A Review on Hypertensive and Antihypertensive drugs

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**Abstract**

One of the main causes of morbidity and early mortality worldwide is hypertension, a complicated, multifaceted, and multisystemic illness. It is defined by major recommendations as having a systolic blood pressure of greater than 130 mmHg and/or a diastolic blood pressure of greater than 80 mmHg. Around 30% of persons globally suffer with hypertension, making it a fairly prevalent condition.

With the availability of several antihypertensive medication classes, hypertension can be successfully treated with few adverse effects. The mechanisms of action and adverse effects of the various pharmacological groups of antihypertensive medications are the two main topics covered in this review. To better understand which type of hypertension a particular pharmacological class of antihypertensive drug is most indicated for, the mechanism of action is analyzed using a pharmacological approach, i.e., the molecular receptor targets, the various sites along the arterial system, and the extra-arterial sites of action. Furthermore, pharmacological mechanisms are used to define and explain side effects in order to better understand how they arise and which patients should not take certain medications.

**Key words** : Hypertension definition, classification, epidemiology, risks factors, symptoms, Anti-hypertensive drug, definition , classification ,mechanism of action , indication, contraindication , adverse effects .

**Introduction**

Numerous antihypertensive drug classes are now available, making it possible to effectively treat hypertension with minimal side effects. This study focuses on two primary topics: the mechanisms of action and side effects of the different pharmacological classes of antihypertensive drugs. A pharmacological approach is used to analyze the mechanism of action, which includes the molecular receptor targets, the different sites along the arterial system, and the extra-arterial sites of action, in order to better understand which type of hypertension a given pharmacological class of antihypertensive drug is most indicated for. Furthermore, in order to better understand how side effects occur and which people should not take particular medications, pharmacological mechanisms are employed to characterize and explain them.

 **Objective [1]**

 Describe the guidelines for using antihypertensive medications and guide the treatment choices for first-line treatment.

* Review the different anti-hypertensive medication classes, summarizing the guidelines for the indication to use combination treatment when mono-therapy fails.
* Outline the significant side effects of each class of antihypertensive medications.
* Identify the approach of the interprofessional team to identify an appropriate care plan for a hypertension patient.[2]
* **Hypertension -**

Definition: According to WHO hypertension is persistent increase in blood pressure i.e. 140 mmHg systolic and 90mm Hg diastolic [3]

* **Classification Of Hypertension-**

| Category | Systolic (mmHg) | Diastolic (mmHg) |
| --- | --- | --- |
| Normal | < 130 | <85 |
| Mild (Stage I) | 140-159 | 90-99 |
| Moderate (Stage II)\_ | 160-179 | 100-109 |
| Severe (Stage III) | 180-209 | 110-119 |
| Very severe (Stage IV) | >210 | >120 |

* **EPIDEMIOLOGY**

In pre-industrial societies, BP levels had narrow distributions with mean values that changed little with age and averaged around 115/75 mmHg .a value that probably represents the normal (or ideal) BP for humans. However, in most contemporary societies, systolic BP levels rise steadily and continuously with age in both men and women. This ubiquitous finding could be explained because age is a proxy for the probability and duration of exposure to the numerous environmental factors that increase BP gradually over time, such as excessive sodium consumption, insufficient intake of dietary potassium, overweight and obesity, alcohol intake and physical inactivity. Other factors, such as genetic predisposition or adverse intrauterine environment (such as gestational hypertension or pre-eclampsia), have small but definite associations with high BP levels in adulthood. Even modest rises in mean population BP lead to large increases in the absolute number of people with hypertension.

As economic development progresses, hypertension initially affects those with a high socioeconomic status, but at later stages of economic development, the prevalence of hypertension and its consequences are greatest in those with lower socioeconomic status; this phenomenon is seen both within and between countries.[4]

**Figure 2. The main neuroendocrine systems involved in the regulation of blood pressure.[4]**



**Risk factors**

Modifiable risk factors include unhealthy diets (excessive salt consumption, a diet high in saturated fat and trans fats, low intake of fruits and vegetables), physical inactivity, consumption of tobacco and alcohol, and being overweight or obese. In addition, there are environmental risk factors for hypertension and associated diseases, where air pollution is the most significant.

Non-modifiable risk factors include a family history of hypertension, age over 65 years and co-existing diseases such as diabetes or kidney disease.[5]

**Symptoms**

Most people with hypertension don’t feel any symptoms. Very high blood pressures can cause headaches, blurred vision, chest pain and other symptoms.

Checking your blood pressure is the best way to know if you have high blood pressure. If hypertension isn’t treated, it can cause other health conditions like kidney disease, heart disease and stroke.

People with very high blood pressure (usually 180/120 or higher) can experience symptoms including:

* severe headaches
* chest pain
* dizziness
* difficulty breathing
* nausea
* vomiting
* blurred vision or other vision changes
* anxiety
* confusion
* buzzing in the ears
* nosebleeds
* abnormal heart rhythm

If you are experiencing any of these symptoms and a high blood pressure, seek care immediately.

The only way to detect hypertension is to have a health professional measure blood pressure. Having blood pressure measured is quick and painless. Although individuals can measure their own blood pressure using automated devices, an evaluation by a health professional is important for assessment of risk and associated conditions.[5]

**Prevention**

Lifestyle changes can help lower high blood pressure and can help anyone with hypertension. Many who make these changes will still need to take medicine.

These lifestyle changes can help prevent and lower high blood pressure.

**Do:**

* Eat more vegetables and fruits.
* Sit less.
* Be more physically active, which can include walking, running, swimming, dancing or activities that build strength, like lifting weights.

