INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Comprehensive Review of Antihypertensive Agents: Mechanisms, Therapeutic Guidelines, And Adverse Effects

K. Arun, P. Haripriya, A. Harikrishnan, T. Madhan, S. Shobhana, V. Harini

G.P. Pharmacy College, Vaniyambadi Main Road, Mandalavadi, Jolarpetai – 635851, Tirupattur District

ARTICLE INFO

Published: 17 Jun. 2026
Keywords:
Hypertension, Antihypertensive Drugs, Blood Pressure Control, Thiazide Diuretics, Calcium Channel Blockers, ACE Inhibitors, Angiotensin Receptor Blockers, Beta-Blockers, Combination Therapy, Resistant Hypertension, Cardiovascular Disease
DOI:
10.5281/zenodo.20729692

ABSTRACT

Hypertension is one of the most common health problems worldwide and is a major risk factor for cardiovascular diseases and premature death. Proper control of blood pressure plays an important role in reducing the risk of serious complications such as coronary artery disease, stroke, heart failure, chronic kidney disease, and diabetes-related vascular disorders. This review provides an overview of the current approaches to the management of hypertension, including blood pressure classification, treatment goals, and the selection of appropriate antihypertensive medications. The review discusses the major classes of antihypertensive drugs, including thiazide and thiazide-like diuretics, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), beta-blockers, loop diuretics, potassium-sparing diuretics, hydralazine, clonidine, minoxidil, and alpha-blockers. Their mechanisms of action, therapeutic uses, dosage considerations, adverse effects, contraindications, monitoring requirements, and toxicity profiles are summarized. In addition, evidence from clinical studies comparing the efficacy and safety of different antihypertensive drug classes is reviewed. The importance of combination therapy and treatment strategies for resistant hypertension is also highlighted. A thorough understanding of antihypertensive medications is essential for achieving effective blood pressure control, reducing treatment-related complications, and improving patient outcomes. Furthermore, a multidisciplinary healthcare approach is important for the successful management of hypertension and the .prevention of long-term cardiovascular complications.

INTRODUCTION

Hypertension (HTN) is recognized as a major contributor to cardiovascular morbidity and mortality. Effective reduction and control of blood pressure significantly decrease cardiovascular risk, and maintaining systolic blood pressure below 130 mmHg has been shown to help prevent complications associated with heart failure,

***Corresponding Author:** P. Haripriya
Address: *G.P. Pharmacy College, Vaniyambadi Main Road, Mandalavadi, Jolarpetai – 635851, Tirupattur District*
Email ✉: haripriyapalani877@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

diabetes, coronary artery disease, stroke, and other cardiovascular disorders. This section reviews the current recommendations for the selection of antihypertensive agents and describes the various drug classes used as first-, second-, and third-line therapies for hypertension. It also outlines their clinical indications, adverse effects, and findings from comparative studies evaluating the efficacy and safety of different antihypertensive drug classes.

Objectives:

- Discuss the current guidelines for the use of antihypertensive drugs and provide recommendations for selecting appropriate first-line therapy.
- Review the major classes of antihypertensive agents and summarize the recommendations for initiating combination therapy when monotherapy does not achieve adequate blood pressure control.
- Describe the important adverse effects associated with each class of antihypertensive medications.
- Explain the role of the interprofessional healthcare team in developing and implementing an effective management plan for patients with hypertension.

Indications

American College of Cardiology and American Heart Association updated the classification of hypertension in 2017, identifying hypertension as a major contributor to cardiovascular morbidity and mortality. According to these guidelines, normal blood pressure is defined as a systolic pressure below 120 mmHg and a diastolic pressure below 80 mmHg. Elevated blood pressure refers to systolic values ranging from 120–129 mmHg with diastolic pressure remaining below 80 mmHg. Stage 1 hypertension is characterized by systolic pressure between 130–139 mmHg or diastolic pressure between 80–89 mmHg, whereas Stage 2 hypertension is diagnosed when systolic pressure is 140 mmHg or higher, or diastolic pressure is 90 mmHg or higher. A hypertensive crisis is considered when systolic blood pressure exceeds 180 mmHg and/or diastolic pressure rises above 120 mmHg.

According to the 2019 guidelines published by the American College of Cardiology and American Heart Association on the primary prevention of cardiovascular disease, lifestyle modification is recommended as the first-line approach for individuals with elevated blood pressure. These modifications include maintaining a healthy body weight, following a cardioprotective diet, engaging in regular physical activity, reducing dietary sodium intake, and limiting alcohol consumption

For individuals diagnosed with Stage 1 hypertension, initiation of antihypertensive therapy is recommended when the estimated 10-year risk of atherosclerotic cardiovascular disease

(ASCVD) is 10% or greater, with the goal of maintaining blood pressure below 130/80 mmHg to reduce the likelihood of cardiovascular complications. In contrast, patients with Stage 1 hypertension who have a 10-year ASCVD risk below 10% are generally advised to manage their condition through lifestyle modifications alone.

Patients diagnosed with Stage 2 hypertension are advised to initiate antihypertensive drug therapy irrespective of their estimated 10-year ASCVD risk, with the treatment goal of reducing blood pressure to below 130/80 mmHg.

For individuals with chronic kidney disease, the recommended blood pressure goal is to maintain values below 130/80 mmHg.

In patients with type 2 diabetes mellitus (T2DM), antihypertensive therapy is recommended when blood pressure exceeds 130/80 mmHg, with the aim of achieving and maintaining BP levels below 130/80 mmHg

Antihypertensive treatment is generally initiated with a single-drug regimen following inadequate blood pressure control through lifestyle modifications alone. Combination therapy is often considered when monotherapy does not achieve the desired therapeutic response

Reduction of blood pressure significantly lowers cardiovascular risk, and maintaining systolic blood pressure below 130 mmHg has been associated with decreased complications in patients with conditions such as heart failure, diabetes mellitus, coronary artery disease, stroke, and other cardiovascular disorders. Additionally, the effectiveness of initial monotherapy may vary depending on factors such as age and race.[1]

Several classes of antihypertensive agents are available for the management of hypertension. Among these, the commonly recommended first-line therapies include thiazide diuretics, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin II receptor blockers (ARBs).

