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Research Article

**ANTIHYPERTENSIVE MEDICATIONS FOR CHRONIC
KIDNEY DISEASE IN PRIMARY CARE PRACTICE**Abdulaziz Saud Alrahili¹, Nasir Ahmad Alsubai², Mishal Mohammed Albaqami³¹Umm Al-Qura University²Umm Al-Qura University³Umm Al-Qura University**Abstract:**

Context: When managing patients with chronic kidney disease, proper management of hypertension that achieves sufficient control of blood pressure is considered to be one of the most important primary care interventions to decrease the severity of kidney disease and reduce the risk of patients developing cardiovascular events. The best mechanism when treating a patient with hypertension and chronic kidney disease is the blockage of the renin angiotensin-aldosterone system, such as angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blocker (ARBs).

Aim of work: We will discuss the importance of managing blood pressure in patients with chronic kidney disease, and emphasize the common medications used for this purpose.

Methodology: We conducted a systematic comprehensive search in literature review using Medline, Pubmed, and Embase from January 1997 till March 2018. We used the terms: chronic kidney diseases, morbidity of kidney failure, ACE inhibitors, ARBs, diuretics

Conclusions: Hypertension is prevalent among patients with chronic kidney disease, and the proper control of blood pressure has been shown to be significantly beneficial in these patients. A goal of keeping blood pressure less than 130/80 mmHg should be targeted in chronic kidney disease patients, especially those who are diabetics. ACEIs and ARBs are considered to be the best lines in the management of hypertension in chronic kidney disease patients. Other drugs include spironolactone and eplerenone, thiazides, CCBs and betablockers.

Keywords: antihypertensive medication, chronic kidney diseases, end stage kidney disease

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INTRODUCTION:

When managing patients with chronic kidney disease, proper management of hypertension that achieves sufficient control of blood pressure is considered to be one of the most important primary care interventions to decrease the severity of kidney disease and reduce the risk of patients developing cardiovascular events. Previous studies have found a high prevalence of blood pressure among patient with renal diseases. A study in Canada has concluded that up to half patients with chronic kidney disease also have hypertension [1]. In another study based on a large US database, more than 80% of patients with chronic kidney disease and albuminuria higher than 3 mg/mmol were found to have hypertension, and the prevalence of hypertension reached 88% in another study on stage 3 chronic kidney disease patients in the UK [2,3].

Proper control of blood pressure has been found to be associated with a significant decline in cardiovascular diseases risk in patients with chronic kidney disease, along with improvements in their prognosis [4]. Therefore, this practice is of extreme importance in primary health care. Generally, blood pressure is controlled using pharmacological agents. In this review, we will discuss the use of these agents in patients with chronic kidney disease.

METHODOLOGY:

We did a systematic search for antihypertensive medications used in primary care for patients with chronic kidney diseases using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>). EMBSE, and Google Scholar search engine (<https://scholar.google.com>) from January 1997 to March 2018. All relevant studies were retrieved and discussed. We only included full articles. The following search terms were used: chronic kidney diseases, morbidity of kidney failure, ACE inhibitors, ARBs, diuretics.

Data Extraction:

two reviewers had independently reviewed the studies, abstracted data and disagreement were resolved by consensus. Studies were evaluated for quality and a review protocol was followed throughout

Blood Pressure Goals in Chronic Kidney Disease

In their latest guidelines, the American College of Cardiology and the American Heart Association

recommended the application of intensive protocols for blood pressure control in any patient with confirmed chronic kidney disease. Moreover, they recommended a lower threshold for the diagnosis of blood pressure in these patients (130/80 mmHg). This management of blood pressure should depend on the risk of having atherosclerotic cardiovascular disease in the patient, along with proper assessment of the blood pressure increases [5].

The recommended target blood pressure level in patients with chronic kidney disease is 125-130 mmHg for systolic blood pressure [6]. Achieving this control has been proven to significantly decrease the risk of developing cardiovascular diseases. When dealing with diabetic patients with a chronic kidney disease, the target blood pressure is 130/80 mmHg, which is associated with improved outcomes in these patients. In some patients with diabetes and a relatively high risk of cardiovascular disease, it is even more beneficial to target blood pressure lower than 130/80 mmHg [7].

On the other hand, evidence on the overall chronic kidney disease population regardless of diabetic status is less conclusive regarding decreasing blood pressure less than 130/80 mmHg. Most of trials conducted on chronic kidney disease patients and hypertension did not show significant improvements when blood pressure reached levels below 130/80 mmHg⁸⁻¹⁰. However, all these studies were successful in proving that achieving blood pressure control less than 140/90 mmHg will lead to significant improvements in outcomes in patients with chronic kidney disease. In addition, more intensive control of blood pressure should be achieved in patients who have proteinuria higher than 1000 mg [11].

Anti-hypertensive Medications

The Renin Angiotensin-Aldosterone System Inhibitors

Chronic kidney disease is considered to be an important predisposing factor for developing a cardiovascular disease, making it an important factor when clinicians decide treatment plans for hypertension. Most adults with chronic kidney disease have a 10% risk of developing an atherosclerotic cardiovascular disease within the next ten years¹². On the other hand, selection of the most proper treatment could be challenging, as the used

drug must have beneficial effects of the kidney.

Generally, the best mechanism when treating a patient with hypertension and chronic kidney disease is the blockage of the renin angiotensin-aldosterone system, as this system has been found and proven to be responsible for significant cardiovascular and renal pathologies. Moreover, agents that manipulate the RAAS system have been found beneficial in improving outcomes in patients with chronic kidney disease and albuminuria, regardless of the presence or absence of diabetes [13].

