IMPACT OF HYPERTENSION AND LIPIDS IN THE PROGRESSION OF CHRONIC RENAL DISEASE

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Abstract: Arterial Hypertension (AH) and lipid abnormalities are among the most important causes that accelerate the progression of chronic renal disease (CRD) and the risk of cardiovascular diseases (CVD). The etiology of arterial hypertension is a multifactorial (near 20-25% of cases with AH the etiology is known, while other cases are due to many other disorders: hormonal, renal, cardiac, infectious, congenital diseases or inherited, different uropstruksionet, RVU etc. Lipid metabolism disorders in patients with CRD are described the first time in 1827 by Dr. Bright, especially in patients with nephrotic syndrome (1). It is known that patients with CRD present the clinical picture of the earlier representation atherosclerosis (Early atherosclerosis) and serious cardiovascular, cerebrovascular complications more frequent and with greater numbers in younger population compared to healthy population. Arterial Hypertension is a independent riskfactor for the rapid pace of CRD with high consequences to cardiovascular disease and high mortality increase (2,3,4). Purpose of the Paper :The purpose of this paper is to verify and document the impact of AH and abnormalities of lipids in preventing and inhibiting the pace of progress of CRD and manifestations of AH against cardiovascular diseases (CVD) The paper also aimed to detect the positive effects and impact of ACE inhibitors in preventing the evolution of the progression of CRD and treatment of arterial hypertension (AH) treated in the Department of Internal Diseases at the Clinical Hospital of Tetova and in the Special Hospital for Nephrology and Hemodialysis ,, Vita Medical Group "of Tetova. The prevalence of CKD in fact is defi-ned by the degree of renal injury randomized according to values of glomerular filtration rate (GFR, Glomerular Filtration Rate) according Coccroft & Gault formula. Patients in stage 1 (GFR of ≥90ml / min / 1.73m ^{2} and 2 and 60-89 ml / min / 1.73m ^{2} of Chronic Kidney Dise-ase (CKD) should show minor damage to the kidney (eg, 1 actor 1 nsive), and , Respectively stage 3, 4, and 5 correspond to the GFR of 30-59, 15-29, and <15 ml / minute, respectively, regardless of any event and show the other symptoms of kidney damage (5)

Index terms: Hypertensioni arterial (AH), CRD, glomerular filtration rate (GFR), lipid profile (total cholesterol (TCH). Triglycerides (TG), HDL-ch (High density lipoprotein cholesterol), LDL-ch (Low Density lipoprotein cholesterol).

1 INTRODUCTION

Arterial Hypertension (AH) remains one most important and common factor of diseases throughout the world. Between normotension and hypetension pressure not any precise definition persists , but based on the preferences and the World Health Organization all the values of systolic press-ure> 140 mmHg and diastolic> 90 mmHg are treated as arterial hypertension. Recent years, a number of studies have verified and documented that between AH and lipid abnormalities and progress of CKD(Chronic Kidney Dise-ase) there is a high positive correlation. There are facts documented that patients with CKD and other consequences besides AH, a large number of them suffer from a hipertre-gliceridemia and dyslipidemia, so it is very necessary examination, treatment, determination and correlation of lipids with AH, that in the initial stages of CRD with the sole purpose of preventing rapid pace of progress towards CRD uremia. Many contemporary studies testify a close conne-ction between pressure and uremic dyslipidemia verifying that the AH with its oscilations significantly affect lipid diso-rder helping their stratification on the wall of blood vessels, thus increasing the risk of aterogenesis of coronary arteries, cerbrale with frequent manifestations of acute myocardial infarction, left ventricular hypertrophy, angina pectoris, heart failure congestive and cerebrovascular brain stroke. Common effects of AH and hyperlipidemia manifestly affect modification and reduce in Renal functions causing nefroangiosklerosis with glomerulosklerosis. It is estimated that 10-13% of elderly patients in the US suffer from CKD and AH without taking to account the degree of CRD. AH during CRF is *volumic type* (with manifestations of cardiovascular complications with hipertensive cardiomyopathy etc. (6), and despite that sometimes it may be as a result of other mechanisms like hipernatremia etc.