Thiazide Diuretics

Thiazide and Thiazide-[like diuretics are widely considered first-line agents for the management of hypertension. According to the Eighth Joint National Committee guidelines, these diuretics may be administered either as monotherapy or in combination with other antihypertensive drugs across all age groups and racial populations. However, in patients with chronic kidney disease, angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) are preferred due to their renal protective effects.[2]

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial identified thiazide diuretics as the preferred initial therapy for hypertension management, except in cases where contraindications are present.

Monotherapy with hydrochlorothiazide at daily doses of 12.5 mg or 25 mg has not demonstrated a significant reduction in morbidity or mortality outcomes.[3]

Evidence indicates that thiazide-type diuretics, particularly chlorthalidone and indapamide, are more effective and cost-efficient in reducing cardiovascular events. Consequently, they are recommended as first-line agents for the management of hypertension. Several studies have also demonstrated that these thiazide-like diuretics possess greater antihypertensive efficacy than hydrochlorothiazide and provide superior cardiovascular protection.[4][5]

Chlorthalidone is widely regarded as a preferred first-line monotherapy for hypertension. Evidence from multiple studies indicates that it is highly effective in lowering blood pressure and reducing cardiovascular morbidity and mortality.[6][7]

Chlorthalidone showed superior blood pressure–lowering efficacy compared with Hydrochlorothiazide based on 24-hour ambulatory blood pressure monitoring results.[4]

Hydrochlorothiazide was found to have a shorter duration of antihypertensive action in studies comparing office blood pressure measurements with 24-hour ambulatory blood pressure monitoring.[8]

Changing therapy from Hydrochlorothiazide to Chlorthalidone has been associated with an

additional reduction in systolic blood pressure of approximately 7–8 mm Hg.[9]

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial demonstrated that Chlorthalidone administered at doses of 12.5–25 mg/day was associated with a lower incidence of cardiovascular complications compared with Amlodipine and Lisinopril

Chlorthalidone is considered a preferred option in elderly patients with osteoporosis because it has been associated with a lower risk of pelvic fractures compared with Amlodipine and Lisinopril.[10]

Compared with Doxazosin and Lisinopril, Chlorthalidone demonstrated superior efficacy in reducing cardiovascular events, including stroke incidence, while also showing greater effectiveness than Amlodipine in preventing heart failure.[11]

Calcium channel blockers CCBs

Similar to thiazide-type diuretics, Calcium Channel Blockers are recommended by the Eighth Joint National Committee as first-line therapy for hypertension, either as monotherapy or in combination with other antihypertensive agents, irrespective of age or race. However, in patients with chronic kidney disease, Angiotensin-Converting Enzyme Inhibitors or Angiotensin II Receptor Blockers are preferred as initial treatment options.[2]

Calcium Channel Blockers have been shown to reduce the risk of most cardiovascular events, with the exception of heart failure, to an extent comparable to thiazide diuretics. They are considered an effective alternative in patients who are unable to tolerate thiazide therapy.[6]

Calcium Channel Blockers are broadly classified into two categories: dihydropyridines and non-dihydropyridines.

Dihydropyridine Calcium Channel Blockers possess stronger vasodilatory effects and are therefore more commonly prescribed for the treatment of hypertension. They exert minimal effects on cardiac contractility and conduction, which further supports their use in blood pressure management. Nifedipine and Amlodipine are among the most frequently used agents in this class.

Non-dihydropyridine Calcium Channel Blockers exhibit weaker vasodilatory activity but have a greater influence on cardiac contractility and conduction. Consequently, they are more commonly used as antiarrhythmic agents and are prescribed less frequently for the management of hypertension.

In patients of African descent with hypertension and no evidence of heart failure or chronic kidney disease, initial antihypertensive therapy is recommended to include either a Calcium Channel Blockers or a thiazide diuretic.[6]

Long-acting Nifedipine has demonstrated a stronger antihypertensive effect compared with Amlodipine.[9]

Dihydropyridine Calcium Channel Blockers are not recommended as primary therapy for congestive heart failure; however, they may be safely used as adjunctive treatment in these patients to improve blood pressure control or manage angina pectoris.

Non-dihydropyridine Calcium Channel Blockers are relatively contraindicated in patients with congestive heart failure and reduced ejection fraction, as well as in those with second- or third-

degree atrioventricular block or sick sinus syndrome.

In comparative studies, Amlodipine demonstrated superior control of 24-hour ambulatory blood pressure compared with Valsartan. Furthermore, the Anglo-Scandinavian Cardiac Outcomes Trial reported that amlodipine was more effective than Atenolol in reducing cardiovascular risk and was associated with a lower incidence of new-onset diabetes.[12]

Compared with thiazide diuretics, Amlodipine demonstrated comparable efficacy in reducing cardiovascular risk across all body weight categories, whereas the effectiveness of thiazide diuretics appeared to be lower in patients with a normal body mass index than in those with obesity [13]

ACE inhibitors and ADRs

Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers are considered the preferred antihypertensive agents for patients with heart failure and chronic kidney disease. They are recommended as first-line therapy in individuals with chronic kidney disease accompanied by proteinuria. According to the Eighth Joint National Committee, these drug classes, together with thiazide diuretics and Calcium Channel Blockers, are recommended as initial treatment options for hypertension in non-Black patients.[2]

Beyond their blood pressure–lowering properties, these agents have been shown to provide cardioprotective benefits in patients at high risk of cardiovascular disease.

