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AN OVERVIEW OF HYPERTENSION IN CHRONIC KIDNEY DISEASE

Anjana Sri Satya Veeravalli*[1], Kuchibhatla Lakshmi Vardhani[1], Amrutha Jampana[1], Beg Karishma[1], Natta Prathibha[2] and Kantamaneni Padmalatha[3]

[1]Pharm D V Year, Department of Pharmacy Practice, Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada - 521 108, Andhra Pradesh, India.

[2]Assistant Professor, Department of Pharmacy Practice, Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada - 521 108, Andhra Pradesh, India.

[3]Professor and Principal, Department of Pharmacology, Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada - 521 108, Andhra Pradesh, India.

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***Corresponding Author**
Anjana Sri Satya Veeravalli
Pharm D V Year, Department of Pharmacy Practice, Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada - 521 108, Andhra Pradesh, India.

ABSTRACT

Chronic kidney disease (CKD) and hypertension are closely related pathophysiological conditions; as a result, hypertension can deteriorate kidney function, and a progressive reduction in renal function can in turn, worsen blood pressure regulation. The prevalence of hypertensive end-stage renal disease keeps rising yearly. Controlling systolic and diastolic hypertension is crucial to lowering this incidence. The prevalence ranges from 60-90% depending on the stage of CKD and its causes. The mechanism of hypertension in CKD includes volume overload, sympathetic dysfunction, and alteration in hormonal systems that regulate blood pressure. This review presents information concerning the pathophysiological mechanism of hypertensive renal disease, the role of salt restriction, and management issues in HTN in patients with CKD including the timing of anti-hypertensive medication dosing, and blood pressure targets. Addressing this salt sensitivity is critical for the management of HTN in CKD whenever possible ACE inhibitors should be part of the treatment. Since these drugs are reno-protective beyond their antihypertensive effect in certain strategies for delaying kidney progression. In order to achieve the target blood pressure levels advised by worldwide recommendations, numerous levels of care, including a number of pharmacological and behavioural changes, are

frequently necessary. The residual cardiovascular risk is substantial even when blood pressure is properly controlled. With the addition of fresh information from clinical research, we will examine both the traditional and novel features of managing hypertension in CKD in the current review.

KEYWORDS: Hypertension, chronic kidney disease, ambulatory blood pressure monitoring, achieving blood pressure, salt restriction.

INTRODUCTION

HTN is the most common comorbidity in patients with CKD, affecting 67-92% of patients. The prevalence of HTN increases with declining renal function. Control of HTN is a major priority in the management of CKD and represents an important modifiable factor in slowing the further loss of kidney function. Elevated blood pressure can occur as a result of CKD but is also a potent risk factor for CKD progression. HTN is common in patients with CKD.[1] The prevalence ranges from 60-90% depending on the stage of CKD and its causes. The mechanism of hypertension in CKD includes volume overload, sympathetic dysfunction, and alteration in hormonal systems that regulate blood pressure. HTN remains a leading attributed cause of end-stage kidney disease (ESKD) in the United States. Uncontrolled hypertension is also associated with a higher risk of cardiovascular morbidity and mortality.[2]

CKD is a global health problem representing the third fastest growing cause of death globally with an estimated prevalence of 8-16% in occidental countries. CKD is defined by the presence of kidney damage or decreased kidney function with an estimated glomerular filtration rate (eGFR) <60ml/min / 1.73m2 for at least 3 months irrespective of the cause.[3]