	+ Get at least 150 minutes per week of moderate-intensity aerobic activity or 75 minutes per week of vigorous aerobic activity.
	+ Do strength building exercises 2 or more days each week.
* Lose weight if you’re overweight or obese.
* Take medicines as prescribed by your health care professional.
* Keep appointments with your health care professional.

**Don’t**:

* eat too much salty food (try to stay under 2 grams per day)
* eat foods high in saturated or trans fats
* smoke or use tobacco
* drink too much alcohol (1 drink daily max for women, 2 for men)
* miss or share medication.

Reducing hypertension prevents heart attack, stroke and kidney damage, as well as other health problems.

Reduce the risks of hypertension by:

* reducing and managing stress
* regularly checking blood pressure
* treating high blood pressure
* managing other medical conditions
* reducing exposure to polluted air.[5]

 **Antihypertensive Drugs-**

 Defination-These are the pharmacological agent which reduce elevated blood pressure(BP) and restore the normal BP.[6]

**Classification-**

| **Class** | **Examples** |
| --- | --- |
| **Targeting renin–angiotensin system** |
|  Angiotensin-converting enzyme inhibitors | Captopril, lisinopril, ramipril |
|  Angiotensin receptor antagonists | Candesartan, losartan, valsartan |
|  Direct renin antagonists | Aliskiren |
| **Adrenoceptor antagonists** |
|  β-Blockers | Atenolol, metoprolol, propranolol |
|  α-Blockers | Doxazosin, labetalol (also a β-blocker), phentolamine, phenoxybenzamine |
| Calcium channel blockers |
|  Phenylalkamines | Verapamil |
|  Dihydropyridines | Amlodipine, nifedipine, nimodipine |
|  Benzothiazepines | Diltiazem |
| Diuretics |
|  Thiazides | Bendroflumethiazide, hydrochlorothiazide |
|  Loop | Furosemide, bumetanide |

**Mechanisum Of Action**-

1. **ACE inhibitors**- decrease blood pressure by inhibiting the angiotensin-converting enzyme this causes a decline in the production of angiotensin II and increases the bradykinin level by inhibiting its degeneration, which leads to vasodilation.
2. **Beta-blockers-** work by inhibiting the catecholamines from binding to the Beta 1, 2, and 3 receptors. Beta-1 receptors are found primarily in the heart muscle, beta-2 receptors are located in the bronchial and peripheral vascular smooth muscles, and beta-3 receptors appear in the adipose tissue of the heart. Cardio-selective beta-blockers (e.g., metoprolol succinate, metoprolol tartrate, atenolol, betaxolol, and acebutolol) inhibit only beta-1 receptors, causing fewer bronchospasms. By inhibiting the catecholamines binding to the beta receptors, the beta-blockers have a negative inotropic effect, which results in a decrease in the heart rate, which helps to reduce oxygen consumption.
3. **Alpha-blockers-**act by inhibiting alpha-1 receptors, which decrease vascular smooth muscle contractions, leading to vasodilation
4. .**Calcium channel blockers- The**mechanism of action of CCBs is related to the inhibition of Ca2+ entry to the cells; this occurs by binding to the L-type voltage-gated calcium channels located in the heart muscle. This effect can cause peripheral vasodilation, which is seen mainly in dihydropyridines, or a negative inotropic effect on the heart muscle in non-dihydropyridines, inhibiting the sinoatrial and atrioventricular nodes, leading to slow cardiac contractility and conduction.
5. **Thiazide and Thiazide like diuretics-**mechanism of action for thiazide-type diuretics is not fully understood. Thiazides inhibit sodium transport in the distal tubule by blocking the Na/Cl channels. Thiazides can have a small effect on the proximal tube by impairing sodium transport, but the main action is on the distal tubule. Thiazides cause initial volume depletion associated with decreased cardiac output, which recovers within 6 to 8 weeks of starting the treatment in a reverse autoregulation mechanism while the blood pressure remains controlled; thiazide diuretics can acutely activate the renin-angiotensin system and cause systemic vascular resistance, which prevents a good response to the diuretic treatment, this increase in renin-angiotensin activity may resolve with chronic thiazide treatment, the addition of an ACE inhibitor or ARB can enhance the blood pressure control. Also, the thiazide-type diuretics have a modest vasodilation effect, although the mechanism is still unclear.
6. **Loop diuretics-** work by increasing the sodium exertion at the level of the medullary and cortical aspects of the thick ascending limb. This action causes a decrease in volume, which leads to decreased blood pressure. [8]

**Indication**

1. Hypertension
2. CHF
3. MI
4. Angina pectoris
5. edema
6. Asthma
7. Liver disease
8. Kidney disease
9. Scleroderma crisis
10. Heart failure
11. Peripheral vascular disease
12. Bradyarrhythmias
13. Diabetic nephropathy
14. Hypertrophic cardiomyopathy
15. Cardiac arrthythmias[6]

**Contraindication**

1. Anuria
2. Liver disease
3. Renal failure
4. Pregnancy
5. Hyperkalaemia
6. Potassium sparing diuretics
7. Diabetics
8. lactation
9. liver cirrhosis
10. asthma
11. acute heart failure
12. bronchitis
13. kidney disease
14. hepatic failure
15. anemia [6]

**Adverse effects**

1. dizziness
2. fatigue
3. electrolyte imbalance
4. vomiting
5. hypotension
6. Hyperkalaemia
7. Dry cough
8. Nausea
9. Urticaria
10. Bowel upset
11. Headache
12. Diarrhea
13. Angioedema
14. Bradycardia
15. Palpitation [6]

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