Both drug classes demonstrate comparable therapeutic efficacy and have similar clinical indications. They are recommended as first-line therapy for patients with left ventricular dysfunction and for those with ST-elevation or non-ST-elevation myocardial infarction, particularly in the presence of diabetes, systolic dysfunction, or anterior wall infarction.

Thiazide diuretics have demonstrated greater efficacy than Angiotensin-Converting Enzyme Inhibitors in reducing blood pressure and preventing stroke. Similarly, Calcium Channel Blockers have shown superior effectiveness over ACE inhibitors in lowering blood pressure and reducing the risk of stroke and heart failure.[6]

Ramipril has been demonstrated to reduce mortality, stroke incidence, and myocardial infarction in patients with symptomatic heart failure as well as in asymptomatic individuals with reduced ejection fraction. Studies have also shown that Perindopril lowers cardiovascular event rates in patients with stable coronary artery disease and preserved systolic function. In comparison with Atenolol, Losartan was associated with greater reductions in morbidity, mortality, and blood pressure levels.

Comparative studies between Ramipril and Telmisartan demonstrated similar therapeutic efficacy in patients with diabetes or heart failure, although telmisartan was associated with a lower incidence of angioedema.[14]

Beta – Blockers

Beta Blockers are generally not recommended as first-line therapy for hypertension unless there are specific clinical indications, such as heart failure or a history of myocardial infarction.[15]

Beta Blockers have been associated with reductions in cardiovascular morbidity and mortality in younger patients; however, their protective effect appears to be diminished in

individuals older than 65 years, with some studies reporting an increased risk of stroke in this population.[15][16][17]

Combination Therapy

In patients whose hypertension is not adequately controlled with monotherapy, combination antihypertensive therapy should be considered. The use of two antihypertensive agents is also recommended as a therapeutic approach for individuals with stage 2 hypertension.[6]

One study demonstrated that combining antihypertensive agents from two different drug classes produced an approximately fivefold greater reduction in blood pressure compared with doubling the dose of a single medication.[18]

Combinations involving an Angiotensin II Receptor Blockers with a diuretic or an Angiotensin-Converting Enzyme Inhibitors with a Calcium Channel Blockers have demonstrated greater efficacy compared with the combination of a Beta Blockers and a diuretic.[19]

The combination of a Beta Blockers with diuretics has been associated with an increased risk of diabetes mellitus. Therefore, such combinations are generally reserved for patients in whom beta-blockers are specifically indicated, including those with heart failure, tachycardia, or a history of myocardial infarction. Additionally, the combination of a thiazide diuretic with a potassium-sparing diuretic has demonstrated antihypertensive efficacy comparable to Calcium Channel Blockers monotherapy and has been associated with a lower incidence of hypokalemia compared with Hydrochlorothiazide monotherapy.[19]

Combination therapies involving Calcium Channel Blockers and diuretics are less commonly used, whereas combinations based on Angiotensin II Receptor Blockers or Angiotensin-Converting Enzyme Inhibitors are generally preferred when combination therapy is indicated. These ACE inhibitor– or ARB-based regimens are particularly recommended for patients with chronic kidney disease.[19] [20]

The combination of Benazepril and Amlodipine has been shown to be more effective than the combination of benazepril and Hydrochlorothiazide in reducing cardiovascular events among high-risk patients, while also slowing the progression of nephropathy.[21][22]

The combination of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers is not recommended because it has been associated with a higher incidence of adverse effects without providing additional clinical benefit.[14][23]

When dual antihypertensive therapy fails to achieve the target blood pressure, a third medication is typically added, usually from another first-line antihypertensive class such as thiazide-like diuretics, Calcium Channel Blockers, Angiotensin-Converting Enzyme Inhibitors, or Angiotensin II Receptor Blockers.

Failure to achieve blood pressure control with a three-drug regimen should prompt evaluation for resistant hypertension, with consideration given to adding a fourth antihypertensive agent from an alternative drug class.[19]

Loop Diuretics

Loop Diuretics are more effective than thiazide diuretics in patients with an estimated glomerular filtration rate below 30 mL/min. They are commonly indicated for the management of peripheral edema associated with congestive heart

failure as well as edema resulting from noncardiac conditions, including hepatic and renal disorders.[24]

Loop Diuretics are generally not recommended as first-line therapy for the management of hypertension.[25]

Potassium Sparing Diuretics

Mineralocorticoid Receptor Antagonists are generally not recommended as first-line agents for hypertension management. However, Spironolactone and Eplerenone have shown effectiveness as add-on therapy in patients with resistant hypertension, particularly when combined with a triple antihypertensive regimen. These agents should be used cautiously in combination with Angiotensin-Converting Enzyme Inhibitors or Angiotensin II Receptor Blockers because of the increased risk of hyperkalemia.[26][27]

Mineralocorticoid Receptor Antagonists are effective in the management of heart failure, as they have been shown to reduce mortality and lower the incidence of hypokalemia. In patients with resistant hypertension, Spironolactone demonstrated greater blood pressure–lowering efficacy than Doxazosin and Bisoprolol when used as an add-on to first-line antihypertensive therapy.[28]

Hydralazine

Hydralazine may be incorporated into the treatment regimen for resistant hypertension, either as monotherapy or in combination with nitrates in patients with heart failure. However, hydralazine therapy is associated with enhanced sympathetic activity and sodium retention; therefore, concomitant use of a Beta Blockers and Loop Diuretics may help mitigate these adverse effects.[9]

Clonidine

Clonidine is a centrally acting alpha-2 adrenergic agonist that is not generally recommended as first-line therapy for hypertension; however, it may be used as an adjunctive agent in patients who do not achieve adequate blood pressure control with combination therapy. The transdermal formulation is often preferred.[9]

Minoxidil

Minoxidil is generally considered in patients who do not respond adequately to Hydralazine therapy. Although it is effective in lowering blood pressure, its use is commonly associated with fluid retention, which may be managed with the addition of a Loop Diuretics. Minoxidil may also increase sympathetic activity, thereby necessitating concomitant therapy with a Beta Blockers.[9]

