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Review Article

Common Adverse Effect of Drugs Used to Treat Hypertension

Snehal Chavhan*, Amruta Bavne, Dr Swati Deshmukh

Shradhha institute of Pharmacy, Kondala Zambre, Washim 444505.

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ABSTRACT

One of the main preventable risk factors for cardiovascular disease is hypertension, which is an increase in systemic arterial blood pressure. As people age, hypertension becomes more common and more severe. Seventy percent of persons aged 65 and older suffer from hypertension, according to the U.S. National Health and Nutrition Examination Survey. Which includes stroke, heart failure, chronic kidney disease, and lowering the blood pressure by antihypertensive drug treatment. Reducing sodium intake, losing weight if the patient is overweight, and getting regular exercise. Drink water and eat potassium-rich food, all recommended lifestyle changes. The antihypertensive medication should be chosen for treatment of hypertension: diuretics (thiazides), ACE inhibitors, calcium channel blockers, and beta-adrenergic blockers.

INTRODUCTION

Hypertension is defined as increase in systolic and diastolic blood pressure or both above normal range it defined persistently high blood pressure.[1] High blood pressure is called as hypertension it causes the serious health problem and increase the risk of heart disease, stroke and even death .Dietary factors and physical in activity contribute to the genetic predisposition, while environmental factors including, drinking, obesity and alcohol, thus making hypertension a preventable cause of morbidity and mortality.[2]The advantages of populations with

hypertension leading a healthy lifestyle cannot be stressed enough, and this includes a controlled diet and regular exercise. The primary goal of treatment is to abolish the risks factors associated with hypertension, without reducing the patient's quality of life. Drugs used for study in hypertension are hydrochlorothiazide, propranolol, amlodipine, nifedipine, prazosin, telmisartan, and losartan.

Adverse effects of the drug:

- Hypokalaemia
- Hypercalcemia

***Corresponding Author:** Snehal Chavhan

Address: Shradhha institute of Pharmacy, Kondala Zambre, Washim 444505.

Email ✉: snehalchavhan68@gmail.com

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- Hyponatremia
- Dehydration
- Hyperglycaemia

Types of Hypertensions:

1. Primary (Essential Hypertension):

Essential hypertension affects approximately 95% of individuals with high blood pressure. There is no recognized medical etiology for this disease. Although it can start earlier, elevated blood pressure typically manifests between the ages of 30 and 50. Essential hypertensive patients typically don't have any symptoms, however they could get regular headaches, fatigue, light-headedness, or nosebleeds. Although the exact origin of essential hypertension is unknown, nutrition, smoking, obesity, and alcohol usage may all be contributing factors.

2. Secondary Hypertension:

This condition affects 5–10% of individuals with high blood pressure. There is a known reason for this syndrome. The most frequent reason for secondary hypertension is an anomaly in the kidney's blood vessel. Additional causes include nosebleeds, disorders and tumours of the adrenal glands, and obstruction of the airway while you sleep. High blood pressure in certain individuals is brought on by an underlying illness. Secondary hypertension is the term for this kind of elevated blood pressure. Secondary hypertension typically results in greater blood pressure than original hypertension and tends to manifest abruptly. Secondary hypertension can result from a number of illnesses and drugs, including such as:

1. Conditions such obstructive sleep apnea, thyroid issues, renovascular disease, kidney issues, and tumours of the adrenal glands.

2. Intoxication, as seen in the use of illegal drugs like cocaine and amphetamines, as well as acute or chronic alcohol consumption.
3. Iatrogenic reasons brought on by specific pharmaceuticals, including decongestants, birth control pills, over-the-counter painkillers, cold treatments, and some prescription medications.
4. Congenital abnormalities that result in blood vessel malformations.

3. Systolic Hypertension Isolated:

Here, the diastolic blood pressure is consistently less than 90 mm Hg and the systolic is consistently around 160 mm Hg. This can happen to elderly adults and is caused by the arteries becoming stiffer with age. Arteriosclerosis is the primary cause of arteries, such as the aorta, losing their flexibility. The underlying cause is said to be the Western food and way of life.