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Multiple clinical studies to have demonstrated that adequate treatment and in time of the AH and dyslipi-demia in patients with CKD they have significantly reduced the frequency of myo-cardial infarction, left ventricular hypertrophy, heart disease, peripheral arterial disease, retino-pathy, trombembolic processes and cerbrovaskular ictus. According to etiology internal medicine practice arterial hypertension is divided in : *1. secondary AH* which appears as a result of various kidney diseases (parenkimatose, nefroskcerosis or blood vessels), various disorders of the endocrine system (feochromocitoma, primary aldosteronismi, Cushing syndrome), coronary diseases, brain diseases (Exces-sive use of hormones and oral contra-ceptives and *2. essential arterial hypertension (idiopathic factor)* whose causes are unknown etiology and this group of *AH* cont-aines near 80- *90%,* although in its etiology are counted many different factors such as genetic predis-position, adiposity , age, sex, sedentarity , psychological stress, socio-economic status ect. Arterial hypertension and also dislipidemias remain a problem with frequency and are more difficulties for treatment of the patients with CRD taking into account the imbalances of electrolytes and in addition the ratio in the system renin-angiotenzin-aldos-teron.In patients with AH and CRD are verified high value-ch LDL and TG and low HDL values in comparisonk with healthy control group. As a result of high concentrations values of LDL-ch we have the appearance of damage of the endothelial cells in the vascular wall, the reduction of prostaglandin synthesis 2 (PGI 2) (with its antithrombotic and fibrinolitic effect) and the effect of stratification of ox LDL (oxidized cholesterol) in macrophages and smooth muscle cells widow (7,8,9). As the causes of endothelial lesions and flatlands of LDL-ox to the walls of blood vessels besides other causes very important role has the AH, in particular its excessive oscillations causing circular movements of blood with injury to the endothelium and early processes of the stratification of fat in the walls of blood vessels. There facts documented that patients with CRD and AH and concentrations of LDL-ch aterogenic, triglicerides (TG) are significantly elevated, while concen-trations of HDL-ch defense (antiaterogenic) are signify-cantly lower (which was also verified in our study) and consequences of cardiovascular disease, cerebrovascular and early atherosclerosis that are highly elevated compa-reed with the healthy population and patients group controller's healthy volunteers (10,11,12,13,). Determination of lipid abnormalities in patients with CRD also accompanied AH in the early stages of the disease, and the discovery of etiopathogenic mechanisms can significantly help in preventing their consequences, with what will be consi-derably decreased to the appearance of cardio-vascular diseases, cerebro-vascular and athero-genetic processes of the blood vessels. According to the definition of the WHO (Clasification of atheroscler-osis, lesions, report of study on definition of terms 1985), athe-rosclerosis (Ath) is defined as a variable of changes of the arterial wall composed of accumulation of lipid, sugars, Blood, blood products, fibrous tissue and calcium deposition asso-ciated with changes in tunica media of the blood vesels. As the final product during Ath is the formation of plaque which in most cases is penetrating the blood vessels intima and comes in contact with blood and its rough surface helps increase the blood vessel and as a product we have the final formation of thrombus or embolus which is the cause of thrombosis of blood vess-els in heart, brain, kidney, liver ect. Atherosclerotic lesions begin with damage to the endothelial cells of blood vessels (14,15). The prevalence of AH in patients with CRD is higher among patients with higher body weight or the BDMix *(Body-Mass - Index BMIx = TT / kg / x TV $^{-2>}$ 24.3 ±5.2 kg / m.* Approximately one in three adults in the United States suffers from AH which represents socio economic prob-lem for state (16). The prevalence of hypertension also varies in Report with CRD and has a high positive corre-lation. Asotiations dealing with, AH and CRD have verify-ed that the highest prevalence of CRD is in patients with renal artery stenosis approxi-mately - 93% -87% in diabetic nephropathy, policystic adult kidney disease by 74% (17). If the AH in patients with CRD is associated with glomerulopathy or diabetic nephropathy then its influence is manifested by a very greater damage to the kidney associated with vascular lesion, nephroar-theros-clerosis and glomerular prolife-ration, with an accelerated pace towsrds uremia when the only treatment is treatment with HD intermitente. This defines in a fundamental way the intense loss of kidney tissue and to the progression of CRD. AH is present in 80% of cases of patients with CKD. Incidence of the AH varies according to the type of under-lying renal disease for example patients with glomerulo-nephritis and with chronic renal policistosis have higher incidence of AH compared with patients who have tubulintersti cial disease (eg Pyelonephritis). For this reason, to treat AH as qualitative effect should not under mind the role and Significance of the balance of Na plays in the pathogenesis of AH. The CRD associated with AH there is a disability eliminate the proper amount of sodium. AH has a major impact on the cardiovascular system and the symptoms of left ventricular failure which may also be accompanied with dyspnoea and pulmonary edema. Treatment of arterial hypertension affects especially the slowing of progression of CRD especially patients who have proteinuria> 1 g / 24h. Recent years have proved that the best effects during treatment AH showed ACE-inhibitors (Skopril, Enalapril, Lisinopril, captopril, ramipril, ...) and a younger group of drugs ARB- receptor antag-onists of Angiotenzin-I (losartan, Irbersartan, candesartan, valsartan, Cossaar ... etc.) compared with other antihyperthonics. In the pace of progress CRF also effect has diabetes, diabetic nephropathy, glomerular hemody-namics disorder, hyperlipidaemia, dietary proteins, hyperfosfatemia, renal anemia, food and consumption of excessive amounts of calories, horrmonet, free radicals, Growth factors (PDGF, platelet-Derived Growth Factor, TGF-b - Transforming Growth Factor-b), coagulation, ammonium, prostaglandins, age ,, gender, race, genetic factors, Consumption of tobacco, renin-angiotensine system (SRA), MIA syndrome (Malnutritio-Inflamatio-Atherosclerosis), inflammation, pro-inflam-matory cytoc-ines influence (Interleukin!, interleukin 1 alpha .Interleukin 6 etc. .From all the causes which lead to CRD can be understood that in its appearance there is not only one mechanism, but the etiology of CRD is extremely multufa-ctorial, therefore early detection of all mechanisms leading to CRD, hygienic-dietary prevention as well as their therapeutic treatment in the initial stages can positively affect the pace, speed and progress of CRD and its complications to the cardiovascular system, brain and early atherosclerosis. In CVD genesis in patients with CRF and AH are counted: high concentrations of oxidized cholesterol t-LDLox, Oxidative stress (R = 1 8) Influence of vasoconstrictor mechanisms such as increased plasma concentration of endothelin-1 (ET-1) (1 9, 20), noradre-naline which counts as one of the most potent vaso-constrictor. The synthesis of nitric oxide (NO) which count as vasodilatator more powerful and more effective in terms of uremia is blocked due to excessive accumulation reduced synthetase nitrogen oxide (NO) by Dimenthyl-L Argenine asymmetric (DMAA) (21,22). There are verif-iable facts and arguments that kidneys play an impor-tant role in long-term regulation of arterial pressure Guy-ton [2 3) and that AH could eventually not be prese-nted to us if it

