



Therapeutic strategies in high blood pressure in patients with chronic kidney disease

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Received: November 11, 2017, Accepted: December 4, 2017

Abstract

The decline in renal function is commonly associated with increased blood pressure and the therapy could rise several problems. In the present study we proposed to study the therapeutic strategies and types of antihypertensive medication used in hypertensive patients with CKD. We studied a group of 30 patients admitted to the Nephrology Department of the Arad County Emergency Clinical Hospital in 2015 for the decompensation of a chronic kidney disease. Patients were classified according to the severity of CKD using the KDIGO classification [6], glomerular filtration rate (GFR) was calculated using the Cockcroft-Gault formula, and we analyzed the types of antihypertensive drugs administered, depending on the associated diseases. Patients had renal impairment of varying degrees, with decrease in creatinine clearance below 60 ml/min, most of them being in the dialysis stage. Analyzing the antihypertension medication used in therapy, we found drugs from almost all classes of antihypertensive drugs. The main classes of antihypertensive used in the study group are: beta blockers: 20/30, diuretic 15/30, ACEI: 15/30, ARBs: 12/30, calcium channel blockers: 10/30. We have to remark that the beta-blockers were largely used in the antihypertensive combination.

Keywords: antihypertensive drugs, CKD

Introduction

Chronic kidney disease (CKD) is not a rare disease, in our country the prevalence in the general population is about 7.3%, but it increases every 10 years by 50% [1].

Hypertension is present in over 80% of patients with chronic kidney disease in advanced disease states, most of these patients having hypertension before glomerular filtration rate reduction [2]. The essential factor involved in the pathogenesis of hypertension is hydrosaline retention and hypervolemia, evidence being the normalization of blood pressure values in over 80% of hypertensives after adequate dialysis [3]. A percentage of approximately 20% of patients do not respond to dialysis because there is another mechanism involved in the pathogenesis of hypertension,

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namely the activation of the renin-angiotensin system. The decline in renal function is commonly associated with increased blood pressure, and sustained increase in blood pressure accelerate the progression of renal function decline [4]. In the present study we proposed to study the therapeutic strategies and types of antihypertensive medication used in hypertensive patients with CKD.

Material and method

We conducted a retrospective study including a group of 30 patients admitted to the Nephrology Department of the Arad County Emergency Clinical Hospital in 2016 for the decompensation of a chronic kidney disease.

All patients were clinically examined, BMI was calculated and the following laboratory tests were performed: haemoleucogram, VSH, fibrinogen, PCR, glycemia, urea, creatinine, uric acid, calcemia, alkaline phosphatase, total protein, serum ionogram, Astrup parameters.

Patients were classified according to the severity of CKD using the KDIGO classification [6].

EKGs were also performed, glomerular filtration rate (GFR) was calculated using the Cockcroft-Gault formula, and we analyzed the types of antihypertensive drugs administered, depending on the associated diseases.

Results

The distribution of hypertensive patients studied by age groups is shown in Table 1.

Patients had renal impairment of varying degrees, with decrease in creatinine clearance below 60 ml/min, most of them being in the dialysis stage (Table 2)

In correlation with the advanced stage of CKD, patients presented clinical signs of uremia, pruritus, tegumentary scarring lesions, denutrition, signs of bone impairment or metabolic acidosis (polypnea, Kusmaul respiration) hyperkalaemia, anemia, as seen in the table 3, to which have been added signs of cardiovascular disease such as: hypertension, left ventricular hypertrophy, cardiomegaly.

Analyzing the antihypertensive medication used in therapy, we found drugs from almost all classes of an-