Most recent guidelines regarding the management and treatment of hypertension recommend the use of an ACE inhibitor or an ARB in any hypertensive patient with albuminuria higher than 300 mg/g [5]. The use of these drugs has proven efficacy in decreasing the levels of protein in the urine, and to stop the progression of kidney disease [14].

On the other hand, when dealing with patients with chronic kidney disease who do not have albuminuria, no evidence is present to support the superiority of ACEIs or ARBs over other anti-hypertensive agents. In addition, it is generally recommended for many proteinuric chronic kidney disease patient that they stop or decrease their dose of ACEIs due to their effects of increasing creatinine levels in blood and causing hyperkalemia. Interestingly, Adverse events associated with ACE inhibitors and ARBs are not strongly associated with administrated doses [6].

Using both ACEIs and ARBs simultaneously is generally not preferred as no evidence has proven any additional efficacy of this regimen ¹⁵. Moreover, studies have found that this regimen can be associated with several side effects as hyperkalemia, hypotension, and worsening kidney functions. In addition, the use of ACEIs and ARBs is contraindicated in pregnant women, as these agents have been found teratogenic. Patients who have a history of angioedema attacks cannot also use ACEIs [6].

Aldosterone Receptor Antagonists

Patients who have proteinuric chronic kidney disease may also benefit from the use of low doses of antagonists of aldosterone receptors like eplerenone and spironolactone. In fact, some recommend the use of spironolactone in combination with an ACEI inhibitor to improve nephropathy and decrease rates of protein excretion in urine. However, these drugs

should be used with caution, as increasing doses of spironolactone will lead to higher risk of developing significant hyperkalemia. Moreover, patients on these drugs should always have their serum potassium levels checked to detect possible increases in serum potassium levels [16].

In cases of hyperkalemia induced by spironolactone, the dose of the drug should be decreased along with using another loop diuretic in severe cases to induce potassium excretion. Impotence and gynecomastia have also been observed with the use of spironolactone. Eplerenone, on the other hand, is not associated with impotence or gynecomastia but needs to be administrated twice daily to achieve therapeutic levels, in contrast to spironolactone [5].

It is preferred to avoid the use of any diuretic that spares potassium in chronic kidney disease patients who have a GFR that is less than 45 mL/min or potassium levels higher than 52 Mmol/L [5]. On the other hand, chronic kidney disease patients who have low potassium levels are recommended to take spironolactone along with an ACE inhibitor in attempts to correct their potassium levels and proteinuria [16].

Diuretics

One significant hallmark in chronic kidney disease patients is having volume overload. Therefore, the use of diuretics is especially important in these patients. Thiazide diuretics are generally preferred in the management and treatment of patients with chronic kidney disease as they have a relatively long-half life. Thiazides have stimulating effects on the RAAS system. Therefore, it is preferred to use them in combination with ACEIs or ARBs to achieve better efficacy. In patients whose GFR is less than 30 mL/min/1.73m, the efficacy of thiazides significantly decreases. Thiazides are contraindicated in patients who have any history of gout attacks. Loop diuretics, on the other hand, have relatively improved efficacy in patients who have advanced chronic kidney disease, and their used is generally preferred in patients who also have congestive heart failure [5].

Calcium Channel Blockers

CCBs are considered to be one of the important drugs for controlling hypertension in patients with chronic kidney disease. Verapamil and diltiazem, which belong to the Non-dihydropyridine CCBs family, have both shown efficacy in decreasing rates of protein excretion in urine, and slowing the

progression of kidney disease ¹⁴; ¹⁷. in addition, Dihydropyridine CCBs, can be used in combination with ACEIs to decrease protein excretion rates in urine in patients with advanced chronic kidney disease [18].

Patients who have stage 3 chronic kidney disease can significantly benefit from the use of CCBs regarding blood pressure control, mortality rates, heart diseases, thrombolytic events, and kidney functions [19]. One limitation of dihydropyridine CCBs is the inability of their use in monotherapy, as they should always be used with ACEIs.

Some guidelines suggest the use of felodipine or amlodipine in patients with chronic kidney disease to improve angina pectoris. However, the use of these drugs is absolutely contraindicated in patients who have systolic heart failure or heart block, as they have a risk of severe bradycardia. They should not also be used with betablockers [5].

Agents Blocking the Sympathetic Nervous System

Beta-blockers

Beta blockers are not among the first line choices for controlling blood pressure in patients with chronic kidney disease, unless there is a heart disease. Generally, beta blockers have been proven efficient in decreasing the mortality in patients who have cardiovascular disease. However, their effects on the kidneys are not well established ²⁰. One beta blocker, nebivolol, has been shown to stimulate vasodilation by nitric oxide [21].

Central Alpha-Adrenergic Agonists

These drugs are generally avoided due to their high rates of side effects in the elderly and low tolerability. Methyldopa is an agent that has been used to control blood pressure in pregnant women due to its safety on the fetus. The use of these drugs is contraindicated in patients who are already on a beta blocker due to the risk of developing bradycardia [22].

Alpha 1-Adrenergic Blockers

Some agents of these drugs family like prazosin and terazosin can be used in patients with chronic kidney disease, especially in patients who also have benign prostatic hyperplasia [23]. However, they have limited benefits on the kidneys especially in diabetic patients, and can induce or worsen heart failure in some patients [24].

CONCLUSIONS:

Hypertension is generally prevalent among patients with chronic kidney disease, and the proper control of blood pressure has been shown to be significantly beneficial in these patients. A goal of keeping blood pressure less than 130/80 mmHg should be targeted in chronic kidney disease patients, especially those who are diabetics. ACEIs and ARBs are considered to be the best lines in the management of hypertension in chronic kidney disease patients. Other drugs include spironolactone and eplerenone, thiazides, CCBs and betablockers. Proper control of blood pressure in chronic kidney disease patients is associated with significant reductions in their risk of developing cardiovascular events.

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