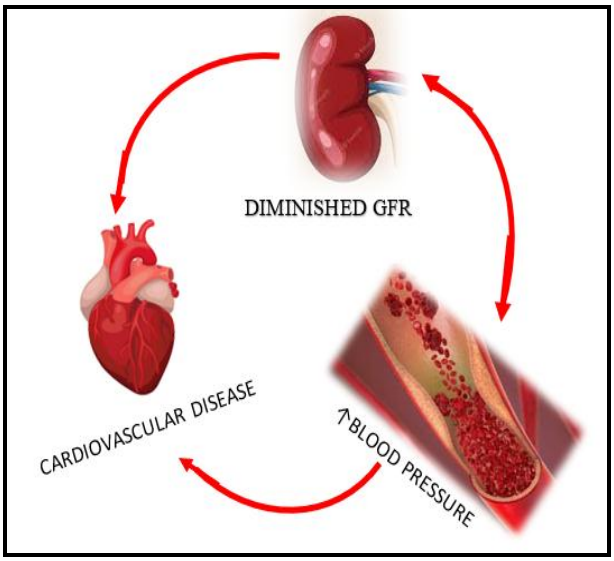
The rise in the incidence of CKD is attributed to an aging population and an increase in hypertension (HTN), diabetes, and obesity within the US population. CKD is associated with a host of complications including electrolyte imbalances, mineral and bone disorders, anemia, dyslipidemia, and HTN. It is well known that CKD is a risk factor for cardiovascular disease (CVD) and that a reduced GFR and albuminuria are independently associated with an increase in cardiovascular and all-cause mortality.[4]

Meanwhile, progressive renal disease can exacerbate uncontrolled HTN due to volume expansion and increased systemic vascular resistance. Multiple guidelines discuss the importance of lowering blood pressure to slow the progression of renal disease and reduce

cardiovascular morbidity and mortality. However, to achieve and maintain adequate BP control most patients with CKD require a combination of anti-hypertensive agents often up to three or four medication classes may need to be employed.[5]

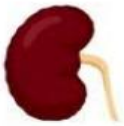
PATHOPHYSIOLOGY

Hypertension is a major cause of CKD due to the detrimental effects of elevated blood pressure on the renal vasculature. Long-term uncontrolled hypertension leads to increased intraglomerular pressure that impairs glomerular filtration. Damage to the glomerulus leads to increased protein filtration, resulting in abnormal protein levels in the urine. Microalbuminuria is the presence of small amounts of albumin in the urine and is often the first sign of CKD. Proteinuria (protein-to-creatinine ratio ≥ 200 mg/g) develops in progressive chronic kidney disease and is associated with a poor prognosis for both renal and cardiovascular disease. As mentioned above, the relationship between CKD and HTN is cyclical, and CKD can contribute to or cause HTN. Elevated blood pressure damages blood vessels throughout the body, not just the kidneys. This damage affects the kidneys' ability to filter fluid and waste products from the blood, increasing the amount of fluid in the blood and increasing blood pressure.[6]



Pathophysiology of CKD in hypertension.

STAGES OF CKD

Stages of CKD	STAGE 1	STAGE 2	STAGE 3	STAGE 4	STAGE 5
eGFR	90 or higher	60-89	45-59	15-29	<15
Level of Kidney damage					
Levels of CKD	Normal function	Mild loss of function	Moderate loss of function	Severe loss of function	Kidney failure

GRADES OF HYPERTENSION

CATEGORY	SYSTOLIC (mmHg)	DIASTOLIC (mmHg)
Optimal	<120	<80
Normal	120-129	80-84
High Normal	130-139	85-89
Grade 1 Hypertension	140-149	90-99
Grade 2 Hypertension	160-179	100-109
Grade 3 Hypertension	>180	>110
Isolated Systolic Hypertension	>140	<90

PROPER BP MEASUREMENT TECHNIQUE

"STANDARDIZED" OFFICE BLOOD PRESSURE MEASUREMENT

Routine in-office BP measurements served as the traditional method for hypertension diagnosis and treatment decisions until recent recommendations favoured the implementation of standardized practices. [(7)] Standardized OBP measurements should include:

(1) Appropriate cuff size (bladder should encircle 80% of the bare arm)

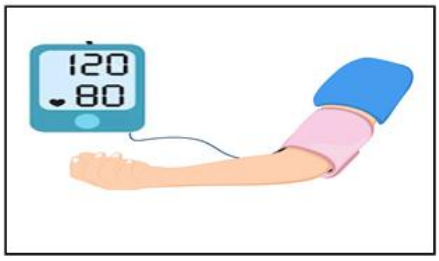
(2) Proper positioning (patient's arm should be supported at the level of the heart while seated with back supported, legs uncrossed, and both feet flat on the floor)

