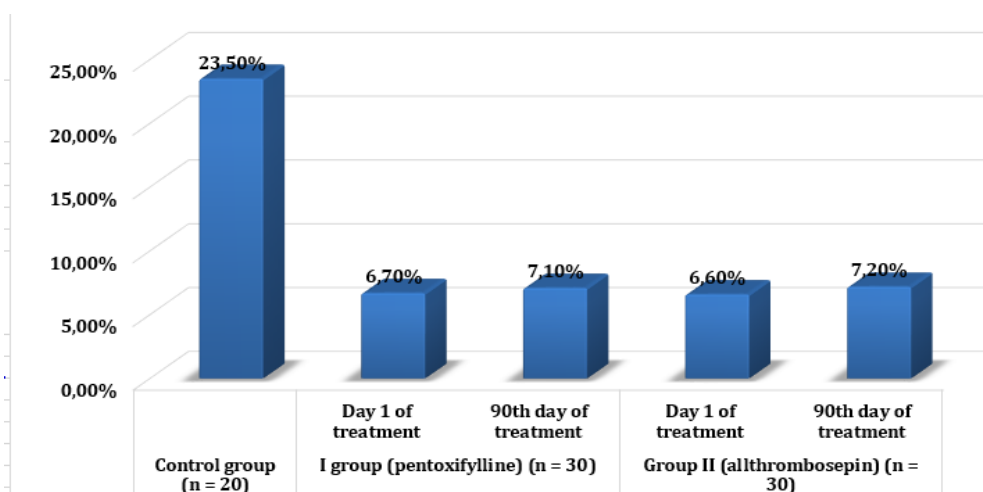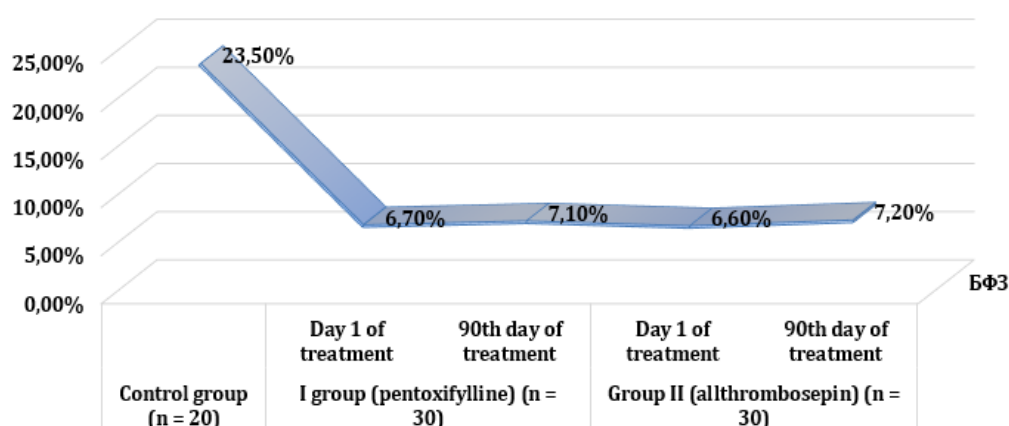
Figure 1. Dynamics of the functional reserve of the kidneys against the background of treatment with antiplatelet agents

Table 1. Results of laboratory tests of group I patients

Parameters		Control group (n = 20)	Group I (pentoxifylline) (n = 30)			
			Day 1 of treatment		Day 90 of treatment	
			Before protein loading	After protein loading	Before protein loading	After protein loading
Creatinine		71,6±1,62 mkmol	169,4±12,41**	164,1±10,72*	156,6±7,05*	151,4±7,22*
Urea		6,8±0,13 mmol/l	11,1±0,47*	10,4±0,34*	9,0±0,55*^	8,9±0,46**^^^
Total protein		69,6±1,35g/l	61,8±1,72*	62,4±1,33*	63,0±1,43*	64,6±1,35*
Proteinuria		0.0±0.01 g/l	1,9±0,78**	1,94±0,64**	0,86±0,28**^	0,90±0,218**^
Main renal artery	RI	0,58±0,07	0,70±0,018***	0,68±0,015***	0,65±0,021***^^^	0,62±0,016***^^^
	PI	1,26±0,18	1,60±0,23**	1,54±0,32**	1,49±0,24**	1,45±0,21**
Segmental renal artery	RI	0,61±0,07	0,69±0,018***	0,68±0,020***	0,64±0,014***^^^	0,62±0,016***^^^
	PI	1,05±0,014	1,21±0,019***	1,20±0,021***	1,16±0,012***	1,14±0,017***
GFR ml/min		103,1±4.99 ml/min	42,1±2,42*	44,9±2,21*	44,9±1,55*	47,8±1,32*
RFR		23,5 %	6,7 %		7,1 %	