does not exist renal injuries and disorders of sodium. In fact, almost all forms of experimental and human hyper-tension disorders are manifested by abnormal secretion of sodium concentrations even during normal blood pres-sure. [2 4). While using large animals in experiments and isolated with AH Guyton showed that there is a rapid normalization of arterial pressure after rapid stimulation and high renal sodium excretion. On the other hand, loading with sodium showed an increased arterial pressure when the renal excretion was conditioned by inhibition of secretion of sodium or the impact of the mechanisms to angiotensin aldosterone either. In these circumstances, the increase in blood pressure was mediated primarily by overloading the volume of extracellular fluid (ECF), despite a reduction in total peripheral resistance. In this case, increased blood pres-sure manifested in heart enlargement and with increased systolic arterial pressure. With time, and normalized volume of extracellular fluid ECF systolic pressure begins to normalize with the impact of increased peripheral resistance , but then we have increased the diastolic pressure . There are documented postmortem studies (during the fatal accidents) that hypertensive patients have had much less functional nephron's compared with individuals who have been dead but normal pressure in a series of autopsy (2 5). The exact nature of the defects of the kidney that are responsible for the inappropriate sodium excretion or factors that mediate the subsequent increase of the peripheral resistance are still unknown. The critical role in volume expansion of extracellular liquids in patients with CRD with manifestation of the cardiovascular system has ultrafiltration , hYpernatremia and excessive amount of salt in the body. The positive balance of salt is dominant, but not the onlu factor in the genesis of hypertension in patients with CRD. [26) In patients with CRD tand AH and treated with hemodialysis (HD) or peritoneal dialysis (The regimes of 3 times a week from 5-6 hours) we see an obvious improvement of AH and the improvement of left ventricular hypertrophy and prevalence reduction of mortality. [27, 28) As mentioned above, experimental evidence shows clearly that the AH in patients with CRD due to the retention of salt and excess water in the body, appears due to increase of peripheral resistance and the impact renin-angiotensin-aldosteron system- - RAA S (29). There are verifiable facts that although renal funcion is stored, activation of RAA S is a important factor in the patho-genesis of AH of patients with polycystic kidney disease and he appears due to vascular overload from permanent increase of the cists (30). Patients with CRD and AH are potential candidate for CVD compared with the general population and in the terminal phase the hemodi-lysis treatment is required with the purpose of normalize-ation of AH reducing cardiovascular disease and with that would be reduced mortality (50-6% due to cardiovascular disease. [3 1) All directions by numerous national associ-ations (JNC VII report of - Joint National Committe on Prevention Detection, Elevation Treatment of High Blood Pressure - 1993), European Society of Hyper-tension (ESH 2003) and European Society of Cardiology (ESC 2003), K / DOQI - Kidney Disease Outcomes Quality Initiative) on prevention, early recognition , evaluation , and early treatment of CRD and AH recommend that the purpose of the treatment to be: Systolic blood pressure <130 mmHg while the diastolic = 80 MHG (32,-33) It is extremely necessary that we prevent progr-ession of CRD in patients with AH except normalization of AH we should evaluate the manifestation proteinuria and its correction . Several studies have documented that patients with AH and CRD (in particular patients> 70 years old with CRD can be in high risk of cardiovascular disease in particular can suffer from acute myocardial infarction if Systolic blood pressure was reduced <120 and diastolic <80 mmHg. (3 4).

Dual therapy (ACE inhibitors and ARBs with) of the AH in patients with CRD affects reduk tion of proteinuria in a larger scale, but there are no documented studies and that the dual therapy affects the preservation of the kidney function , or preventes cardiovascular damage, compared with the therapy of ACE inhibitors Combined with any diuretic (which affects the treatment of volume overload or hyperkaliemia (35). For adequate treatment of AH in patients with CRD should always have in mind the nature of the underlying renal disease. The goal of the treatment with ACE inhibitors or ARBs should aim at a tension <130/80 mm Hg while the blood pressure of <140/90 mm Hg is acceptable to a large number of patients and other forms of CRD. Double or triple treatment of the AH should generally be avoided. Studies of AH treatment of patients with CRD are controversial and still not exactly know to what degre should the arterial pressure be lowered to be protected the kidney . The aforementioned uncertainty exists about the quantitative relationship between blood pressure levels and progressive renal failure . Many epidemiological studies have verified a high positive correlation between AH and hypercreatininemia. Despite the different opinions that are existing as qualitative approach to AH in patients with CKD, it is accepted that control of hypertension at under 140/90 mm Hg significantly affects reduction of CRD and apperance of CVD. Because the treatment of hypertension and norma-lization of hyperlipidemia has shown positive effects on the slowdown in the progress of the CRD and lowering of hipercreatininemia patients who receive care and antihype-rtensive therapy in time while preserving the values of the pressure of: 120 ... 130/85 mm Hg *(Preferred values for patients with renal impairment).* Besides slowing down the pace of normalization of CRD significantly affects the prevention of cardiovascular diseases (acute myocardial infarction, angina pectoris congestive heart failure s, etc. cerebrovascular brain stroke. Last Years of Progress in prevention of CRD and increased glomerular filtration of patients with CRD and AH big role has shown the protein intake restriction which affects and lowers the pace of progress of CRD. Similar results were observed in hypertensive patients with CRD with a minimum dosage of antihypertensives before bedtime. hese results , together are evidence which verify conclusions of many scientists on the positive correlation salt consumption with AH of the patients with malignant hypertension and in patients with CKD form strong reasons for reducing the consumption of salt as a mechanism to slow the progress and pace of progress of diabetic nephropathy. *daily protein human consumption must not passe a value of 0.5 - 0.6 g / kg / day..* During the aforementioned diseases ACE inhibitors are used as qualitative choices and having in mind that some ACE inhibitor have shown high positive effects compared to other groups of drugs in slowing the pace of progress of CRD and reduce the morbidity and mortality of patients with diseases aforementioned. Prevention of progression of CRD requires treatment and medication of arterial hypertension (AH) that the arterial pressure in patients with proteinuria of 0.25-1.0 g / 24 hours should be ≤ 130/80 while patients with proteinuria of ≥ 1.0 g / 24 org / 24 hours should be ≤ 125/75 mmHg. Proteinuria is not the only dominant factor which indicates renal damage but is independent risk factor of rhythm and speed of progress of CRD .At the same time proteinuria shows the efficiency of action and impact of ACE -frenuesëve while as parameter serves the elimination of reduce protein in urine during 24 hours. We can say that the regression is achieved when through urine protein loss is *<0.3 g / 24* hours, and when we have improvement of the degree glomerular filtration (GF).