(3) Patient preparation (patient should relax for 5 minutes, abstain from caffeine, exercise, and smoking in the preceding 30 minutes, and ensure his or her bladder is empty

(4) Multiple measurements 2 readings at least 1-2 minutes apart) in both arms while using a validated device that is appropriately calibrated, importantly, these measurements should be done without the white coat provider being in the room.[8]

Many studies have demonstrated the lack of correlation between routine and standardized OBP measurement.[9] Compared routine versus standardized BP measurements in 275 participants from the Systolic Blood Pressure Intervention Trial (SPRINT). The mean systolic blood pressure (SBP) and diastolic blood pressures (DBP) in routine office measurements were 12.7 and 12 mm Hg higher, respectively than the standardized measurements performed on the same day. Additionally, research indicates that medical staff are inadequately competent to follow standardized blood pressure monitoring protocols and require regular retraining.[10]

AMBULATORY BLOOD PRESSURE MONITORING



STANDARDIZED BLOOD PRESSURE MONITORING

Ambulatory blood pressure monitoring

Due to the stronger association between blood pressure measurements from ABPM and cardiovascular and renal outcomes, 24-hr ABPM has been considered the preferred metric of blood pressure in both the general population and patients with CKD, 24-hour blood pressure involves wearing an appropriately sized blood pressure cuff 24 hours a day and taking measurements every 15-20 minutes during the day and every 30-60 minutes during sleep.[11] Therefore, the advantage of ABPM is that it provides adequate nocturnal physiological preoccupation (blood pressure must drop >10% during sleep) and intra-sleep measurements that allow assessment of blood pressure variability. The presence of masked hypertension (defined as normal BPS in the office but elevated BPS outside the office) is associated with an increased risk of cardiovascular disease, with and without CKD.[12] Both nocturnal hypertension and non-immersion conditions are also associated.

SYMPTOMS

Symptoms of CKD with high blood pressure include

- Edema of the legs, feet, ankles, hands, or face
- Muscle cramps

- Loss of appetite
- Nausea and vomiting
- Headache and difficulty concentrating
- Increased blood pressure
- Excessive urination
- Drowsiness and difficulty sleeping
- Itching associated with dry and darkened skin
- Chest pain
- Shortness of breath

BLOOD PRESSURE TARGETS IN CKD

Blood Pressure goals in CKD-National Kidney Foundation focuses on discontinuation of BP threshold Fuchs treatment, but overtreatment of HIN in CKD potency can be harmful. In his cohort of more than 65,650,000 Amerson veterans with chronic kidney disease, he had both extreme hypertension and hypotension associated with improved Mook, with the high polarity of pork pressure having the highest mortality rate with dready. Blood that is too diastolic may not be beneficial.[13]

GOALS OF THERAPY

Non-diabetic and diabetic CKD patients should have a target blood pressure of less than 130/80 mmHg.[14] Ultimately, the rationale for lowering blood pressure in all CKD patients is to reduce both renal and cardiovascular morbidity and mortality. Maintaining blood pressure control and minimizing proteinuria in CKD and HTN patients is critical to prevent the progression of kidney disease and the onset or exacerbation of CVD.[15]

Recent literature suggests that BP targets in diabetic and non-diabetic CKD may need to be individualized based on the presence of proteinuria. Several studies have compared achieving a blood pressure target of <130/80 mmHg.[16] with reducing blood pressure to <140/90 mmHg for cardiovascular or renal outcomes in diabetic and non-diabetic patients with CKD, failing to demonstrate a reduction in the outcome. However, patients with proteinuria are less likely to experience worsening renal function, renal failure, or death if hypotension goals are achieved. Future guidelines state that the goal may be to reduce blood pressure by more than half.[17]

TREATMENT OF HYPERTENSION: PHARMACOLOGICAL TREATMENT

Drugs that not only lower blood pressure but also reduce proteinuria are recommended as first-line therapy for most CKD and HTN patients.[18] Agents that target the renin-angiotensin-aldosterone system ("RAAS"), such as considered. Kidney disease with or without diabetes and with or without proteinuria.[19]