Note: * - the differences are significant relative to the control group (* - P <0.05, ** - P <0.01, *** - R <0.001) ^ - the differences are significant relative to the group prior to treatment (^ - R < 0.05, ^^ - R <0.01, ^^^ - R <0.001).

Table 2. Dynamics of RFR indicators in group II patients

Parameters		Control group (n = 20)	Group II (allthrombosepin) (n = 30)			
			Day 1 of treatment		Day 90 of treatment	
			Before protein loading	After protein loading	Before protein loading	After protein loading
Creatinine		71,6±1,62 mkmol	166,5±10,87*	160,6±11,43*	158,9±7,09*	153,4±6.31*
Urea		6.8±0.13 mmol/l	11,3±0,45**	10,4±0,34**	9,0±1,52*^	8,8±0,52**^^
Total protein		69,6±1,35g/l	62,3±1,68*	63,2±1,24*	64,1±1,39*	65,2±1,33*
Proteinuria		0,0±0,01 g/l	2,3±0,63**	2,32±0,64**	1,72±0,72**^	1,73±0,311**^
The main renal artery	RI	0,58±0,07	0,69±0,022***	0,68±0,012***	0,64±0,019***^^^	0,62±0,016***^^^
	PI	1,26±0,18	1,59±0,28**	1,52±0,22**	1,46±0,16**	1,43±0,19**
Segmental renal artery	RI	0,61±0,07	0,69±0,022***	0,68±0,012***	0,64±0,019***^^^	0,62±0,016***^^^
	PI	1,05±0,014	1,20±0,024***	1,19±0,018***	1,15±0,016***	1,14±0,017***
GFR ml/min		103,1±4,99 ml/min	42,1±2,16**	44,8±2,32**	44,8±1,28**	47,9±2,08**
RFR		23,5%	6,6 %		7,2 %	

Note: * - the differences are significant relative to the control group (* - P <0.05, ** - P <0.01, *** - R <0.001) ^ - the differences are significant relative to the group prior to treatment (^ - R < 0.05, ^^ - R <0.01, ^^^ - R <0.001).

Another key criterion that we should pay attention to in the diagram images is that we have observed that RFR is at least slightly better preserved in group 2 patients, who received alltrombosepin as an antiaggregant agent, than in group. It has been shown that long-term administration of the antialgregant drug Alltrombosepin to patients not only improves the functional state of the kidneys, but also has a significant effect on maintaining the functional reserve of the kidneys.

5. Discussion

The version of this template is V1. Most of the formatting instructions in this document have been compiled by SAP Productions. SAP Productions offers A4 templates for Microsoft Word. SAP Productions has tried its best efforts to ensure that the templates have the same appearance.

SAP Productions permits the distribution and revision of these templates on the condition that SAP Productions is credited in the revised template as follows: "original version of this template was provided by courtesy of SAP Productions".

6. Conclusions

In the early stages of chronic kidney disease, it is advisable to monitor the state of the functional reserve of the kidneys.

Long-term use of alltrombosepin antiaggregant drug in patients during treatment achieves better preservation of renal functional reserve.

In patients with the use of the drug Alltrombosepin, renal functional reserve is well maintained and the progression of chronic kidney disease is slowed.

REFERENCES

[1]   Gojenko A.I., Gojenko E.A., Functional renal reserve in physiology and pathology of the kidney. Bukov. med., t. 16.3 (63): 2015. 18st.

[2]   Ivanov D.D., Kuryata A.V., Garmish I.P. (2018) RAAS blockers: CKD and cardiac-vascular risk. Pochki. Kidneys, 2: 13–22.

[3]   Karimov M.M. Progression of chronic kidney disease from the perspective of some links of pathogenesis // Bulletin of the Tashkent Medical Academy. - Tashkent, 2014. - № 4. - C. 7-19.

[4]   Karimov M.M., Daminov B.T., Kayumov U.K. Chronic kidney disease as a medical and social problem and risk factors and its development // Bulletin of the Tashkent Medical Academy. - Tashkent, 2015. - № 2. - C. 8-12.

