



## Antihypertensive Drugs: An Overview

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### ABSTRACT

Many antihypertensive medications with few adverse effects are useful in the treatment of hypertension. The mechanism of action and adverse effects of these medications are the two main topics of this review. After taking into account the targets and locations of action of each drug class, the mechanisms of action are examined to decide which form of hypertension each is most appropriate for. To determine which patients should avoid taking a certain medication, side effects are explained by their pharmacological causes. The review includes information on major drug classes: diuretics, ACE inhibitors, beta-blockers, and calcium channel blockers. It also briefly describes other classes: centrally acting agents, and direct vasodilators.

Keywords: Hypertension, ACE inhibitors, Beta blockers, Side effects, Calcium channel blockers.

### Introduction

Hypertension, a common chronic condition that often comes with serious heart and kidney problems, becomes more common with age. It is usually found along with new cardiovascular risk factors. Diagnosing hypertension now often uses automated blood pressure measurement techniques. Essential hypertension occurs because the kidneys can't excrete sodium appropriately except blood pressure is higher than normal. One important risk factor for cardiovascular disorders is hypertension. It raises the risk of peripheral arterial disease, heart failure, stroke, congestive heart failure, and renal failure. Usually, hypertension is also frequently linked to other risk factors, such as diabetes.

**Normal blood pressure:** Systolic pressure of less than 120 mmHg and diastolic pressure of less than 80 mmHg are considered normal blood pressure values.

**High blood pressure:** Systolic between 120 and 129 mmHg, and diastolic less than 80 mmHg.

#### Symptoms of high BP:

- Severe headache
- Severe anxiety
- Shortness of breathe
- Nosebleeds

#### Types of hypertension:

Mainly two type of hypertension

- **Primary hypertension:** Primary hypertension that is not related to any medical condition.
- **Secondary hypertension:** Secondary hypertension related to medical condition that causes high blood pressure mainly in kidneys, arteries, heart or endocrine system.

#### Cause of BP:

Some genetic or lifestyle related factors

- Use of more alcohol
- Old age
- Overweight
- Obesity
- Use of more salt
- Family history of high blood pressure

#### Condition related factors:

**Hyperthyroidism:** Hyperthyroidism is produced because of thyroid gland that produces too much thyroid hormone. This can result in hypertension, mostly systolic hypertension.

**Hyperaldosteronism:** Aldosterone is essential hormone that is produced in the adrenal gland and it is important to control blood pressure and electrolyte balance. Because of abnormal growth of adrenal gland can cause hypertension and in some cases cause low level of potassium resulting in hyperkalaemia.

**Chronic kidney disease:** Chronic kidney disease may be occurring because of temporary or permanent damage of kidney that resulting in loss of normal kidney function.

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#### The physiological processes that give rise to essential hypertension:

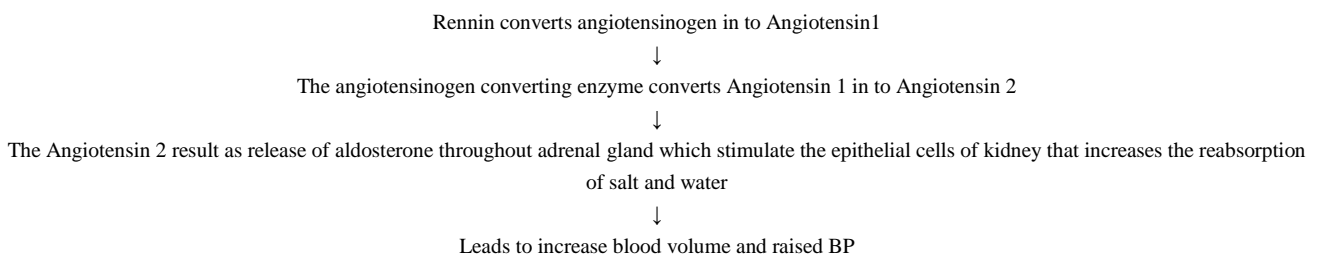
**Heredity:** Hypertension can be caused because of genetically. Especially parental history of hypertension increases the chances of hypertension. Different studies have suggested that in hypertension, 60% is family relationship and 40% is environmental association.

**Over activity of the sympathetic nervous system:** The over activity of sympathetic is related to cardiac output, peripheral resistance, increased heart rate, plasma and urinary NE(nor adrenaline) levels, peripheral postganglionic sympathetic nerve discharge. Because of over activity of sympathetic, the primary hypertension connected with obesity, sleep apnea, and early type 2 diabetes mellitus and pre- diabetes, chronic kidney disease and heart failure.

**Renal processes include pressure natriuresis and excessive salt consumption:** Due to consumption of high salt diet kidneys are enabling to excrete the excess sodium level. It is based on different studies people who consume little sodium have little or no hypertension. Some of the studies show reduction in salt intake placed as a reduction in BP. Over consumption of sodium occurs hypertension by increasing fluid volume and preload, which increased cardiac output.

In normotensive people, the consumption of high salt increases blood pressure that leading to high sodium and water excretion by the kidneys. This process called pressure- natriuresis helps go back blood pressure to normal.

**Angiotensin-converting enzyme system (RAAS) is one of the hormone pathways:** Rennin is a circulating enzyme (protease) that participates in maintains extracellular amount and arterial vasoconstriction.