2 MATERIAL AND METHODS

In-prospective cohort study (,, cross-section ") were included in total N^O = 100 (from whom 55 were male with an average age of: 59.80 ± 13.50), male while 44 were girls the average age: 57.50 ± 15.00)). In the study we had the control group N^O = 100 healthy individuals (55 male and 45 female with an average age of 57.40 ± 11.80) that served for comparison of values obtained from examinated parameters . Patients with AH and CRF that were treated with ACE inhibitors in the Clinical Hospital of Tetovës-Ward Internal and in the Special Hospital for Nephrology and Hemodialysis ,, Vita Medical Group "of Tetova Patients were divided according to the levels of hypertension, according to the criteria of the report of the JNC-VII Joint National Committe on Prevention Detection, Elevation Treatment of High Blood Pressure year 2003.On the examined patients did the examination of proteinuria, serum urea, creatinine in serum, uric acid, electrolytes, lipide profile of Total Lipids (LT), total cholesterol (ChT), triglycerides (TG), HDL-ch, LDL-ch with aim to verify their influence in the appearance of arterial hypertension as complementary factors in the etiology of CRD

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Table number. 1: Presentation of patients according to gender, average age(N^O= 100) and control group N^O = 100

Gender	Total number N^o = 120 (100%)	The average age ± SD	The average age of the control group ± SD
Male	N^0 = 55 (55%)	59.80 ± 13.50	57.40 ± 11.80
Female	N^0 = 45 (45%)	57.50 ± 15.00	57.40 ± 11.80

The average age of patients in males was 59.80 ± =13.50 while the female gender was 57.50 ± 15.00, the average age difference between male and female according to statistics is nonsignificant *p = 0.0005,* which indicates for a homogeneous group (tab. number 1).

3 GAINED RESULTS

Results from measurements obtained are presented in tabular.

Table number 2 . The definition of progress, remission and regression of the chronic nephropathies manifested by proteinuria

Settings	Progression	Remission	Regression
Proteinuria	> 1.9 g / 24 h	<1.0 g / 24 h	<0.40 g / 24 h
FGR	GFR reduced	GF stable	GF increased
Kidney structure	GFR deteriorated	GF stable	GF improved

Table number 3: Presentation of average values obtained from patients with AH, total- (N^O = 100) Total lipid (TL), total cholesterol (CHT), triglycerides (TG), HDL-ch, LDL-ch

Settings examined	Number tot. of patients	Minimum	Maximum	Average	± *SD*
LT	100	4.90	6.50	6.70	1.40
TG	100	3.40	4.30	3.90 ↑	1.70
CHT	100	5.80	8.40	6.40 ↑	2.08
HDL-ch	100	0.80	1.12	1:02 ↓	0.60
LDL-ch	100	4.30	4.80	4.60 ↑	0.90

From the table number 3 of the patients examined we can see a ***significant increase*** p <0.0001 the fraction of LDL-ch, CHT, and TG while we have a decrease to a statistically significant difference with p <0.0001 for HDL-ch.with reference to lipid values.

Table number 4: Presentation of proteinuria values of 100 patients (55 males, 45 females) obtained from patients before use and after use of ACE inhibitors p r j 20 mg and values control group of 100 healthy individuals.

Proteinuria	Before therapy with ACE inhibitor 20 mg	After 24 months therapy with ACE inhibitors	Group controller - (healthy) N^O- 100
Male N^O = 55	> 3.20 g / 24 h ↑□↑	1.09 g / 24 h ↓□	< 0. 36 g / 24 h
Female N^O = 45	> 3.50 g / 24 h ↑□↑	1. 12g / 24 h ↓□	

Table number 5: Presentation of average values of patients (N^O = 100) for glycemia, urea, uric acid, kreatinine and treatment before starting the arterial hypertension

Settings	Females N^O= 45 (45 %)		Males N^O = 55 (55%)		Total pati-ents N^O= 100	100 (100%)
	Average	± SD	Average	± SD	Average	± SD
Glycemia	6.90	2.60	6.90	3.00	6.40	2.70
Urea	17.30	2.80	17.80	4.02	16.50	3.90
Creatinine	340.40	12.50	290.80	29.70	318.00	13.60
Uric acid	39.500	362.00	420.00	36.4	375.00	39.50

Table number 6: Presentation of average values of patients (N^o = 100) for glycemia, urea, creatinine and uric acid after 24 months of treatment with AH

Settings	Female = 45 (45%)		Males = 55 (55%)		Total = 100 (100%)	
	Average	± SD	Average	± SD	Average	± SD

Glycemia	6.50	1.20	6.70	2.40	6.60	1.40
Urea	18.20	2.40	8.40	4:50	15.30	2.80
Creatinine	340.00	17.00	295.80	23.80	3 58.00	24.00
Uric acid	380 .00	396.80	390.40	4 2.60	390 .80	42.60

From the table itself is noticed a slight increase in nitrogen products (urea, creatinine uric acid but are nonsignifikant and shows a chronic renal failure non progressive .