Alpha Blockers

Alpha Blockers are not recommended as first-line agents for the treatment of hypertension because they are less effective than other first-line antihypertensive therapies in reducing cardiovascular events.[6]

Mechanism of action

Thiazide and thiazide-like diuretics

Thiazide and thiazide-like diuretics primarily act on the distal tubule, where they inhibit sodium reabsorption by blocking the Na+/Cl− cotransporter, although a minor inhibitory effect on proximal tubular sodium handling has been reported [29]. Their antihypertensive effect initially reflects volume depletion with reduced cardiac

output; cardiac output typically returns to baseline within 6–8 weeks while blood pressure control persists, suggesting a compensatory autoregulatory process. Early treatment can transiently stimulate the renin–angiotensin system and increase systemic vascular resistance, which may blunt the acute antihypertensive response; this neurohormonal activation often diminishes with sustained thiazide therapy, and combining thiazides with an ACE inhibitor or ARB frequently improves blood pressure lowering. In addition, thiazide-type agents exert modest vasodilatory effects, although the precise mechanisms underlying this vasodilation remain incompletely defined.

Calcium channel blocker

Calcium channel blockers exert their effects by inhibiting cellular Ca2+ influx through L-type voltage-gated calcium channels in cardiac and vascular smooth muscle. Dihydropyridine CCBs predominantly produce peripheral vasodilation, whereas non-dihydropyridine agents have notable negative inotropic and chronotropic effects, suppressing sinoatrial and atrioventricular nodal activity and slowing myocardial contractility and conduction[30]

ACE inhibitors

ACE inhibitors lower blood pressure primarily by blocking angiotensin-converting enzyme, which reduces angiotensin II synthesis and concurrently decreases bradykinin breakdown; the resulting fall in angiotensin II and accumulation of bradykinin promote vasodilation[31]

ARBs

Angiotensin receptor blockers (ARBs) lower blood pressure by preventing angiotensin II from activating AT1 receptors, thereby blocking angiotensin II–mediated effects; unlike ACE inhibitors, ARBs do not alter kinin metabolism.

Beta blockers

Beta-adrenergic blockers antagonize catecholamine action at β1, β2, and β3 receptors. β1 receptors predominate in myocardium, β2 receptors are abundant in bronchial and vascular smooth muscle, and β3 receptors are present in cardiac adipose tissue. Cardioselective agents (for example, metoprolol, atenolol, betaxolol, and acebutolol) preferentially block β1 receptors and thus carry a lower risk of bronchospasm. By inhibiting β-receptor signaling, beta-blockers exert negative inotropic and chronotropic effects, reducing heart rate and myocardial oxygen demand [32]

Loop diuretics

Loop diuretics reduce blood pressure by inhibiting sodium reabsorption in the thick ascending limb of the loop of Henle (both medullary and cortical segments), promoting natriuresis and volume depletion [24].

Potassium-sparing diuretics

Potassium-sparing diuretics act on principal cells of the late distal tubule and collecting duct to reduce sodium reabsorption while conserving potassium and hydrogen ions. Spironolactone and eplerenone function as mineralocorticoid receptor antagonists, blocking aldosterone-mediated effects at these sites.

Hydralazine

Hydralazine is an arteriolar vasodilator that reduces vascular smooth muscle contractility by decreasing cytoplasmic Ca2+ availability, thereby inhibiting calcium-mediated contraction[33].

Clonidine

Clonidine activates α2-adrenergic receptors in the rostral ventrolateral medulla, diminishing central sympathetic outflow and lowering plasma norepinephrine levels, which in turn reduces cardiac output.

Minoxidil

Minoxidil acts as an arteriolar vasodilator by opening ATP-sensitive potassium channels in vascular smooth muscle, leading to membrane hyperpolarization and relaxation.

Alpha- blockers

Alpha-adrenergic antagonists block α1 receptors on vascular smooth muscle, reducing vasoconstriction and producing vasodilation. [34]

Administration

Thiazide-type diuretics are administered orally. Hydrochlorothiazide is commonly available in 12.5 mg and 25 mg tablet formulations, with a maximum recommended daily dose of 50 mg. Chlorthalidone is supplied in 25 mg and 50 mg tablets, and its daily dosage may be increased up to 100 mg when required.[29]

Dihydropyridine calcium channel blockers are administered through the oral route. Amlodipine is commonly prescribed with a maximum recommended daily dose of 10 mg.[35]

The extended-release formulation of Nifedipine can be administered up to a maximum daily dose of 120 mg.[36] Non-dihydropyridine calcium channel blockers are available in both oral and intravenous formulations. The intravenous form of Diltiazem is particularly useful for controlling heart rate in patients with cardiac arrhythmias, while its maximum recommended oral dose is 480 mg per day.[37] Verapamil is available in both oral and intravenous formulations. The intravenous preparation is commonly used in the management of tachyarrhythmias, particularly atrial fibrillation. The maximum recommended oral dose of verapamil is 480 mg per day.[38]

All angiotensin-converting enzyme (ACE) inhibitors are administered orally, except Enalapril, which is also available in an intravenous formulation.[31] In contrast, all angiotensin II receptor blockers (ARBs) are available only in oral dosage forms.[39]

Beta-blockers are available in both oral and intravenous formulations.[32]Loop diuretics are available in both oral and intravenous formulations, whereas potassium-sparing diuretics are primarily administered as oral dosage forms.[24]

Hydralazine can be administered through both oral and intravenous routes. The maximum recommended oral dose is 300 mg per day.[33]

The transdermal formulation of Clonidine is generally preferred, as oral administration may increase the risk of rebound hypertension.[9]

The maximum transdermal clonidine dose is 0.3 mg weekly, while the oral immediate-release form maximum dose is 0.3 mg three times daily. [40]

Minoxidil is administered orally in the treatment of hypertension. Similarly, alpha-blockers used for hypertension management are available only in oral dosage forms.[41]

Adverse Effects

Thiazides – Side Effects Thiazide and thiazide-like diuretics are associated with several adverse effects, many of which are dose-dependent. The most frequently observed metabolic disturbances

include hypokalemia and hyponatremia. Other important side effects include hyperuricemia, hypomagnesemia, hyperlipidemia, and elevated blood glucose levels.[42,29]

A study reported that Chlorthalidone was associated with a higher risk of hospitalization due to severe hypokalemia in elderly patients. Additional adverse effects that are not dose-dependent include sexual dysfunction and sleep disturbances.