4. Malignant Hypertension:

The most dangerous type of hypertension is malignant hypertension. It is characterized by a dangerously abrupt increase in blood pressure. Frequently, diastolic pressure exceeds 130 mm Hg or greater. However, if the increase is very abrupt, malignant hypertension can also happen at lower, less concerning levels. Malignant hypertension, in contrast to other types of high blood pressure, is typically accompanied by severe symptoms headache, dyspnoea, chest discomfort, nausea, vomiting, impaired vision, or even blindness, convulsions, and unconsciousness. Malignant hypertension is a life-threatening illness. Malignant hypertension patients need to be admitted to the hospital right away. People are instantly at danger for heart attacks, strokes, heart failure, irreversible kidney damage, haemorrhagic



strokes, and brain enlargement. Less than 1% of individuals with high blood pressure go on to develop malignant hypertension. Malignant hypertension is rarely the initial indication that a person has excessive blood pressure. Although the etiologic of this ailment is typically unknown, it can occasionally be attributed to the body's reaction to quitting a blood pressure medication or to substance addiction, such as cocaine.

5. Resistant Hypertension:

If a triple-drug antihypertensive medication regimen fails to reduce blood pressure to less than 140/90 mm Hg, the condition is referred to as resistant hypertension. Resistance to hypertension may develop in 20–30% of cases of high blood pressure. Obese women, older adults, and people with underlying medical disorders like diabetes or kidney disease are more likely to have it. There might be a genetic component as well.

6. Hypertension During Pregnancy:

Between 6% and 8% of pregnancies result in high blood pressure, and in the majority of these cases, the diagnosis is made during the first trimester. High blood pressure during pregnancy can be brought on by hormonal changes or by preeclampsia, a dangerous pregnancy complication that includes artery tightness in the mother and placenta as well as erratic blood clotting.

Risk factor:

Although the precise causes of high blood pressure are unknown, a number of Circumstances and events could contribute to its development, such as:

- Smoking
- Being overweight or obese

- Not exercising
- Eating a diet high in salt
- Drinking too much alcohol
- Being stressed
- Having a family history of high blood pressure
- Having chronic renal failure
- Thyroid problems.

Secondary hypertension is common in individuals with renal problem. The body's salt and water balance is controlled by the kidneys. The blood pressure rises if the kidneys are unable to eliminate too much water and salt from the body. The salt and water balance can be upset by kidney infections, renal artery stenosis, a constriction of the arteries supplying blood to the kidneys, and other kidney diseases. Hypertension can result from elevated level of adrenal gland hormones, such as cortisol, adrenaline, and aldosterone, which are frequently caused by Cushing's disease and pituitary and adrenal gland tumours. Hypertension can be brought on by a number of medications, including birth control pills, decongestants, cold treatments, over-the-counter pain relievers, and some prescription pharmaceuticals; illegal drugs, including cocaine and amphetamines; persistent alcohol use; obstructive sleep apnea and pregnancy.

Pathophysiology of Hypertension:

Age-related increases in arterial stiffness are a major factor in the development of hypertension in the elderly. The gradual mechanical senescence of the elastic network, changes in the cross-linking of extracellular matrix components, fibrosis, and calcification of Elastic fibres are thought to be the causes of the increased stiffness. Large arteries



capacitance is decreased and pulse wave velocity is increased when they harden. A pressure (pulse) wave is produced during ventricular systole and moves from the heart periphery at a pace (referred to as pulse wave velocity) that is determined by the conduit arteries' elastic characteristics. The reflected wave reaches the aortic valve before to closure when the wave velocity is significantly increase (>13 m/s). This lowers diastolic blood pressure while increasing systolic, afterload blood pressure. This phenomenon explains why older adults frequently have higher systolic and pulse blood pressures and lower diastolic blood pressures (isolate systolic hypertension) than younger adults. Another significant factor raising blood pressure in the elderly is endothelial dysfunction. Vasoconstrictors like endothelin-1 rise with age, and the bioavailability of the vasodilator nitric oxide declines. Increased arterial stiffness and the emergence of isolated systole hypertension has been linked to these metabolic alterations. It has been proposed that arterial stiffness and diastolic dysfunction, left atrial remodelling, and consequent cardiovascular risk are related in a potentially significant way. According to Abhaya Ratna et al., greater arterial stiffness was linked to more severe left ventricular diastolic dysfunction (LVDD) in an aged group that had a clinical profile of being at high-risk for cardiovascular events. The latter condition is a major predictor of cardiovascular events and incident heart failure and is frequently observed in the community, particularly among older adults. According to reports, the most significant risk factor for LVDD in the general population is hypertension. Crucially, LVDD is thought to represent a crucial connection between heart failure and hypertension, especially in patients who have both heart failure and a preserved left ventricular ejection fraction.