Table number 7. Separation of patients (n^{O} = 100) examined with AH (Arterial Hypertension) according to the JNC VII (National Joint Committe - 2003).

Grade of Hypertension	Male N^{O} =55	Female N^{O} = 45
AH	20	17
AH first grade mild	1 6	10
AH second grade -average	8	6
AH third grade severe isolated systolic	6	9
AH isolated systolic	5	3

Table number 8. Values obtained for GFR * ml / min / 1.73m ^{2} *according to Cockroft & Gault formula after* treatment with ACE inhibitor for 24 months

The value of AH before therapy	M * N^{O} = 55	F * N^{O} = 45	Therapy 20 mg ACE inhibitor	GFR * before the therapy	GFR values and AH after 24 months use of ACE in the dose of 20 mg
AH high risk 220/120 mmHg	25	18	2x1 plu s diuretic	GFR-19	GFR-28 ↑ TA = 150/95 mmHg
AH very high 180/110 mmHg	14	13	2x1 plus diuretic	GFR- 42	GFR-54 ↑ TA = 140/90 mmHg
AH high 160/100 mmHg.	9	8	2x1	GFR- 65	GFR-76 ↑ TA = 135/90 mmHg
AH mild 145/90 mmHg	7 9	6	1 x1	GFR- 78	GFR-88↑ TA = 135/80 mmHg

M*-male; F*-female; * GFR, Glomerular Filtration Rate

4 DISCUSSIO

Arterial hypertension (AH) still remains the most common cardiovascular event during the CKF. In the terminal phase of uremia comes to hyperhidration, namely comes to the increase of the extracellular fluid volume, which results in AH and edema syndro-me . AH during CKF most commonly is *volume type,* and despite that sometimes it may be as a result of other mechanisms as is during hypernatriemia, renine- angiotensine system disorders aldosteron ect. Prevalence of AH which is a main risk factor of cardiovascular

diseases (CVD) is found in 28% of the adult population. In the United States from AH suffer more than 37-39% while in the world of AH suffer total of 1 billion inhabitants. It is assumed that the prevalence of AH will increase, which will increase the prevalence of CRD, CVD, cerebral insults (36,37, 38). This fundamentaly determines the quantity of loss of kidney tissue and leads to progression of CRD. The volumic type hypertension that most often appears with uremia is associated with cardiovascular complications, hypertensive cardiomyopathy, ventricular hypertrophy. AH damages the kidney causing nephroartherosclerosis which leads up to CRD terminalis when the only medication is HD. AH is therefore present in 80% of cases of patients with CRD. AH incidence varies according to the type of underlying kidney disease. For example patients with chronic glomerulonephritis have higher incidence of AH compared with patients with tubulointerstitial disease (Eg Pyelonephritis). For this reason, to treat AH with good effect we must have in mind the important role of the balance of Na in the pathogenesis of AH. In general the kidney diseases are of associated with the AH, as is glomerulonephritis (GMN), are accom-panied with the retention type of Na , while kidney disease who do not have frequent manifest-tations of AH (tubulointerstitiale disease), are not associated with the retention of Na. At the basic diseases associated with AH there is an inability of kidneys to eliminate the right amount of Na. Symptoms of AH that accompanies CRF do not differ from those of the AH with other etiology. The other symptoms are: enlarged heart, eye with hypertonic lesions (fundus hyper-toniccus) with different degree depending on the duration of AH. Treatment of AH is of great importance to preserve residual renal function and prevent damage of blood vessels. The impor-tant symptoms and complications that appear during CRF is important to note the CHF which is the result of increased intake of salt . This is also proved during the use of HD and ultra filtra-tion (fluid extraction) when the congestive heart failure is improved. AH in patients with renal disturbance occurs to the 80% average of them.This phenomenon is positively correlated with progressive loss of kidney function namely the nefrones. In the manifestation of hypertensive syndrome affect several mechanisms: water, electrolyte disorders and disorders of the ratio between the quantity of sodium and Renine-Angiotensine-Aldosteron system, disorder of the ,, autoregulation " function and peripheral resistence, increased intake of salt, dyslipidemia etc. Malignant AH remains the most commonly complication and is a volumic type, although it could be the hipereninemike origin and mechanism. Diagnosis is based not only on the absolute values of arterial pressure but also on the basis of symptoms its accompanying such as: cefaleja, nausea, vomitusi, confusion, acute left ventricular failure, pulmonary edema, etc. Aforementioned complications grow if AH is associated with hyperlipidemia, diabetes, hyperfibrinemia and MIA syndrome (Malnutritio-Inflamatio-atherosclerosis) . Systolic arterial hypertension is defined when systolic is ≥□140mmHg and diastolic is ≥□90 mmHg. Numerous studies have shown that increased peripheral vascular resistance is closely connected to the renine-angiotensine-aldosterone system and disorders between the concentrations of calcium and parathyroid hormone (HPT) and disorders of the vasodilatators, Quinine, prostaglandines and disorders of the neuromuscular system of the arterioles. There are a large number of studies on the effects and actions of antihypertensive drugs to patients with AH, action and effect of ACE-inhibitors of 10 mg or 20 mg or ACE inhibitors in combination with diuretics however ACE remains as one of favourite medications during AH crysis and treatment of patients with CRD. Drugs of this action groups develop their hypotensive effect by blocking the effect of dipeptide-carboxy-Peptidasis and with increasing levels of obstruction of converting of the Angitensine -I (AI) in Angiotensine-II, slowing the conversion of bradykinine and Other quinine and reduce sympathetic activity thus also reduce and prevent negative effects of hyper-tension on kidney hemodynamically. The role of AH as a risk factor in increasing the rate of progression of CRF, cardiovascular and cerebrovascular accidents in the general population is undoubtful. The duration of hypertension also seems to have a reducing effect on renal function. Besides AH and hypercholesterolemia and unbalanced diabetes appears as a dominant factor and complement of the performance and rapid pace of CRD. In our paper we verified that quality treatment, adequate and in proper time of AH with ACE inhibitors in patients with CRD is closely correlated with the slowdown in the pace of progress of the disease by decreasing proteinuria and side effects of AH related to CVD .