CCB Side Effects

Treatment with dihydropyridine calcium channel blockers (CCBs) commonly causes peripheral edema. Among these agents, long-acting nifedipine has a greater tendency to produce edema compared to amlodipine, and the occurrence of edema increases with higher doses of the CCB. This edema is not caused by sodium or fluid retention and is not an indication of heart failure.[9]Because edema caused by calcium channel blockers (CCBs) is not due to an increase in body fluid volume, treatment with diuretics is usually ineffective. However, combining CCBs with ACE inhibitors or, to a lesser extent, ARBs has been shown to reduce the risk of peripheral edema. Dihydropyridine CCBs may also produce adverse effects such as dizziness, flushing, headache, and gingival hyperplasia. [30]

Non-dihydropyridine calcium channel blockers are commonly associated with bradycardia and may cause constipation in nearly 25% of patients.

Calcium channel blockers can also inhibit platelet aggregation, which may increase the risk of gastrointestinal bleeding. Therefore, these drugs should be used cautiously in elderly patients and in individuals who are at a greater risk of bleeding.

ACE Is and ARBs Side Effects

The predominant adverse effects associated with ACE inhibitors include persistent cough, low blood pressure, fatigue, and azotemia. Transient renal dysfunction is also frequently observed, particularly in patients who experience fluid loss due to conditions such as diarrhea or vomiting.

Cough is a common adverse effect observed in up to 20% of patients receiving ACE inhibitor therapy, and it may take approximately 14–28 days to resolve after discontinuation of treatment. The incidence of cough is lower with angiotensin receptor blockers (ARBs). Studies comparing Losartan with Hydrochlorothiazide reported a similar frequency of cough between the two drugs. ARBs are also considered safe in patients with asthma, as Candesartan was not associated with an increased incidence of cough when compared with calcium channel blockers. Furthermore, Ramipril demonstrated a higher occurrence of cough than Telmisartan.[14]

Treatment with angiotensin-converting enzyme (ACE) inhibitors is commonly associated with mild hyperkalemia. The risk of developing hyperkalemia is further increased in patients with renal impairment, diabetes mellitus, or congestive heart failure, even when baseline renal function is normal.[43] Ramipril and Telmisartan show comparable rates of hyperkalemia, acute kidney injury, and syncope. However, telmisartan has been associated with a higher incidence of symptomatic hypotension.[14]

Angioedema is an uncommon adverse effect associated with ACE inhibitor therapy and has been reported in approximately 0.3% of patients receiving Ramipril. In comparison, angiotensin receptor blockers (ARBs) are associated with a lower risk of angioedema than ACE inhibitors. [14]

In Black patients, angiotensin receptor blockers (ARBs) have been associated with a lower incidence of both cough and angioedema.[6]

Beta-Blockers – Side Effects

Common adverse effects associated with beta-blockers include bradycardia, constipation, depression, fatigue, and sexual dysfunction. These agents may also cause bronchospasm and aggravate symptoms of peripheral vascular disease. In addition, beta-blockers can precipitate or worsen Raynaud Syndrome.[32]`

Loop directics

Loop diuretics are commonly linked with electrolyte disturbances, particularly hypokalemia, hyponatremia, hypomagnesemia, and hypochloremia.[24] Other metabolic side effects of loop diuretics include dehydration, hyperuricemia, and hyperlipidemia. In some cases, treatment with loop diuretics may also lead to ototoxicity and hearing loss.[25]

Side effects of the Mineralocorticoid receptor antagonists:

The major adverse effect of mineralocorticoid receptor antagonists is hyperkalemia. These drugs may also produce metabolic acidosis by reducing the excretion of hydrogen ions. Additional side effects include erectile dysfunction and gynecomastia in men, as well as menstrual irregularities in women.

Hydralazine:

Hydralazine may produce adverse effects such as headache, flushing, palpitations, dizziness, and symptoms of hypotension, mainly due to stimulation of the sympathetic nervous system.[33]Hydralazine has also been linked to drug-induced lupus erythematosus, hemolytic anemia, and various other immune-mediated reactions.[33]

Clonidine

Common adverse effects of clonidine include drowsiness, headache, dizziness, irritability, nausea, vomiting, constipation, upper abdominal discomfort, and bradycardia. In rare cases, serious reactions such as angioedema, atrioventricular block, and severe hypotension may also occur.[40]

Minoxidil

Minoxidil treatment is commonly associated with hirsutism, characterized by excessive hair growth.[44]

Alpha-blockers

Alpha-blockers may cause tachycardia and orthostatic hypotension due to venous dilation.[34]

Contraindication

Thiazide-type diuretics are contraindicated in anuric patients and in those with known sulfonamide hypersensitivity[29].

