Mini Review

MANAGING HIGH BLOOD PRESSURE WITH ACE INHIBITORS: WHAT YOU NEED TO KNOW?

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How to cite this article: Nagar A. Managing High Blood Pressure with Ace Inhibitors: What You Need to Know? Innov Pharm Planet (IP-Planet) 2020;08(2)17-21.

Source of Support: Nil.
Conflicts of Interest: None declared.

Date of Submission: 15-04-2020
Date of Revision: 07-05-2020
Date of Acceptance: 16-05-2020

ABSTRACT:

Hypertension remains a leading cause of cardiovascular morbidity and mortality worldwide, necessitating effective and long-term management strategies. Angiotensin-converting enzyme (ACE) inhibitors are widely used as first-line agents in controlling high blood pressure due to their proven efficacy and beneficial effects on multiple organ systems. This review provides an in-depth analysis of ACE inhibitors in the management of hypertension, including their mechanism of action through the inhibition of the renin-angiotensin-aldosterone system, which results in vasodilation and reduced blood pressure. We discuss the clinical efficacy of ACE inhibitors in comparison to other antihypertensive classes, highlighting their added benefits in cardiovascular and renal protection, particularly in patients with comorbidities such as diabetes and chronic kidney disease. The safety profile of ACE inhibitors, including common and serious side effects like cough, Hyperkalaemia, and angioedema, is also examined, alongside contraindications and drug interactions. Special considerations for elderly patients and those with multiple health conditions are addressed, emphasizing the role of ACE inhibitors in personalized treatment. Finally, emerging research on new ACE inhibitors and combination therapies, as well as the potential for genetic-based treatment approaches, is explored. ACE inhibitors remain a cornerstone in hypertension management, offering both efficacy and protection against long-term complications.

KEYWORDS: Hypertension, ACE inhibitors, blood pressure control, cardiovascular protection, renal benefits.

INTRODUCTION

Hypertension, commonly known as high blood pressure, is defined as a persistent elevation in arterial pressure, specifically when systolic blood pressure (SBP) is 130 mm Hg or higher and/or diastolic blood pressure (DBP) exceeds 80 mm Hg. It is a prevalent chronic medical condition affecting approximately 1.28 billion adults globally, with a significant portion residing in low- and middle-income countries. The condition is notably underdiagnosed, with around 46% of adults unaware of their hypertensive status, and less than half receiving appropriate treatment. Managing hypertension is critical due to its association with severe complications such as cardiovascular diseases, stroke, and kidney damage; it accounts for about 7.5 million deaths annually, making it a leading cause of morbidity and mortality worldwide. Pharmacotherapy plays a crucial role in managing hypertension, with various classes of antihypertensive medications available. Among these, ACE inhibitors (Angiotensin-Converting Enzyme inhibitors) are frequently recommended as a first-line treatment option due to their Efficacy in lowering blood pressure and reducing the risk of cardiovascular events.

Other classes include diuretics, beta-blockers, calcium channel blockers, and angiotensin II receptor blockers (ARBs). The choice of medication often depends on individual patient factors, including the presence of comorbidities and the specific characteristics of the hypertension. Effective management through pharmacotherapy not only helps in controlling blood pressure but also significantly reduces the risk of associated complications.[1]

Access this article online	
Website: https://innovationaljournals.com/index.php/ip	**e-ISSN:** 2348-7275

UNDERSTANDING ACE INHIBITORS

ACE inhibitors, or Angiotensin-Converting Enzyme inhibitors, function primarily by interrupting the renin-angiotensin-aldosterone system (RAAS), a critical regulator of blood pressure and fluid balance. At the biochemical level, ACE inhibitors block the action of the angiotensin-converting enzyme, which catalyses the conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor that increases blood pressure by narrowing blood vessels and stimulating the secretion of aldosterone, leading to sodium and water retention. By inhibiting this enzyme, ACE inhibitors reduce the levels of angiotensin

II, resulting in vasodilation (widening of blood vessels) and decreased secretion of aldosterone. This mechanism not only lowers blood pressure but also decreases preload and afterload on the heart, ultimately reducing cardiac workload and improving outcomes in patients with hypertension and heart failure.[2]

In terms of pharmacokinetics and pharmacodynamics, ACE inhibitors exhibit unique absorption, distribution, metabolism, and excretion characteristics. Most ACE inhibitors are administered orally in prodrug forms, which are converted into their active metabolites in the liver. For example, ramipril is converted to ramiprilat, its active form, which binds to ACE with high affinity. The absorption rates vary among different ACE inhibitors; typically, around 35% of an oral dose is absorbed into systemic circulation. The distribution of these drugs is influenced by their binding to plasma proteins and tissue compartments, with less than 2% of total body ACE found in plasma. Metabolism occurs predominantly in the liver, while renal clearance plays a significant role in excreting active metabolites. The pharmacodynamic effects include sustained inhibition of ACE activity, leading to prolonged reductions in blood pressure that can last for 24 hours or more after dosing. Overall, ACE inhibitors are effective in managing hypertension and preventing cardiovascular complications through their multifaceted actions on the RAAS and their favorable pharmacokinetic profiles.[3]