Treatment and medication of AH in patients with CRD should be started in the early stages of disease. Besides drug therapy in preventing and slowing CRD measures like (reducing the consumption of excess fluids and salt , correction of dyslipidaemia, correction of glycose values in diabetics, hypoprotein diet , Ca. restriction) have also an important role. In patients with CRD and AH reducing the intake of proteins helps decreasing in the body substances that come from increased protein catabolism .For this reason daily consumption of proteins should not exceed the capacity of urea excretion from kidney . Daily intake of proteins in grams is calculated by multiplying it three times the value of urea in the urine during 24 hours. During the food consumption in patients with CRD essential amino acid consumption is preferably of whom one third of daily protein should be of animal origin. With the progress of CRD the amount of protein consumed should gradually and continuously redused . Daily protein human consumption must not pass a value of 0.5 - 0.6 g / kg / day. According to the facts and studies about AH treatment of patients with CRF all groups of antihypertensive medications are effective but the last few years most effects in the treatment of AH and less side effects have shown ACE - inhibitors and combined medications that block AT – 1 receptors , angiotensine II [or the so called ARB: losartan, valsartan, candesartan, Eprosartan, Ibersartan, Cossaar, telmisartan), Xalec + HCT (candesartan 8 mg + 12.5 hidrohlorothiazid)] which modify the effect of renine-angiotensine- aldosterone system- (RAAS) who during AH is disturbed (39,40.) There have been many studies on the

positive effects of various antihypertensive medications, their effects and actions and all have witnessed and verified that ACE inhibi - tors-Angiotenzin-Converting-Enzyme are medications most preferred for the treatment of renal origin AH and patients with C RD.

Therefore we can conclude that treatment-Decrease and normalization of arterial pressure significantly affects the reducing of their effects on the cardiovascular system, renal and ACE-inhibitors have minimal side effects while their advantages are that this group of drugs may be combined with calcium blocker and a large number of diuretics. In the market there are medications ACE inhibitors combined with diuretics whose priority is that they are used once a day and are highly effective in reducing arterial pressure. Different ways AH correction and crises in patients with CRF constitute the most important part of CRD progression rhythm where important role has the treatment and prevention of disease. The role of AH and his inadequate treatment in patients with CRD risk in the manifestation of CVD and acceleration of the pace of renal disease is undeniable (41.42)

5 CONCLUSION

Cardiovascular diseases (heart attack, CVD-, ventricular hypertrophy, congestive heart failure, cerebrovascular stroke) in epidemic form are manifested in patients with AH, hypercholesterolemia and CRD and are five times more frequent than people with gender and age the same general population which suffers from AH but are not with CRD - Fragmingham study 43). Common factors of cardiovascular disease in patients with CRD compared with general population are: age, sex, hypertension, diabetes , consumption of tobacco, hyperlipide-mia, apolipoproteinemy disorders while as specific factors are : hyperparathyroidism secondary anemia, hyperhomocysteinemia, hyperfibrinemia, oxidative stress, malnutrition, trombogenic factors, and chronic inflammation . Higher mortality in patients with CRD mos commonly happ-ens from ischemic cardiomyopathy coupled with hypertension ((44,45,46), ischemic cardio-myopathies is explicitly linked to: old age, male gender, AH, diabetes mellitus, tobacco, anemia, oxidative stress, dyslipidemia and hyperhomocysteinemia (47, 48). Uremic cardiomyopathy is closely associated with the action of AH, the actions of uremic toxins, proinflam-matory cyto-kines, secondary hyperparatyroidism, and MIA syndrome (Malnutritio-Inflamatio-Athero-sclersis (49, 50, 51, 52.53). It is verified that in patients with uraemia, the occurrence of myocardial infarction is 10 times more frequent than in patients with other primary disease (54.55, 56.) Statistical studies published in the US in 1997 on the occurrence of mortality in patients with terminal chronic renal failure treated with HD showed that 53% of mortality is caused due to cardiovascular disease, 16% due to infections, 4% of carcinomas and 27% from other causes in patients up to age 64 years (57.58)

REFERENCES

1. Chan MK, Varghese Z, Moorhead JF. Lipid abnormalities in uremia, dialysis and transplantation. *Kidney Int. 1981; (19): 119- 625.*
2. AM Sinclair, CG Isles, I. Brown, H. Cameron, Murray GD, and JW Robertson, "Secondary hypertension in a Blood Pressure Clinic," Archives of Internal Medicine, vol. 147, pp. 1289-1293, 1987.
3. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY and, "Chronic Kidney Disease and the Risks of death, cardiovascular events, and hospitalization," New England Journal of Medicine, vol. 351, no. 13, pp. 1296-1305, 2004.
4. SS Anavekar, JJV McMurray, Velazquez EJ et al., "Relation Between renal dysfunction and cardiovascular Outcomes After myocardial infarction," New England Journal of Medicine, vol. 351, no. 13, pp. 1285-1295, 2004.
5. AS Levey, J. Coresh, K. Bolton et al., "K / doqi clinical practice guidelines for Chronic Kidney Disease: Evaluation, Classification, and stratification," American Journal of Kidney Diseases, vol. 39, no. 2, pp. S1-S266, 2002.
6. J. Coresh, E. Cypress, LA Stevens et al., "Prevalence of Chronic Kidney Disease in the United States," Journal of the American Medical Association, vol. 298, no. 17, pp. 2038-2047, 2007.