Calcium channel blockers are contraindicated in patients with a known hypersensitivity to these agents[30]. Non-dihydropyridine calcium channel blockers are contraindicated in patients with heart failure or reduced left ventricular ejection fraction, sick sinus syndrome, and second- or third-degree atrioventricular block.[30] Dihydropyridine calcium channel blockers should be avoided in cardiogenic shock, severe aortic stenosis, and unstable angina. Caution is also advised when prescribing these agents in patients with hepatic impairment[36][35]

ACE inhibitors are contraindicated in patients with prior hypersensitivity to these agents, a history of ACE inhibitor–associated angioedema or other

forms of angioedema, pregnancy, or concurrent use of aliskiren.[45] Relative contraindications include volume depletion, impaired renal function, and aortic valve stenosis.[45] ARBs are contraindicated in pregnancy[39]. Concomitant use of ACE inhibitors and ARBs is generally discouraged. Relative contraindications to ARB therapy include volume depletion, concomitant use of agents that increase serum potassium, and impaired renal function[39].

Beta-adrenergic antagonists are contraindicated in patients with asthma, particularly with nonselective agents. Relative contraindications include hypotension and bradycardia, and some clinicians advise avoiding beta-blockers in the setting of cocaine-induced coronary vasospasm .[32]

Loop diuretics are contraindicated in individuals with sulfonamide hypersensitivity, in anuric patients, and in those with hepatic coma.[24]

Potassium-sparing diuretics should not be used in patients with chronic kidney disease or preexisting hyperkalaemia, and they require caution when coadministered with ACE inhibitors, ARBs, or aliskiren[46].This drug class is contraindicated in patients with a known hypersensitivity to its agents.

Clonidine is contraindicated in individuals with hypersensitivity to alpha-2 agonists and should be used with caution or avoided in patients with depression or those who have recently experienced a myocardial infarction. [40]

Hydralazine is contraindicated in individuals with a documented hypersensitivity to the drug. It may provoke sympathetic activation in patients with coronary artery disease, and in those with rheumatic mitral valve disease it can raise pulmonary artery pressure[47][33].

Minoxidil is contraindicated in pregnant and breastfeeding women and in patients with known hypersensitivity to the drug[44].

Alpha-adrenergic blockers are contraindicated in patients with a history of orthostatic hypotension and in those concurrently taking phosphodiesterase inhibitors.[41]

Monitoring

Thiazide and loop diuretics frequently produce hypokalaemia, whereas potassium-sparing agents are associated with hyperkalaemia [24][29]. Patients taking diuretics require regular electrolyte monitoring, and those on thiazide or loop diuretics should also have serum uric acid checked[24][26]. Patients receiving loop diuretics should be assessed for ototoxic effects, including hearing loss, as part of routine monitoring [24].

Hyperkalaemia is a recognized complication of ACE inhibitor and ARB therapy, and the risk is amplified when these drugs are coadministered with potassium-sparing diuretics. In patients with chronic kidney disease, serum potassium should be monitored closely when prescribing ACE inhibitors, ARBs, or potassium-sparing agents [39]. ACE inhibitors and ARBs can precipitate acute kidney injury; therefore renal function should be monitored regularly during treatment [45][39].

Patients treated with dihydropyridine calcium channel blockers should be monitored for hypotension and peripheral oedema. Heart-rate surveillance is important with non-dihydropyridine CCBs and beta-blockers because both classes can cause bradycardia, particularly when used together. Additionally, QTc monitoring is indicated for patients receiving sotalol .[30][32]

Patients prescribed alpha-adrenergic antagonists should be monitored for orthostatic hypotension and the emergence of tachyarrhythmias [34][41].

When patients are treated with hydralazine, periodic complete blood counts and antinuclear antibody testing are recommended.[33] Heightened vigilance is warranted if patients develop arthralgia, fever, or other systemic symptoms, as these may signal serious adverse effects [48]

Toxicity

Thiazide and loop diuretic toxicity commonly produces electrolyte disturbances—primarily hypokalaemia and hyponatremia—and can lead to hyperchloremic metabolic alkalosis and marked volume depletion. No specific antidotes exist; management is supportive, focusing on fluid resuscitation and correction of electrolyte imbalances.[24]

Toxicity from potassium-sparing diuretics typically manifests as significant hyperkalaemia. Management involves discontinuing agents that raise serum potassium, initiating IV fluids, and administering stabilizing and shifting therapies such as IV calcium gluconate, IV insulin with glucose, and sodium bicarbonate as indicated, along with potassium-binding resins or other removal strategies[46].

Non-dihydropyridine calcium channel blocker overdose primarily impairs myocardial contractility and conduction, producing bradycardia, hypotension, and potentially complete heart block or idioventricular rhythms. Dihydropyridine toxicity mainly produces profound peripheral vasodilation with marked hypotension and less direct chronotropic effect. Initial management includes IV fluid resuscitation for hypotension, IV atropine or temporary transcutaneous/transvenous pacing for bradycardia, and IV calcium chloride or calcium gluconate if hemodynamic status does not respond to fluids. If hypotension persists, vasopressor support should be considered.[30]

ACE inhibitor and ARB overdose may produce marked hypotension, hyperkalaemia, and hyponatraemia. There are no specific antidotes; treatment is supportive with intravenous fluids and appropriate measures to manage hyperkalaemia. [31]

Beta-blocker overdose, similar to calcium channel blocker toxicity, typically produces hypotension and bradycardia and can progress to second- or third-degree atrioventricular block. Initial therapy includes IV glucagon; additional supportive measures such as fluid resuscitation and temporary pacing may be required if patients do not respond.[32]

Hydralazine overdose may produce profound hypotension, reflex tachycardia, and cutaneous flushing, and in severe instances can progress to cardiogenic shock or myocardial ischemia. No specific antidote exists; management is supportive with IV fluids and vasopressors for refractory hypotension, and beta-blockers may be employed to control marked tachycardia.[33]

Clonidine overdose typically presents with lethargy, hypotension, bradycardia, and miosis, and may progress to respiratory depression in severe cases. Management is supportive, including IV fluids and vasopressors (commonly dopamine or norepinephrine); IV atropine can be used for significant bradycardia, and temporary pacing reserved for atropine-refractory cases.[49]

Minoxidil overdose typically produces tachycardia and hypotension; treatment is supportive, focusing on IV fluids and vasopressor therapy as needed.[44]