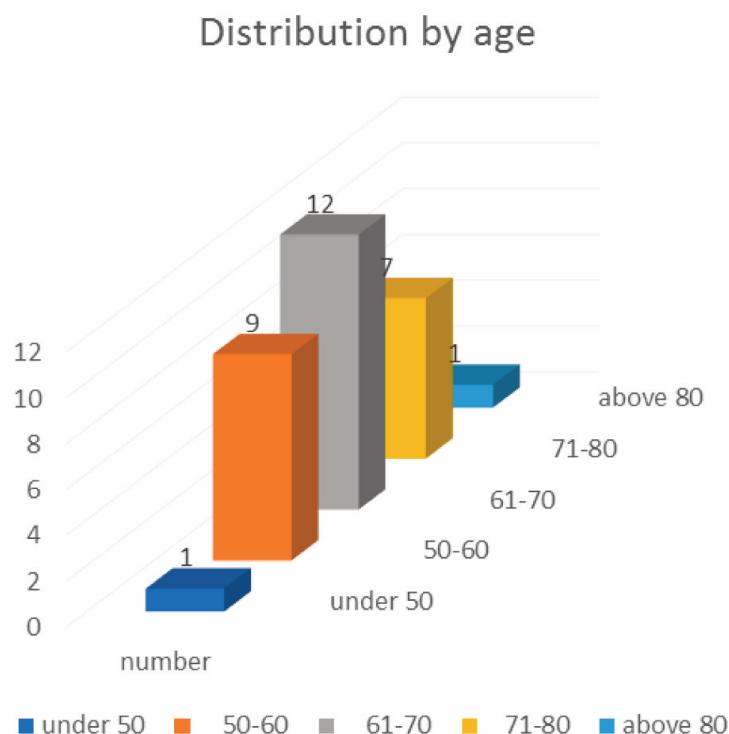


Table 1. Distribution by age.

GFR categories of CKD

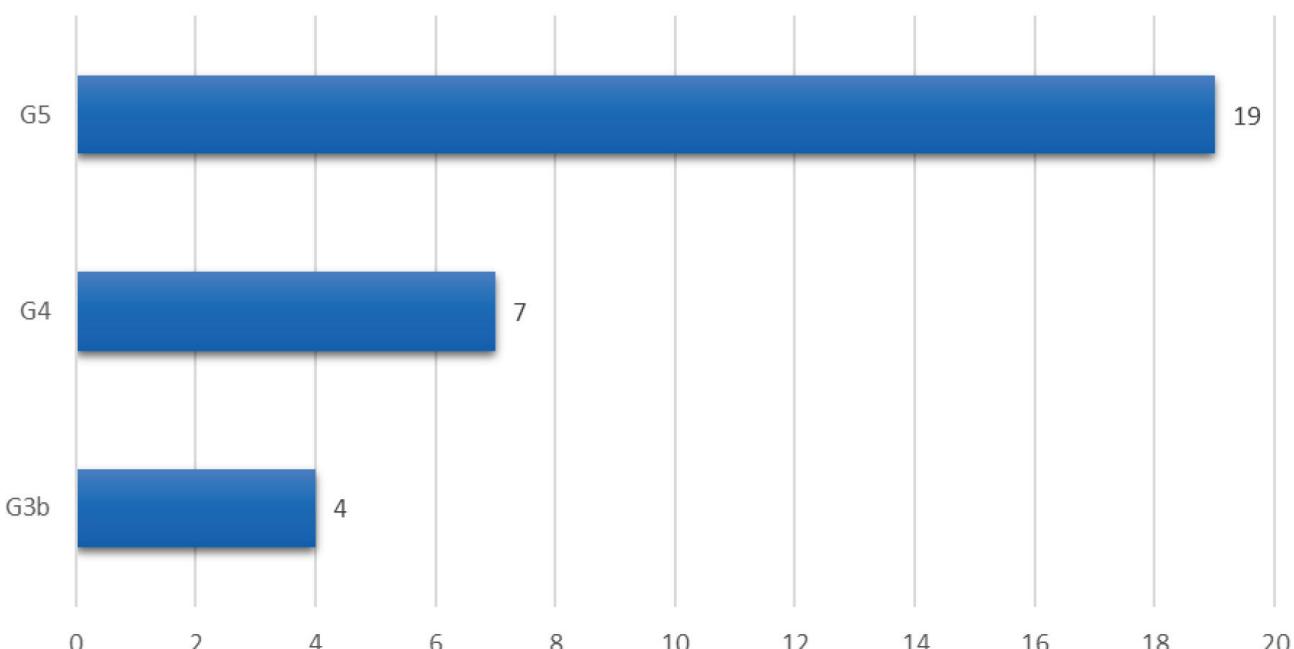


Table 2. GFR categories using KDIGO classification.

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Discussions

The therapeutic strategy and antihypertensive classes used in the treatment of hypertension depend on the CKD stage. The therapeutic target recommended by KDIGO and KDOQI is to maintain blood pressure values below 130/80 mmHg for patients with CKD with or without diabetes, regardless of the degree of proteinuria [3]

According to the Eight Joint National Committee published in 2014, a less aggressive target value of less than 140/90mmHg is recommended in patients under 60 years of age with diabetes and CKD and below 150/90 in patients over 60 years of age or black [3].

CKD and hypertension (HTN) are closely associated with a cause-effect relationship.

CKD affects the population irrespective of age, the majority being in the group of 61-70 years, as also found in our study.