7. Defeyter PJ, Vos P: Progressio and regression of the arterosclerotic plaque Eur. *Heart J, 16 (suppl. I): 26 to 30.1995.*

8. JJ Snyder and AJ Collins, "KDOQI hypertension, dyslipidemia, and diabetes care guidelines and care Current Patterns CKD in the United States Population: National Health and Nutrition Examination Survey 1999-2004," American Journal of Nephrology, vol. 30, no. 1, pp. 44-54, 2009.
9. NO SARAFIDIS, S. Li, SC Chen et al., "Hypertension Awareness, Treatment, and Control in Chronic Kidney Disease," American Journal of Medicine, vol. 121, no. 4, pp. 332-340, 2008.
10. J. Guyton New advences in 1 actor 1 nsive. *Am. J. Card. 1998; vol.82 12A*
11. Sommer JB, Aitken JM et. Al. Lipoprotein lipids in Chronic renal failure and hemodialysis: The influence of etiology and implification of atherogenesis *. Atherosclerosis 34: 353.1979.*

12. Huttenen JK, Pastemack A et al. Lipoprotein metabolism in patients with Chronic uremia. *Acta Med SCANDIA 204-211; 1978.*

13. Castelli: the Framingham heart study update: cholesterol, tryglicerides, lipoproteins and risk of coronary heart Disease, *1998* .

14. WOD D. *European and Ammerican revommandation for CHD Prevention 19 (suppl A) A 12 EUR: Heart J, 1998.*

15 .. F. Turnbull, "Effects of Different Blood-Pressure-lowering regimens on major cardiovascular events: Results of