ARB'S VS ACE INHIBITORS

Studies have shown that antihypertensive drugs that target the renin-angiotensin system are more effective than other drugs in preventing kidney function decline, even when similar blood pressure goals are achieved.[20] Based on these results, guidelines recommend ACE inhibitor or ARB therapy as first-line treatment for patients with diabetes or non-diabetic renal disease, HTN, and proteinuria. and ARBs are equally effective in lowering blood pressure and reducing proteinuria.[21]

These results were determined in patients with HTN and were not in patients with additional comorbidities such as CKD, which did not apply. Therefore, the choice of any given drug depends on patient-specific factors such as potential side effects and cost. Concomitant use of ACE inhibitors and ARBs has been shown to worsen renal function and is not recommended. Combination therapy with ACE inhibitors and ARBs did not reduce cardiovascular mortality or morbidity compared with ACE inhibitors alone.[22]

ACE Inhibitors and ARBs are generally well tolerated. ACE inhibitors can cause a dry cough, which unfortunately often requires a change in treatment. ARBs are not associated with a dry cough. Angioedema is very rare. However, patients starting ACE inhibitors or ARBs should be informed of the signs and symptoms that may occur with angioedema. If angioedema is unlikely, but swelling of the face (often including the eyelids) or extremities is present, the patient should be advised to stop treatment and seek immediate medical attention.[23]

THIAZIDE VS LOOP DIURETICS

For patients without proteinuria, preferred first-line therapy has not been established. Patients with CKD and HTN often experience fluid retention or fluid overload. As a result, diuretics are often required in treatment regimens. Thiazide is recommended for patients with CKD stages 1–3 (GFR ≥30 mL/min) and is established as an effective agent to reduce the risk of BP and CVD. Loop diuretics are recommended for patients with CKD stage 4 or 5 (GFR <

30 mL/min). This is because it is highly effective in reducing extracellular fluid volume in patients with significantly reduced GFR.[24]

Thiazide diuretics (chlorthalidone, hydrochlorothiazide) and loop diuretics (bumetanide, furosemide, torsemide) all cause hyperuricemia (increased urination). This increased water loss can lead to electrolyte imbalance. Patients taking these drugs must monitor their electrolytes to ensure they are not experiencing electrolyte abnormalities such as hyperkalemia or hypomagnesemia, which can occur in response to antihypertensive drugs. However, it is common in diuretics. Advising patients starting diuretic treatment to rise slowly from a sitting position is important.[25]

CALCIUM CHANNEL BLOCKERS

Calcium channel blockers (CCBs) are considered second-line or third-line therapy in the treatment of HTN in chronic kidney disease patients. Although there may be no difference in effects on blood pressure lowering between non-dihydropyridine CCBs (ND-CCBs; e.g., diltiazem, verapamil) and dihydropyridine CCBs (e.g., amlodipine, nifedipine), ND-CCB significantly increased proteinuria has been shown to reduce either alone or in combination with ACE inhibitors or ARBs. ND-CCB may reduce proteinuria and should be considered as second-line or third-line therapy in patients with diabetic CKD or non-diabetic CKD with proteinuria, in addition to its antihypertensive effect.[26] Dihydropyridine CCB can be used as second-line therapy in non-diabetic CKD patients without proteinuria. Common side effects include edema and constipation with ND-CCB (particularly verapamil) and flushing and peripheral edema with dihydropyridine drugs.[27]

ALDOSTERONE ANTAGONISTS

Aldosterone plays a very detrimental role in the progression of chronic kidney disease. Aldosterone receptor antagonists (eg, spironolactone, eplerenone) may be used to treat CKD if blood pressure targets are not achieved with first- and second-line therapy. These agents have been shown in human studies to cause a decrease in proteinuria.[28] when added to ACE inhibitors and ARB'S Aldosterone antagonists are potassium-sparing diuretics, especially increasing the risk of hyperkalemia when used with ACE inhibitors or ARBs. Patients starting potassium-sparing diuretics must have their potassium levels checked to ensure that they are not experiencing electrolyte imbalances. Symptoms of hyperkalemia include irregular heartbeat and severe muscle weakness. Unfortunately, hyperkalemia can occur asymptomatically, underscoring the importance of monitoring.[29]