In our group, the majority of patients had a GFR <15 ml/ min/1.73 m² being in stage G5, respectively 64% (19/30), most of them being in the hemodialysis program (Table 2).

Stage G4 represents 23% of patients (7/30) with a GFR of 15-29 ml/ min/1.73 m², and in stage G3b 13% (4/30) with a GFR between 30-44 ml/ min/1.73m².

As far as clinical manifestations are concerned, the damage to all organs and systems is evident, which characterizes chronic kidney disease. (Table 3), with a special focus on cardiovascular diseases.

The presence of hyperstension is seen in over 90% (25/30) of patients studied with advanced kidney disease. We did not notice significant therapeutic differences in relation to the etiology of renal failure, because it is difficult to establish the etiology of high blood pressure in the advanced stages of chronic kidney disease.

Appropriate treatment of hypertension in patients with CKD has a double benefit: reduction in the rate of CKD progression and reduction of cardiovascular risk.

The main classes of antihypertensive used in the study group are: beta blockers: 20/30, diuretic 15/30, ACEI: 15/30, ARBs: 12/30, calcium channel blockers: 10/30.

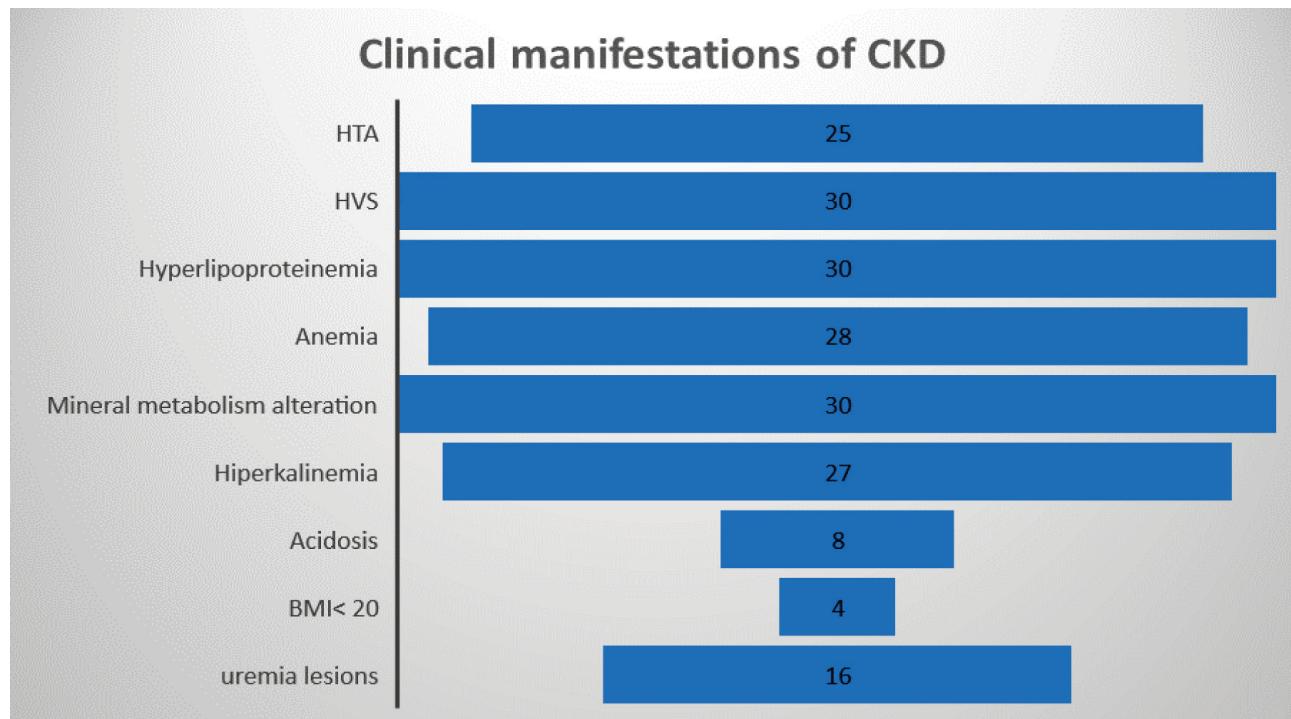


Table 3. Clinical manifestations of CKD.