CLINICAL EFFICACY OF ACE INHIBITORS IN HYPERTENSION

Effectiveness in Reducing Blood Pressure

Angiotensin-converting enzyme (ACE) inhibitors are widely recognized for their efficacy in managing hypertension. Numerous clinical studies and meta-analyses have demonstrated their effectiveness in lowering blood pressure and reducing cardiovascular risks. For instance, a meta-analysis of randomized clinical trials indicated that ACE inhibitors lead to significant reductions in all-cause mortality and cardiovascular mortality among hypertensive patients, showcasing a 10% reduction in all-cause mortality. This underscores the importance of ACE inhibitors not only in blood pressure management but also in improving overall survival rates.

Moreover, ACE inhibitors function by blocking the formation of angiotensin II, a potent vasoconstrictor, thereby promoting vasodilation and reducing blood pressure. Their effectiveness is further supported by findings from large-scale studies such as the HOPE trial, which demonstrated significant reductions in cardiovascular events among high-risk patients treated with ramipril, an ACE inhibitor. Additionally, ACE inhibitors have shown comparable efficacy to other antihypertensive classes in lowering blood pressure while also providing protective effects against renal disease and heart failure.[4]

Comparison with Other Antihypertensive Agents

When comparing ACE inhibitors to other classes of antihypertensive medications such as diuretics, calcium channel blockers (CCBs), and beta-blockers several key differences emerge regarding efficacy, side effects, and patient outcomes.

Efficacy: Both ACE inhibitors and diuretics have been shown to effectively lower blood pressure; however, ACE inhibitors may provide additional benefits in terms of cardiovascular protection and mortality reduction. For example, while diuretics are effective for initial treatment, ACE inhibitors are often preferred for patients with comorbid conditions such as diabetes or heart failure due to their protective effects on the kidneys. In head-to-head trials, some studies suggest that angiotensin receptor blockers (ARBs) may offer superior cardiovascular protection compared to ACE inhibitors, although both classes exhibit similar antihypertensive effects.

Side Effects: ACE inhibitors are associated with specific side effects such as cough and angioedema due to increased bradykinin levels. In contrast, ARBs tend to have a better side effect profile with lower rates of discontinuation due to adverse events. Diuretics can lead to electrolyte imbalances and dehydration, while beta-blockers may cause fatigue and bradycardia.

Patient Outcomes: Studies indicate that ACE inhibitors are linked to lower rates of all-cause mortality compared to other antihypertensive agents. A meta-analysis revealed that ACE inhibitors reduced all-cause mortality by 10% compared to controls, while ARBs did not demonstrate a similar effect. Furthermore, the reno-protective effects of ACE inhibitors make them particularly beneficial for patients with chronic kidney disease.[5]

BENEFITS BEYOND BLOOD PRESSURE CONTROL

Cardiovascular Protection

ACE inhibitors offer substantial cardiovascular protection beyond their primary function of lowering blood pressure. They are effective in reducing the risk of major cardiovascular events, such as myocardial infarction (MI) and stroke, particularly in high-risk populations. For example, the HOPE trial demonstrated that ramipril significantly lowered the incidence of cardiovascular events in patients with a history of cardiovascular disease or diabetes, leading to a notable reduction in all-cause mortality by approximately 14% compared to placebo.

Additionally, ACE inhibitors improve heart health by decreasing afterload and preload, which enhances cardiac output without increasing heart rate. This is particularly beneficial in patients with left ventricular dysfunction, as ACE inhibitors mitigate cardiac remodelling and hypertrophy by reducing levels of angiotensin II and aldosterone, which are responsible for vascular smooth muscle hypertrophy and fibrosis. Their ability to increase bradykinin levels also contributes to vasodilation, further promoting cardiovascular health.[6]

Renal Benefits

ACE inhibitors play a critical role in protecting kidney function, especially in patients with hypertension-related kidney damage or diabetes. By inhibiting the renin-angiotensin-aldosterone system (RAAS), ACE inhibitors reduce glomerular capillary pressure, which is beneficial for preserving renal function. Studies have shown that these medications can slow the progression of diabetic nephropathy, significantly reducing the combined endpoints of dialysis, transplantation, and death in patients with insulin-dependent diabetes mellitus.