Hypertension symptoms include:

1. Light-headedness
2. Blurred eyesight
3. Pain in the chest
4. Bleeding nose
5. Experiencing nausea and vomiting
6. Exhaustion

Treatment:

Antihypertensive agents A class of medications known as antihypertensives is used to treat hypertension (high blood pressure). Antihypertensive Therapy aims to stop the effects of high blood pressure, such as myocardial infarction, stroke, Heart failure, and kidney failure. According to the evidence, lowering blood pressure by 5 Mm/hg can decrease the risk of stroke by 34%, ischemic heart disease by 21%, dementia, Heart failure, and cardiovascular disease mortality. Antihypertensives come in a variety of Classes and work to reduce blood pressure in various ways. Research Through innovation Thiazide diuretics, calcium channel blockers, ACE inhibitors, angiotensin II receptor Antagonists (arbs), and beta blockers are some of the most significant and popular Medicines.

Treatment of Hypertension:

1. Diuretics

A. Thiazide & Thiazide-like Diuretics

- Hydrochlorothiazide
- Chlorthalidone
- Indapamide

B. Loop (High-Ceiling) Diuretics



- Furosemide
- Bumetanide
(Used when renal function is poor or for edema with hypertension)

C. Potassium-Sparing Diuretics

- Amiloride
- Spironolactone
- Eplerenone

2. Beta-Adrenergic Blockers (β -Blockers)

- Metoprolol (β_1 -selective)
- Atenolol
- Propranolol (non-selective)
- Nebivolol (β_1 -selective + nitric oxide-mediated vasodilation)
(Useful in young patients, post-MI, or with arrhythmias)

3. Alpha-Adrenergic Blockers (α_1 -Blockers)

- Prazosin
- Terazosin
- Doxazosin
(Also beneficial in patients with hypertension + benign prostatic hyperplasia)

4. Calcium Channel Blockers (CCBs)

Dihydropyridines (mainly vasodilators):

- Amlodipine
- Nifedipine

Non-dihydropyridines (reduce heart rate):

- Diltiazem
- Verapamil

5. Angiotensin II Receptor Blockers (ARBs)

- Losartan
- Irbesartan
- Telmisartan
- Valsartan
- Candesartan
- Olmesartan

6. Angiotensin-Converting Enzyme Inhibitors (ACEIs)

- Enalapril
- Lisinopril
- Ramipril
- Perindopril

(ACEIs and ARBs are not used together.)

Firstline Drug Treatment:

1. Furosemide

Class: Loop Diuretic

Mechanism of Action:

Furosemide inhibits tubular reabsorption of sodium and chloride in the proximal and distal tubules and the thick ascending loop of Henle by inhibiting the sodium-chloride cotransport system resulting in excessive excretion of water along with sodium, chloride, magnesium, and calcium.

Administration:



Furosemide is available in oral and intravenous formulations. The administration of oral furosemide can be in the form of tablets or an oral solution. Intravenous furosemide is twice as potent as oral furosemide. In patients with normal renal function, the oral dose equivalence of furosemide relative to other oral diuretics is as follows:

- 40 mg of furosemide = 20 mg of torsemide = 1 mg of bumetanide
- Furosemide oral tablet formulations are available in 20 mg, 40 mg, and 80 mg.
- Furosemide oral solution is available as 10 mg/ml or 8 mg/ml, i.e., 40 mg furosemide/5 ml of solution.

Adverse Effects:

Adverse reactions are categorized below by the system organ classification system(soc) and listed by decreasing severity. The following are potential adverse effects associated with furosemide use:

Gastrointestinal System

- Hepatic encephalopathy in patients with cirrhosis
- Pancreatitis
- Jaundice (intrahepatic cholestatic jaundice)
- Increased liver enzymes
- Anorexia
- Oral and gastric irritation
- Cramping
- Diarrhoea
- Constipation
- Nausea

- Vomiting

Systemic Hypersensitivity Reactions

- Severe anaphylactic or anaphylactoid reactions (e.g., with shock)
- Systemic vasculitis
- Interstitial nephritis
- Necrotizing angitis

Central Nervous System

- Ototoxicity
- Paresthesias
- Vertigo
- Dizziness
- Headache
- Blurred vision
- Xanthopsia

Hematologic Reactions

- Aplastic anemia
- Thrombocytopenia
- Agranulocytosis
- Hemolytic anemia
- Leukopenia
- Anemia
- Eosinophilia