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#### Adrenoceptor Antagonists: Overview and Clinical Applications

**B-blockers:** B blockers do not use as first line antihypertensive. These are used in this case like after myocardial infarction, or tachyarrhythmias such as atrial fibrillation. Another various uses include stable heart failure, thyrotoxicosis, oesophageal, anxiety, and glaucoma. B-Blockers block the effects of catecholamine at  $\beta$ -Adrenoceptor. These Gs type G-protein-coupled receptors are classified as B1; these are mainly present with in the heart and kidneys. B2 are present in the lungs, blood vesicles and muscles. B-blockers categorized according to cardio selectivity. Metoprolol, atenolol and esmolol have more affinity in B1 then B2. Metoprolol, atenolol, and esmolol are examples of  $\beta$ 1-selective medications, in contrast to non-cardioselective medications like as propranolol and sotalol. While pindolol and timolol exhibit some agonist activity, the majority of  $\beta$ -blockers are pure antagonists. Classified as Vaughan-Williams class I antiarrhythmics, several  $\beta$ -blockers, including propranolol and metoprolol, also block sodium channels. Both  $\beta$ - and  $\alpha$ -blocking properties are present in labetalol. Although  $\beta$ -blockers help individuals with stable heart failure, they can exacerbate

symptoms in some patients by decreasing cardiac output. They can also have negative effects on the central nervous system, such as fatigue and vivid nightmares, as well as adverse effects like poor peripheral circulation and bronchospasm.

**Diuretics:** The most common diuretics used in hypertension are thiazide (bendroflumethazide, hydrochlorothiazide) and thiazide-like (chlortalidon, indapamide). These are used in heart failure or at the risk of heart failure. These are also added to drugs in patients who have not responded to first and second line antihypertensive treatments. Thiazide diuretics act on the proximal part of the distal tubule that inhibits the reabsorption of sodium and chloride, and results in a reduction in water reabsorption leading to diuresis. The effect of diuretics depends on their excretion in the renal tubule and is as a result reduced in renal impairment.

Thiazide diuretics have many clinically related biochemical side effects, hypocalcaemia, hypercholesterolemia, hyperuricaemia, hypochloraemic alkalosis; plasma loss may precipitate dehydration and acute kidney injury.

**Calcium channel blockers:** Calcium channel blockers are first line treatment for primary hypertension for the patient of over age 55 and black patient of African and Caribbean family. Diltiazem and verapamil are rate-controlling CCBs that are used in tachyarrhythmia and angina where their negative inotropic and chronotropic effects improve the myocardial oxygen supply: demand ratio. CCBs have a few specific non-cardiac indications like; nimodipine is used to reduce cerebral vasospasm after spontaneous subarachnoid haemorrhage in patients and verapamil is used to treat cluster headache in neurology. Calcium channel blockers (CCBs) come in a variety of chemical forms. These comprise dihydropyridines (such as amlodipine and nifedipine), phenylalkylamines (such as verapamil), and benzothiazepines (such as Diltiazem). The pharmacokinetic characteristic of CCBs varies. Due to first-pass metabolism, the majorities that are taken orally have low bioavailability. Certain medications are accessible as intravenous versions, such as verapamil, nimodipine, and nicardipine. It is possible to deliver nifedipine sublingually. All CCBs have half-lives less than 12 hours, with the exception of amlodipine, which has a somewhat longer half-life.

**ACE Inhibitors:** ACE inhibitors are the first line treatment in 55 years old among primary hypertension. These are also used in heart failure, post myocardial infarction, diabetic neuropathy and chronic kidney disease. The effects of ACE inhibitors are greater in case of renal and cardiac than the arterial pressure control. ACE is a metalloproteinase enzyme that occurs among the pulmonary vasculature. By the inhibition of ACE, the cleavage of peptide hormone Angiotensin I to Angiotensin II is reduced and also the metabolism of peptide bradykinin to inactive substances. The reduction of Angiotensin II is responsible for the therapeutic effect. The bradykinins have some therapeutic advantages through vasodilatation but it's also responsible for dry cough in susceptible individuals. ACE inhibitors have some side effects, skin rashes, agranulocytosis, hyperkalaemia due to reduced aldosterone secretion, and taste disturbance.

**Centrally acting agents:** Centrally acting agents include Clonidine ( $\alpha_2$  Adrenoceptor agonist), methyldopa (precursor of a  $\alpha_2$  Adrenoceptor agonist), and moxonidine (agonist at imidazoline binding sites). These have little use in primary hypertension while methyldopa is used to treat hypertension in pregnancy. Centrally acting drugs have little use because of common side effects. Clonidine is an analgesic and sedative drug that reduces the minimum alveolar concentration of inhalation anaesthetic agents, and the side effects are dry mouth and sedation. Methyldopa contains immunological side effects like, pyrexia, haemolytic anaemia, and hepatitis. Termination of treatment with Clonidine can cause rebound hypertension.

**Vasodilator:** The directly acting vasodilators are used rarely because of their side effects. For example, hydralazine, minoxidil, and sildafinil. Hydralazine is used in secondary hypertension that is caused by pre-eclampsia and also minoxidil is used to treat male pattern baldness. Vasodilators are helpful in the relaxation of vascular smooth muscle in resistance vessels. Vasodilators are poorly tolerated. These have some side effects, headache, fluid retention, and oedema. Other specific side effects are, left ventricular hypertrophy, pericardial, and pleural effusions caused by minoxidil and hydralazine caused in case of peripheral neuropathy, blood dyscrasia, and a lupus-like reaction.

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## Conclusion:

In this review article we discussed about the various classes of drug that are used in hypertension and also learnt about the cause of hypertension, symptoms and types of hypertension. In this review we were also discussed about the drug safety, therapeutic efficacy and comparative effectiveness. The choice of antihypertensive therapy is depend on the patient profile. A successful treatment of hypertension is possible with minute side effects

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