Furthermore, ACE inhibitors are recommended as first-line therapy for hypertension in diabetic patients due to their ability to reduce proteinuria and delay the onset of end-stage renal disease. Their protective effects on the kidneys are particularly important given that hypertension is a leading cause of chronic kidney disease (CKD). The use of ACE inhibitors has been associated with improved renal outcomes and decreased serum creatinine levels in hypertensive patients with albuminuria.[7]

Improvement in Heart Failure and Post-Myocardial Infarction

ACE inhibitors are essential in managing heart failure and preventing complications following myocardial infarction. They have been shown to reduce mortality and hospitalizations in patients with heart failure with reduced ejection fraction (HFrEF). Large-scale trials have consistently demonstrated that ACE inhibitors decrease overall mortality rates among heart failure patients by improving hemodynamics and reducing cardiac workload.

In the context of post-MI care, ACE inhibitors are recommended for all patients with left ventricular dysfunction or heart failure following an MI. They significantly lower the risk of subsequent cardiovascular events and slow the progression to congestive heart failure after an MI. For instance, studies indicate that early initiation of ACE inhibitor therapy post-MI can lead to substantial reductions in both all-cause mortality and cardiovascular mortality. This underscores the importance of incorporating ACE inhibitors into treatment protocols for patients recovering from myocardial infarction to enhance long-term outcomes.[8]

SAFETY AND SIDE EFFECTS OF ACE INHIBITORS

Common and Serious Side Effects

ACE inhibitors are associated with several common and serious side effects. The most frequently reported adverse effects include:

Dry Cough: Occurring in approximately 10% to 20% of patients, this persistent cough is believed to be linked to increased bradykinin levels. It can develop within weeks to months after starting treatment and may persist even after discontinuation of the medication for some patients.

Hyperkalemia: This condition, characterized by elevated potassium levels, occurs in about 2% to 6% of patients. It is particularly concerning for those with renal impairment or those taking potassium-sparing diuretics or potassium supplements.

Angioedema: A rare but potentially life-threatening reaction, angioedema affects about 0.1% to 0.2% of patients. It involves swelling of the face, lips, and airway, which can lead to airway obstruction. Patients with a history of angioedema related to ACE inhibitors are at increased risk if treated again with these medications.

Less common but serious side effects include:

Acute Kidney Injury: ACE inhibitors can cause transient increases in blood urea nitrogen (BUN) and serum creatinine levels, particularly in patients with pre-existing renal impairment or those on diuretics.

Hematologic Effects: Rarely, ACE inhibitors can lead to neutropenia or agranulocytosis, especially in patients with additional risk factors such as renal disease.

Hypotension: This is a common effect that can occur, particularly in patients who are volume-depleted or have heart failure.

Contraindications

There are specific situations where ACE inhibitors should not be prescribed:

Pregnancy: ACE inhibitors are contraindicated during pregnancy due to the risk of teratogenic effects, including congenital malformations and fetal death. They are classified as Category D by the FDA, indicating potential harm to the fetus when taken during any trimester.

Bilateral Renal Artery Stenosis: The use of ACE inhibitors in patients with bilateral renal artery stenosis can lead to acute renal failure due to decreased renal perfusion.

History of Angioedema: Patients who have previously experienced angioedema associated with ACE inhibitor therapy should not be re-exposed to these medications due to the heightened risk of recurrence.

Hypersensitivity: Individuals with known hypersensitivity to ACE inhibitors or components of their formulation should avoid these drugs.

Drug Interactions

ACE inhibitors can interact with various medications, leading to increased risks of adverse effects:

Diuretics: The concurrent use of diuretics, especially potassium-sparing types, can enhance the risk of Hyperkalemia and hypotension. Caution is advised when initiating ACE inhibitor therapy in patients already on diuretics.

Potassium Supplements: Due to the potential for Hyperkalemia, potassium supplements should be used cautiously under medical supervision when a patient is on an ACE inhibitor.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): NSAIDs can reduce the antihypertensive effects of ACE inhibitors and may increase the risk of acute kidney injury when used together, particularly in volume-depleted or elderly patients.

Other RAAS Blockers: Combining ACE inhibitors with angiotensin receptor blockers (ARBs) or direct renin inhibitors like aliskiren is generally discouraged due to an increased risk of Hyperkalemia and acute kidney injury.
These interactions necessitate careful monitoring and management strategies when prescribing ACE inhibitors alongside other medications.[9]

CONCLUSION

ACE inhibitors are highly effective in managing hypertension, offering significant cardiovascular and renal protective benefits. They remain a cornerstone therapy for patients with high blood pressure, particularly those with comorbidities like diabetes and chronic kidney disease. While generally well-tolerated, careful consideration of side effects, contraindications, and drug interactions is essential. Future research on personalized medicine and novel ACE inhibitor formulations holds promise for enhancing patient outcomes in hypertension management.

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