[5]   Melnik A. A. Kidneys. p-ISSN 2307-1257, e-ISSN 2307-1265 № 3 (17) 2016.

[6]   Mixaylova I. E.. Antiplatelet drugs in the prevention and treatment of coronary atherothrombosis. Literature review // Bulletin of St. Petersburg University. Series 11. Medicine. - 2014.

[7]   Popova L.V., Bokarev I.N. Application of antiplatelet agents in clinical practice, Practical medicine, Cardiology, '6 (82) September 2014g, 22.

[8]   Rogova I. V., Fomin V. V., Damulin I. V., Shashkova E. V. Features of cognitive impairment in patients with chronic kidney disease at the pre-dialysis stages: scientific publication // Therapeutic archive. - 2015. - Tom 85 № 6. - C. 25-30.

[9]   Savitska L.M. (2017) Vzaêmozv'yazok míj funktsionalnim nirkovim rezervom, rívnem sechovoï acidi ta yakístyu jittya patsíêntív íz xroníchnoyu xvoroboyu nirok Í– ÍÍÍ stadíí. Nirki, 6 (2): 32–39.

[10]   Sharapov O. N., Mirzaeva G. P., Sabirov M. A. Study of hypoazotemic efficacy of the drug tsinarozid in clinical conditions: a scientific publication // Vestnik Tashkentskoy Meditsinskoy Akademii. - Tashkent, 2014. - N1. - C. 54-56. - Bibliogr.: 12 nazv.

[11]   Azpiazu D, Role of pyrophosphate in vascular calcification in chronic kidney disease //Nefrologia] 2018 May - Jun; Vol. 38 (3), pp. 250-257.

[12]   Chiang C., The use of bone turnover markers in chronic kidney disease-mineral and bone disorders The use of bone turnover markers in chronic kidney disease-mineral and bone disorders // [Nephrology (Carlton)] 2017 Mar; Vol. 22 Suppl 2, pp. 11-13..

[13]   Garcfa-Bello JA, Ortiz-Flores J, Anemia and hypoalbuminemia as risk factors for left ventricular diastolic dysfunction in children with chronic kidney disease on peritoneal dialysis // Nefrologia] 2018 Jul - Aug; Vol. 38 (4), pp. 414-419.

[14]   Lapina E.S., Batyushin M.M., Terentev V.P., Clinical features of therapy of anemia and the significance of its fluctuation in the development of anemia in dialysis patients // Georgian Medical News. 2017. № 272. C. 64-68.

[15]   Matsumoto-Miy azaki J, Miyazaki N., Traditional Thermal Therapy with Indirect Moxibustion Decreases Renal Arterial Resistive Index in Patients with Chronic Kidney Disease // J Altern Complement Med] 2016 Apr; Vol. 22 (4), pp. 306-14.

[16]   Mayta-Tristan P, Early mortality in patients with chronic kidney disease who started emergency haemodialysis in a Peruvian population: Incidence and risk factors // Nefrologia] 2018 Jul - Aug; Vol. 38 (4), pp. 425-432.

[17]   National Kidney Foundation (2015) GFR Calculator (https://www.kidney.org/professionals/kdoqi/gfr_calculator).

[18]   Noor S, Role of Leptin and dyslipidemia in chronic kidney disease // Pakistan Journal Of Pharmaceutical Sciences [Pak J Pharm Sci] 2018 May; Vol. 31 (3), pp. 893-897.

[19]   Oliveira EA, Mak RH. Progression of chronic kidney disease in children - role of glomerular hemodynamics and interstitial fibrosis. Curr Opin Pediatr. 2018 Apr; 30(2): 220-227.

[20]   Role of glomerular hemodynamics and interstitial fibrosis.. // Curr Opin Pediatr] 2018 Apr; Vol. 30 (2), pp. 220-227.

[21]   Sata Y., Role of the Sympathetic Nervous System and Its

Modulation in Renal Hypertension // Front Med (Lausanne)] 2018 Mar 29; Vol. 5, pp. 82.

[22] Vavilova T.P., Geva O.N., Pushkina A.V., Tkachev G.A., Koretskaya N.A.: Diagnostic and prognostic value of antioxidant enzyme assay in erythrocytes of patients with end stage renal disease treated with hemodialysis// Biomed Khim. –2016. –Mar-Apr. –52(2). –P219-22.