Dermatologic-hypersensitivity Reactions



- Toxic epidermal necrolysis
- Stevens-johnson syndrome
- Erythema multiforme
- Drug rash with eosinophilia and systemic symptoms
- Acute generalized exanthematous pustulosis
- Exfoliative dermatitis
- Bullous pemphigoid
- Purpura
- Photosensitivity
- Rash
- Pruritus
- Urticaria

Cardiovascular System

- Alcohol, barbiturates, or narcotics may aggravate orthostatic hypotension.
- Increase in cholesterol and triglyceride serum levels

Renal Disorders

- Acute kidney injury due to fluid loss

Metabolic Disorders

- Hyperglycaemia
- Hyperuricemia
- Hypokalaemia
- Hypomagnesemia

Contraindications

- Contraindications to furosemide use include patients with documented allergies to furosemide and patients with anuria.
- A boxed warning suggests the cautious use of furosemide as it is a potent diuretic, which can predispose to excessive loss of water and electrolytes, resulting in dehydration with electrolyte depletion.
- According to Beers Criteria, caution is necessary when administering diuretics to patients 65 years and older to avoid potential adverse effects of inducing hyponatremia by causing or exacerbating syndrome of inappropriate antidiuretic hormone secretion (SIADH); therefore, close monitoring of serum sodium is advisable at initiation or during the dose adjustment in older adults.
- Ototoxicity can occur with the use of furosemide, but the following conditions predispose patients to a higher risk of reversible or irreversible hearing impairment:
 - Use of a higher than the recommended dose of furosemide or a fast infusion rate of the drug,
 - Hypoalbuminemia comorbid illnesses
 - The concomitant use of ethacrynic acid, aminoglycosides, or other ototoxic drugs
 - Patients with underlying severe renal impairment
- Caution is also necessary for patients with underlying liver disease, especially those with decompensated liver disease, as rapid electrolytes imbalance secondary to furosemide use can precipitate hepatic encephalopathy and hepatic coma. In patients



with hepatic coma, the prescriber should delay giving furosemide until there is an improvement in the patient's mental status.

- Patients with the advanced renal disease with fluid overload should be closely monitored for oliguria, azotemia, and volume status. If either oliguria or azotemia develops, furosemide should be discontinued to prevent kidney injury.
- In patients with primary adrenal insufficiency with hypertension, diuretics are a practice clinicians should avoid to treat hypertension. Alternatively, the dosage of glucocorticoid/mineralocorticoid requires adjustment, and, if needed, the Clinician should prefer other classes of antihypertensive agents over diuretics to treat hypertension.
- High-risk patients for radiocontrast-induced nephropathy are more predisposed to having a worsened kidney function if furosemide is given before contrast administration than high-risk patients receiving gentle hydration before contrast exposure.
- Patients with a known history of urinary retention due to, for example, benign prostatic hyperplasia, neurogenic bladder with bladder evacuation abnormalities, or urethral and ureteral strictures should be observed closely during the initial days of furosemide treatment. After that, they require observation for worsening symptoms as excessive diuresis and urine retention can lead to acute urinary retention leading to acute kidney injury.
- The risk of hypokalemia increases with a high dose of furosemide, decreased oral potassium intake in patients with hyperaldosteronism states (liver abnormalities or licorice

ingestion), or concomitant use of corticosteroid, ACTH, and laxatives.

- Furosemide at high doses, i.e., more than 80 mg per day, inhibits thyroid hormone binding to thyroid binding protein leading to a transient increase in free thyroid hormones that subsequently causes a mild decrease in total thyroid hormone.

How to overcome adverse effect of Furosemide

Careful monitoring of the patient's clinical condition, daily weight, fluids intake, urine output, electrolytes, i.e., potassium and magnesium, kidney function monitoring with serum creatinine and serum blood urea nitrogen level is vital to monitor the response of furosemide. For example, if indicated for diuresis with furosemide, replete electrolytes lead to electrolyte depletion, and adjust the dose or even hold off on furosemide if laboratory work shows signs of kidney dysfunction. Similarly, patients who are on furosemide treatment in an ambulatory care setting need close monitoring to evaluate the response to treatment, intermittent electrolytes and kidney function monitoring to replete electrolytes and manage the dose of furosemide as indicated, and to assess for other adverse effects of the furosemide treatment and manage it accordingly.

CONCLUSION:

This article summarises drugs used in treatment of diseases with adverse effects which gives guidance for therapy management.

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