Although the blood pressure reduction obviously achieves renal and cardiovascular protection, the optimal values are still controversial. There are few studies

that included hypertensive patients with CKD. In the AASK study, calcium channel blockers such as amlodipine compared with angiotensin converting enzyme

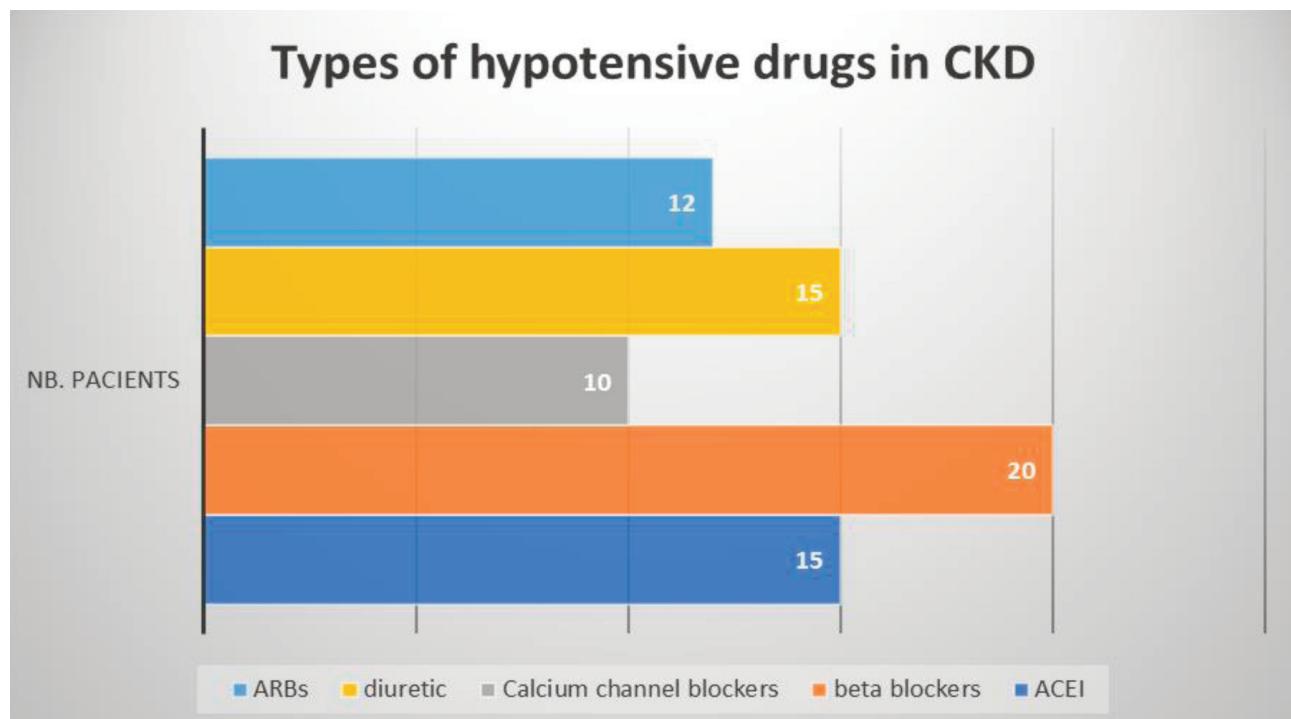


Table 4 Classes of antihypertensive drugs used in patients with chronic kidney disease.