Alpha-adrenergic antagonist overdose can result in profound hypotension; management is supportive, with IV fluid resuscitation and vasopressor therapy as first-line measures.[50]

REFERENCES

1. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, Chalmers J, Rodgers A, Rahimi K. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet. 2016 Mar 05;387(10022):957-967. [PubMed]
2. Armstrong C., Joint National Committee. JNC8 guidelines for the management of hypertension in adults. Am Fam Physician. 2014 Oct 01;90(7):503-4. [PubMed]
3. Messerli FH, Bangalore S. Antihypertensive efficacy of aliskiren: is hydrochlorothiazide an appropriate benchmark? Circulation. 2009 Jan 27;119(3):371-3. [PubMed]
4. Ernst ME, Carter BL, Goerdt CJ, Steffensmeier JJ, Phillips BB, Zimmerman MB, Bergus GR. Comparative antihypertensive effects of hydrochlorothiazide and chlorthalidone on ambulatory and office blood pressure. Hypertension. 2006 Mar;47(3):352-8. [PubMed]
5. Olde Engberink RH, Frenkel WJ, van den Bogaard B, Brewster LM, Vogt L, van den Born BJ. Effects of thiazide-type and thiazide-like diuretics on cardiovascular events and mortality: systematic review and meta-analysis. Hypertension. 2015 May;65(5):1033-40. [PubMed]
6. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA, WilliamsonJD,WrightJT.2017ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018 Jun;71(6):e13-e115. [PubMed]
7. Kaplan NM. Chlorthalidone versus hydrochlorothiazide: a tale of tortoises and a hare. Hypertension. 2011 Dec;58(6):994-5. [PubMed]
8. Finkielman JD, Schwartz GL, Chapman AB, Boerwinkle E, Turner ST. Lack of agreement between office and ambulatory blood pressure responses to hydrochlorothiazide. Am J Hypertens. 2005 Mar;18(3):398-402. [PubMed]
9. Carey RM, Calhoun DA, Bakris GL, Brook RD, Daugherty SL, Dennison-Himmelfarb CR, Egan BM, Flack JM, Gidding SS, Judd E, Lackland DT, Laffer CL, Newton-Cheh C, Smith SM, Taler SJ, Textor SC, Turan TN, White WB., American Heart Association Professional/Public Education and Publications Committee of the Council on Hypertension; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Genomic and Precision Medicine; Council on Peripheral Vascular Disease; Council on Quality of Care and Outcomes Research; and Stroke Council. Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. Hypertension. 2018 Nov;72(5):e53-e90. [PMC free article] [PubMed]
10. Puttnam R, Davis BR, Pressel SL, Whelton PK, Cushman WC, Louis GT, Margolis KL,

Oparil S, Williamson J, Ghosh A, Einhorn PT, Barzilay JI., Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) Collaborative Research Group. Association of 3 Different Antihypertensive Medications With Hip and Pelvic Fracture Risk in Older Adults: Secondary Analysis of a Randomized Clinical Trial. JAMA Intern Med. 2017 Jan 01;177(1):67-76. [PubMed]

11. Wright JT, Probstfield JL, Cushman WC, Pressel SL, Cutler JA, Davis BR, Einhorn PT, Rahman M, Whelton PK, Ford CE, Haywood LJ, Margolis KL, Oparil S, Black HR, Alderman MH., ALLHAT Collaborative Research Group. ALLHAT findings revisited in the context of subsequent analyses, other trials, and meta-analyses. Arch Intern Med. 2009 May 11;169(9):832-42. [PMC free article] [PubMed]
12. Dahlöf B, Sever PS, Poulter NR, Wedel H, Beevers DG, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E, Ostergren J., ASCOT Investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. Lancet. 2005 Sep 10-16;366(9489):895-906. [PubMed]
13. Weber MA, Jamerson K, Bakris GL, Weir MR, Zappe D, Zhang Y, Dahlof B, Velazquez EJ, Pitt B. Effects of body size and hypertension treatments on cardiovascular event rates: subanalysis of the ACCOMPLISH randomised controlled trial. Lancet. 2013 Feb 16;381(9866):537-45. [PubMed]
14. ONTARGET Investigators. Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, Dagenais G, Sleight P, Anderson C. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med. 2008 Apr 10;358(15):1547-59. [PubMed]
15. Khan N, McAlister FA. Re-examining the efficacy of beta-blockers for the treatment of hypertension: a meta-analysis. CMAJ. 2006 Jun 06;174(12):1737-42. [PMC free article] [PubMed]
16. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure-lowering treatment on cardiovascular outcomes and mortality: 14 - effects of different classes of antihypertensive drugs in older and younger patients: overview and meta-analysis. J Hypertens. 2018 Aug;36(8):1637-1647. [PubMed]
17. Lindholm LH, Carlberg B, Samuelsson O. Should beta blockers remain first choice in the treatment of primary hypertension? A meta-analysis. 2005 Oct 29-Nov 4Lancet. 366(9496):1545-53. [PubMed]
18. Wald DS, Law M, Morris JK, Bestwick JP, Wald NJ. Combination therapy versus monotherapy in reducing blood pressure: meta-analysis on 11,000 participants from 42 trials. Am J Med. 2009 Mar;122(3):290-300. [PubMed]
19. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I., ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018 Sep 01;39(33):3021-3104. [PubMed]
20. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie TD, Ogedegbe

O, Smith SC, Svetkey LP, Taler SJ, Townsend RR, Wright JT, Narva AS, Ortiz E. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014 Feb 05;311(5):507-20. [PubMed]