RENIN-INHIBITORS

Aliskiren is currently the only renin inhibitor on the market. Indicated for the treatment of HTN as monotherapy or in combination with valsartan. Recent data from the ALTITUDE trial suggest the use of ACE inhibitors or ARBs in patients with diabetes or renal impairment (GFR <60 mL/min) because of the increased risk of renal impairment, hypotension, and hyperkalemia. (30) It is taboo. Aliskiren can be considered if the patient cannot take her ACE inhibitors or ARBs. However, it is not recommended for use in patients with stage 4 or 5 renal failure.[31]

BETA-BLOCKERS

Beta-Blockers: Data that evaluate the effect of beta-blockers on the progression of CKD and proteinuria are limited. While beta-blockers are not included in these agents can be considered as second- or third-line therapy if the patient has a compelling indication for a beta-blocker such as coronary artery disease or chronic heart failure.[32]

NONPHARMACOLOGICAL RECOMMENDATIONS

Chronotherapy: This type of therapy takes into consideration circadian BP patterns, and institutes the administration of antihypertensive medication concerning the daily patterns, moving away from the administration of all antihypertensive medications in the morning. Trials have demonstrated improved 24-hour BP control in patients administering CCBs in the evening rather than in the morning.[33] Additional studies have identified benefits from the nighttime administration of other antihypertensive medications such as ACE inhibitors or ARBs.[34] Chronotherapy may warrant some consideration for those unable to achieve their BP goal when administering all antihypertensive agents in the morning. If patients are on more than two antihypertensive agents, it may be appropriate to administer two agents in the morning and the additional agents in the evening.

ROLE OF SALT RESTRICTION IN HTN

Consuming less than 5 grams of salt per day for adults lowers blood pressure and lowers the risk of cardiovascular disease, stroke, and coronary heart attack. The main benefit of salt reduction is a corresponding reduction in hypertension. Excessive sodium intake (more than 2 grams per day, equivalent to 5 grams of salt per day) and insufficient potassium intake (less than 3.5 grams per day) contribute to high blood pressure and increase the risk of heart disease and stroke. Salt is the main source of sodium in our diet, but it may come from monosodium glutamate, which is used as a flavoring agent in many parts of the world.[35]

Most people eat too much salt. That's an average of 9-12 grams per day, or about double the maximum recommended amount of salt reduction has been identified as one of the most cost-effective actions countries can take to improve the health of their populations. A key salt reduction measure could give him an extra year of healthy living at a cost below average annual income or gross domestic product per capita. An estimated 2.5 million deaths could be avoided each year if global salt consumption were reduced to recommended levels.[36]

LIFESTYLE CHANGES

Increased physical activity, weight loss, and dietary changes are recommended for all her HTN patients. The Diet to Stop Hypertension (DASH) diet emphasizes increased fruit and vegetable consumption, low-fat dairy and lean protein intake, and restriction of saturated fats. This diet has been shown to significantly reduce systolic blood pressure, roughly equivalent to the reductions achieved with antihypertensive monotherapy.[37] Furthermore, reducing sodium and alcohol intake has been shown to reduce blood pressure. It is an effective means of lowering blood pressure. Increased daily activity may enhance the benefits of antihypertensive therapy and may play an important role in achieving blood pressure goals.[38]

CONCLUSION

Hypertension management in CKD lowers incident CV risk and reduces kidney disease progression. Existing guidelines have moved closer to consensus BP targets and placed more emphasis on accurate BP measurements and more dependence on home and ABPM. Pharmacologic therapies offer varying degrees of risk reduction in CKD, and lifestyle interventions should be encouraged to augment these health benefits. Most importantly, patient engagement with out-of-office BP measurements, as well as more informed and shared decision-making, will lead to long-term success. Taking all these aspects together and considering both pharmacological and non-pharmacological treatment concepts of hypertension in chronic kidney disease, the progression of chronic kidney disease is reduced and further improvement is yet to come.

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CONFLICTS OF INTEREST

The authors confirm that this article's conflict has no conflict of interest.

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