prospectively-Designed overviews of 1 actor 1 nsi Trials," The Lancet, vol. 362, no. 9395, pp. 1527-1535, 2003.
16. PA SARAFIDIS, S. Li, SC Chen et al., "Hypertension Awareness, Treatment, and Control in Chronic Kidney Disease," American Journal of Medicine, vol. 121, no. 4, pp. 332-340, 2008].
17 PA SARAFIDIS, S. Li, SC Chen et al., "Hypertension Awareness, Treatment, and Control in Chronic Kidney Disease," American Journal of Medicine, vol. 121, no. 4, pp. 332-340, 2008).
18. ND Vaziri, "Roles of oxidative stress and antioxidant therapy in Chronic Kidney Disease and hypertension," Current Opinion in Nephrology and hypertension, vol. 13, no. 1, pp. 93-99, 2004.
19. M. AB Chapman, A. Johnson, PA Gabow, and RW Schrier, "The renin-angiotensin-aldosterone system and autosomal dominant polycystic Kidney Disease," New England Journal of Medicine, vol. 323, no. 16, pp. 1091-1096, 1990.
20. E. Kohan, "Endothelins in the normal and diseased Kidney," American Journal of Kidney Diseases, vol. 29, no. 1, pp. 2-26, 1997.
21. MP Blaustein, J. Zhang, L. Chen et al., "The pump, the exchanger, and endogenous ouabain: Mechanisms That link signaling salt retention to hypertension," hypertension, vol. 53, no. 2, pp. 291-298, 2009.
22. ND Vaziri, "Effect of Chronic renal failure on ETHYLENE Oxide metabolism," American Journal of Kidney Diseases, vol. 38, no. 4, pp. S74-S79, 2001.
23. AC Guyton, TG Coleman, DB Young, TE Lohmeier, and JW DeClue, "Salt balance and long-term Blood Pressure Control," Annual Review of Medicine, vol. 31, pp. 15-27, 1980.
24. JE Hall, "The Kidney, hypertension, and obesity," hypertension, vol. 41, no. 3, pp. 625-633, 2003.
25. G. Keller, G. Zimmer, G. Mall, Ritz E., and K. Amann, "Nephron number in patients with primary hypertension," New England Journal of Medicine, vol. 348, no. 2, pp. 101-108, 2003.
26, E. Saad, B. Charr, and DSC Raj, "hypertension control with daily dialysis," Seminars in Dialysis, vol. 17, no. 4, pp. 295-298, 2004.
27. Al Günal, S. Duman, M. Özkahya et al., "Strict control volume normalizes hypertension in peritoneal dialysis patients," American Journal of Kidney Diseases, vol. 37, no. 3, pp. 588-593, 2001.
28.. Vasavada N. and R. Agarwal, "Rule of Excess volumes in the pathophysiology of hypertension in Chronic Kidney Disease," Kidney International, Vol. 64, no. 5, pp. 1772-1779, 2003.
29. EC Kim, G. Onesti, AB Schwartz, JL Chinitz, and C. Swartz, "Hemodynamics of hypertension in end-stage renal Chronic Disease," Circulation, vol. 46, no. 3, pp. 456-464, 1972.
30. RA Augustyniak, M. Tuncel, W. Zhang, RD Toto, and RG Victor, "Sympathetic overactivity or a Cause of hypertension in Chronic renal failure," Journal of hypertension, vol. 20, no. 1, pp. 3-9, 2002.
31. Keith DS, Nichols GA, Gullion CM, JB Brown, and DH Smith, "longitudinal follow-up and Outcomes Among a Population with Chronic Kidney Disease in a Large Managed Care Organization," Archives of Internal Medicine, vol. 164, no. 6, pp. 659-663, 2004.
32. Chobanian AV, Bakris GL, Black HR et al., "The SEVENTH Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report," Journal of the American Medical Association, vol. 289, no. 19, pp. 2560-2572, 2003.
33. Levey AS, MV Rocco, S. Anderson et al., "K / doqi clinical practice guidelines on hypertension and Antihypertensive Agents in Chronic Kidney Disease," American Journal of Kidney Diseases, vol. 43, no. 5, pp. S1-S290, 2004].
34. DE Weiner, H. Tighiouart, AS Levey et al., "Lowest systolic Blood Pressure is Associated with stroke in Stages 3 to 4 Chronic Kidney Disease," Journal of the American Society of Nephrology, vol. 18, no. 3, pp. 960-966, 2007. ·
35. .R. Kunz, C. Friedrich, M. Wolbers, and JFE Mann, "Meta-Analysis: effect of monotherapy and Combination therapy with inhibitors of the renin-angiotensin system on proteinuria in renal Disease," Annals of Internal Medicine, vol. 148, no. 1, pp. 30-48, 2008.
36. AS Levey, J. Coresh, K. Bolton et al., "K / doqi clinical practice guidelines for Chronic Kidney Disease: Evaluation, Classification, and stratification," American Journal of Kidney Diseases, vol. 39, no. 2, pp. S1-S266, 2002.
37. Hajjar I, Kotchen TA. Trends in 1 actor 1 nsi, Awareness, Treatment,
and control of hypertension in the United States 1988-2000. JAMA 2003; 290: 199-206.
38. Fogo AB. Progressio versus Chronic Kidney Disease regression of Nephrol Dial Transplant 2006; 21 (2): 281-4.
39. FM Tedla[1] et al.Chronic Kidney Disease hypertension: Navigating the Evidence. International Journal of hypertension, Volume 2011 (14-02-2011), Article ID 132405, 9 pages.
40. Measures Blood Pressure and Risk of Chronic Kidney Disease in men. Nephrol diile Transplant.2008; 23-1246-1251.).
41. Essential hypertension, Progressive Renal Disease, and Uric Acid: A pathogenetic Link? J Am.Soc. Nephrol.2005; 16: 1909-1919;
42. hypertensive nephrosclerosis-a Cause of End-Stage Renal Disease? Nephrol Dial Transplant. 2000; 15: 1515-1517.
43. Levey AS, Eknoyan G. Cardiovascular Disease in Chronic Renal Disease. *Nephrol Dial Transplant. 1999; 14: 828-33* .
44. Parfrey PS, Foley RN. Risk Factors for cardiac dysfunction in dialysis patients: implications for patient care. *Semin Dial. 1997; 10: 137-41* .
45. Brenner RM, EM Wrona. The epidemic of cardiovascular Disease in End-Stage Renal Disease. *Curr Opin Nephrol Hypertens. 1999; 8: 365-9.*

46. London GM, Drueke TB. Atherosclerosis and arteriosclerosis in Chronic renal failure. *Kidney Int. 1997; 51: 1678-95.*
47. Parfrey PS, Foley RN. The clinical cardiac Epidemiology of Disease in Chronic renal failure . *J Am Soc Nephrol. 1999; 10: 1606-15.*
48. Parfrey PS, Harnett JD, Foley RN. Heart failure and ischemic Heart Disease in Chronic uremia. *Curr Opin Nephrol Hyperten. 1995; 4: 105-10* .
49. Parfrey PS, Foley RN, Harnett JD, et al. Outcome and Risk Factors of ischemic diseas in Chronic uremia. *Kidney Int. 1996; 49: 1428-34* .
50. Foley RN, Parfrey PS. Cardiovascular Disease and Mortality in ESRD. *J Nephrol. 1998; 11: 239-45.*
51. Wheeler DC. Cardiovascular Disease in patients with Chronic renal failure. *Lancet.1996; 348: 1673-4* .
52. Wizemann V. Coronary artery Disease in dialysis patients. *Nephron. 1996; 74: 642-51.*
53. Locatelli F, Del Vecchio L, Manzoni C. Morbidity and Mortality on Maintenance Haemodialysis. *contrib Nephrol. 1998; 124: 166-89.* 54,55,56,57.58.59)
54. Lindner A, B Charr, Sherard D, Scribner B. ACCELERATED atherosclerosis in prolonged Maintenance hemodialysis. *N Engl J Med. 1974; 290: 697-701.*
55. Rostang SG, Gretes JC et al. Ishemic Heart Disease in patients with uremia undergoing hemodialysis Maintenance. *Kidney Int.1979; 16: 600-11*
56. Ritz E, Deppisch R, Stier E, Hansch G. Atherogenesis and cardiac death: are broke Related to dialysis procedure and bioincompatibility? *Nephrol Dial Transplant. 1994; 9: 165-72* .
57. USRDS 1999 Annual Data Report. *Am J Kidney Dis. 1999; 34: S20-S152.*
58. Attman YES, Alaupovic P, Tavella M, Knight-Gibson C. abnormal lipid and apolipoprotein composition of Major density lipoprotein classes in patients with Chronic renal failure. *Nephrol Dial Transplant. 1996; 11: 63-9* .

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