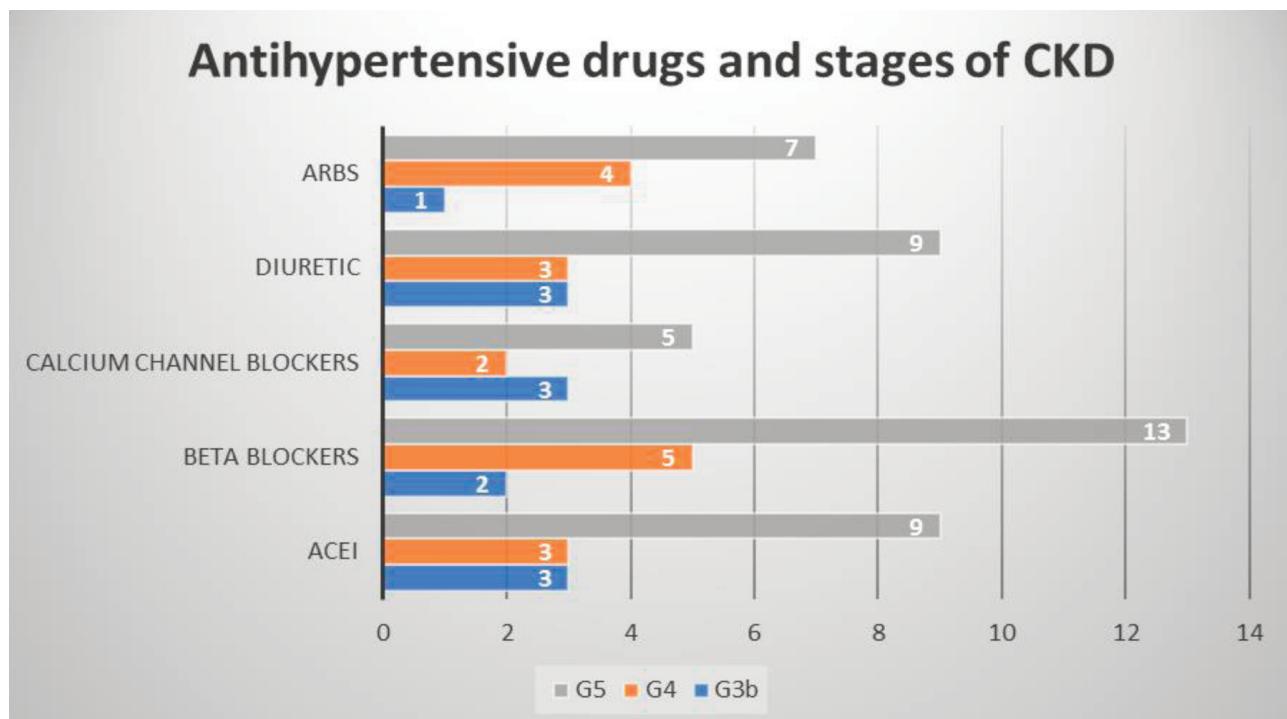


Table 5 Antihypertensive drugs and stages of CKD.

(ramipril) and beta blockers (metoprolol) have been shown to reduce the rate of renal failure progression, with ramipril having the best slowing effect in GFR decline[8].

However, observational studies have shown that lowering the blood pressure below 120 mmHg may increase the risk of stroke or death [9].

In ESC / ESH 2013 [10], it is recommended to initiate antihypertensive therapy with a diuretic to which one or more other antihypertensive of the other classes may be added: converting enzyme inhibitors, ARBs, beta blockers or calcium channel blockers.

Unfortunately, in patients with renal impairment, the use of thiazides or thiazide-like diuretics is often ineffective, in case of creatinine clearance below 30 ml/min, and excessive induced salt depletion can trigger a vasoconstrictor mechanism and activation of the RAA system. That's why loop diuretics remain the most used, with ionogram control and several doses daily.

Beta blockers reduce cardiovascular risk, inhibit renin secretion, but often reduce cardiac output, vasodilating beta blockers such as carvedilol and nebivolol being preferred in doses heart rate dependent.

Calcium channel blockers (CCB) are effective in lowering blood pressure, have antianginal effects, but

non-dihydropyridine drugs increase variability in blood pressure values, an important risk factor for stroke, therefore dihydropyridines (amlodipine and nifedipine retard) are preferred.

Blocking of the Renin Angiotensin System with Angiotensin-Converting Enzyme Inhibitors(ACEI) or Angiotensin Receptor Blockers(ARBs) has been shown to be an effective therapy, reducing CKD progression and death rate.

However, the risk of hyperkalaemia in patients with CKD, the risk of angioedema for ACEI and the potential for fetal malformations should be considered.

In European guidelines, the most recommended classes of antihypertensive agents are ACE inhibitors, ARBs, CCB, diuretics and beta-blockers.

In the NICE guide a different tactic was adopted [11], it is recommended to initiate treatment with ACEI or thiazide in caucasian patients younger than 55 years of age, and for black people is recommended CCB as initial therapy.

Obtaining target blood pressure in hypertensive patients with CKD is preferably done with agents that reduce proteinuria [12].

Fixed combinations appear to be also one choice for patients with CKD, regardless of etiology, but as

shown by the ONTARGET and ALTITUDE studies, the double blocking of the renin angiotensin system with an ACEI plus ARB is not much effective than monotherapy, adding greater risks to adverse effects.

In patients with resistant hypertension, which associates over 3 antihypertensive drugs, the hydroelectrolyte balance and the possibility of excess salt and water should be considered.

Conclusions

In conclusion, most hypertensive patients with CKD require long-term therapy

which will significantly reduce the risk of cardiovascular events and slow the progress of renal impairment, but this treatment should be closely monitored due to the numerous complications or side effects that may occur in patients with advanced kidney disease

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