21. Jamerson K, Weber MA, Bakris GL, Dahlöf B, Pitt B, Shi V, Hester A, Gupte J, Gatlin M, Velazquez EJ., ACCOMPLISH Trial Investigators. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. N Engl J Med. 2008 Dec 04;359(23):2417-28. [PubMed]
22. Bakris GL, Sarafidis PA, Weir MR, Dahlöf B, Pitt B, Jamerson K, Velazquez EJ, Staikos-Byrne L, Kelly RY, Shi V, Chiang YT, Weber MA., ACCOMPLISH Trial investigators. Renal outcomes with different fixed-dose combination therapies in patients with hypertension at high risk for cardiovascular events (ACCOMPLISH): a prespecified secondary analysis of a randomised controlled trial. Lancet. 2010 Apr 03;375(9721):1173-81. [PubMed]
23. Phillips CO, Kashani A, Ko DK, Francis G, Krumholz HM. Adverse effects of combination angiotensin II receptor blockers plus angiotensin-converting enzyme inhibitors for left ventricular dysfunction: a quantitative review of data from randomized clinical trials. Arch Intern Med. 2007 Oct 08;167(18):1930-6. [PubMed]
24. Huxel C, Raja A, Ollivierre-Lawrence MD. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 22, 2023. Loop Diuretics. [PubMed]
25. Sica DA, Carter B, Cushman W, Hamm L. Thiazide and loop diuretics. J Clin Hypertens (Greenwich). 2011 Sep;13(9):639-43. [PMC free article] [PubMed]
26. Chapman N, Dobson J, Wilson S, Dahlöf B, Sever PS, Wedel H, Poulter NR., Anglo-Scandinavian Cardiac Outcomes Trial Investigators. Effect of spironolactone on blood pressure in subjects with resistant hypertension. Hypertension. 2007 Apr;49(4):839-45. [PubMed]
27. Khosla N, Kalaitzidis R, Bakris GL. Predictors of hyperkalemia risk following hypertension control with aldosterone blockade. Am J Nephrol. 2009;30(5):418-24. [PubMed]
28. Williams B, MacDonald TM, Morant S, Webb DJ, Sever P, McInnes G, Ford I, Cruickshank JK, Caulfield MJ, Salsbury J, Mackenzie I, Padmanabhan S, Brown MJ., British Hypertension Society's PATHWAY Studies Group. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. Lancet. 2015 Nov 21;386(10008):2059-2068. [PMC free article] [PubMed]
29. Patel P, Preuss CV. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 6, 2025. Thiazide Diuretics. [PubMed]
30. McKeever RG, Patel P, Hamilton RJ. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Feb 22, 2024. Calcium Channel Blockers. [PubMed]
31. Herman LL, Padala SA, Ahmed I, Bashir K. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 31, 2023. Angiotensin-Converting Enzyme Inhibitors (ACEI) [PMC free article] [PubMed]
32. Farzam K, Jan A. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Aug 22, 2023. Beta Blockers. [PubMed]
33. Herman LL, Bruss ZS, Tivakaran VS. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Mar 28, 2023. Hydralazine. [PubMed]

34. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. National Institute of Diabetes and Digestive and Kidney Diseases; Bethesda (MD): Jan 8, 2018. Alpha 1 Adrenergic Receptor Antagonists. [PubMed]
35. Bulsara KG, Patel P, Cassagnol M. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Apr 21, 2024. Amlodipine. [PubMed]
36. Khan KM, Patel JB, Patel P. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 6, 2025. Nifedipine. [PubMed]
37. Talreja O, Cassagnol M. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Aug 28, 2023. Diltiazem. [PubMed]
38. Fahie S, Cassagnol M. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Feb 6, 2023. Verapamil. [PubMed]
39. Patel P, Launico MV. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 5, 2025. Angiotensin II Receptor Blockers (ARB) [PubMed]
40. Patel P, Saadabadi A. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Dec 13, 2025. Clonidine. [PubMed]
41. Taylor BN, Cassagnol M. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 10, 2023. Alpha-Adrenergic Receptors(Archived) [PubMed]
42. Leung AA, Wright A, Pazo V, Karson A, Bates DW. Risk of thiazide-induced hyponatremia in patients with hypertension. Am J Med. 2011 Nov;124(11):1064-72. [PubMed]
43. Desai AS, Swedberg K, McMurray JJ, Granger CB, Yusuf S, Young JB, Dunlap ME, Solomon SD, Hainer JW, Olofsson B, Michelson EL, Pfeffer MA., CHARM Program Investigators. Incidence and predictors of hyperkalemia in patients with heart failure: an analysis of the CHARM Program. J Am Coll Cardiol. 2007 Nov 13;50(20):1959-66. [PubMed]
44. Patel P, Nessel TA, Kumar D D. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Feb 24, 2023. Minoxidil. [PubMed]
45. Singh B, Cusick AS, Goyal A, Patel P. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 4, 2025. ACE Inhibitors. [PubMed]
46. Almajid AN, Patel P, Cassagnol M. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Feb 28, 2024. Amiloride. [PubMed]
47. Kandler MR, Mah GT, Tejani AM, Stabler SN, Salzwedel DM. Hydralazine for essential hypertension. Cochrane Database Syst Rev. 2011 Nov 09;(11):CD004934. [PubMed]
48. Iyer P, Dirweesh A, Zijoo R. Hydralazine Induced Lupus Syndrome Presenting with Recurrent Pericardial Effusion and a Negative Antinuclear Antibody. Case Rep Rheumatol. 2017;2017:5245904. [PMC free article] [PubMed]
49. Manzon L, Nappe TM, DelMaestro C, Maguire NJ. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jun 26, 2023. Clonidine Toxicity(Archived) [PubMed]
50. Yang CH, Raja A. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Mar 13, 2023. Terazosin. [PubMed]

HOW TO CITE: K. Arun, P. Haripriya, A. Harikrishnan, T. Madhan, S. Shobhana, V. Harini, Comprehensive Review of Antihypertensive Agents: Mechanisms, Therapeutic Guidelines, And Adverse Effects, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 6, 4126-4142. https://doi.org/ 10.5281/zenodo.20729692