



A DETAILED UPDATED REVIEW ON ANTIHYPERTENSIVE DRUGS AND THEIR CLASSIFICATION

Azharruddin Mohammed*¹ and Akthar Sulthana Mohammad²

¹Pharmacist, Abeer Medical Center, Doha, Qatar.

²Pharmacist, Al Fathimiya Pharmacy, Doha, Qatar.

*Corresponding Author: Azharruddin Mohammed

Pharmacist, Abeer Medical Center, Doha, Qatar.

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ABSTRACT

Antihypertensives are a class of drugs that are used to treat hypertension (high blood pressure). Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke and myocardial infarction. Evidence suggests that reduction of the blood pressure by 5 mmHg can decrease the risk of stroke by 34%, of ischaemic heart disease by 21%, and reduce the likelihood of dementia, heart failure, and mortality from cardiovascular disease. There are many classes of antihypertensives, which lower blood pressure by different means. Among the most important and most widely used medications are thiazide diuretics, calcium channel blockers, ACE inhibitors, angiotensin II receptor antagonists (ARBs), and beta blockers. Which type of medication to use initially for hypertension has been the subject of several large studies and resulting national guidelines. Established treatment of hypertension is feasible with limited side effects given the supply of multiple antihypertensive classes. Current review describes the varied pharmacological classes of antihypertensive drugs. Major pharmacological classes of antihypertensive drugs are detailed here: beta-blockers, diuretics, angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists, and calcium channel blockers etc. Four additional pharmacological classes are described in a shorter manner: renin inhibitors, alpha-adrenergic receptor blockers, centrally acting agents, and direct acting vasodilators.

KEYWORDS: Hypertensive drugs, treatment, cardiovascular diseases, Angiotensin-converting enzyme inhibitor; Calcium channel blocker; Diuretic.

INTRODUCTION

The fundamental goal of treatment should be the prevention of the important endpoints of hypertension, such as heart attack, stroke and heart failure. Patient age, associated clinical conditions and end-organ damage also play a part in determining dosage and type of medication administered.^[1-3] The several classes of antihypertensives differ in side effect profiles, ability to prevent endpoints, and cost. The choice of more expensive agents, where cheaper ones would be equally effective, may have negative impacts on national healthcare budgets.^[4] As of 2018, the best available evidence favors low-dose thiazide diuretics as the first-line treatment of choice for high blood pressure when drugs are necessary.^[5] Although clinical evidence shows calcium channel blockers and thiazide-type diuretics are preferred first-line treatments for most people (from both efficacy and cost points of view), an ACE inhibitor is recommended.^[6] Chlorothiazide was discovered in 1957, but the first known instance of an effective antihypertensive treatment was in 1947 using Primaquine, an antimalarial.^[5] Vaccinations are being trialed and may become a treatment option for high

blood pressure in the future. CYT006-AngQb was only moderately successful in studies, but similar vaccines are being investigated.^[5-6]

The following are the enlisted class of antihypertensive drugs.

Diuretics

Diuretics help the kidneys eliminate excess salt and water from the body's tissues and blood.

1) Loop Diuretics

- a) Bumetanide
- b) Ethacrynic Acid
- c) Furosemide
- d) Torsemide

2) Thiazide Diuretics

- a) Eptizide
- b) Hydrochlorothiazide And Chlorothiazide
- c) Bendroflumethiazide
- d) Methyclothiazide
- e) Polythiazide

3) Thiazide-Like Diuretics

- a) Indapamide
- b) Chlorthalidone
- c) Metolozone
- d) Xipamide
- e) Clopamide

4) Potassium-Sparing Diuretics

- a) Amiloride
- b) Triamterene
- c) Spironolactone
- d) Eplerenone

Calcium Channel Blockers

Calcium channel blockers block the entry of calcium into muscle cells in artery walls.

1) Dihydropyridines

- a) Amlodipine
- b) Cilnidipine
- c) Clevidipine
- d) Felodipine
- e) Isradipine
- f) Lercanidipine
- g) Levamlodipine
- h) Nicardipine
- i) Nifedipine
- j) Nimodipine
- k) Nisoldipine
- l) Nitrendipine

2) Non-Dihydropyridines

- a) Diltiazem
- b) Verapamil

ACE Inhibitors

ACE inhibitors inhibit the activity of angiotensin-converting enzyme (ACE), an enzyme responsible for the conversion of angiotensin I into angiotensin II, a potent vasoconstrictor.

- 1) Captopril
- 2) Enalapril
- 3) Fosinopril
- 4) Lisinopril
- 5) Moexipril
- 6) Perindopril
- 7) Quinapril
- 8) Ramipril
- 9) Trandolapril
- 10) Benazepril

ACE inhibitors (and angiotensin II receptor antagonists) should not be a first-line treatment for black hypertensives without chronic kidney disease.^[7] Notable side effects of ACE inhibitors include dry cough, high blood levels of potassium, fatigue, dizziness, headaches, loss of taste and a risk for angioedema.^[1]

Angiotensin II Receptor Antagonists

Angiotensin II receptor antagonists work by antagonizing the activation of angiotensin receptors.

- 1) Azilsartan
- 2) Candesartan
- 3) Eprosartan
- 4) Irbesartan
- 5) Losartan
- 6) Olmesartan
- 7) Telmisartan
- 8) Valsartan
- 9) Fimasartan

Adrenergic Receptor Antagonists**1) Beta Blockers**

- a) Acebutolol
- b) Atenolol
- c) Bisoprolol
- d) Betaxolol
- e) Carteolol
- f) Carvedilol
- g) Labetalol
- h) Metoprolol
- i) Nadolol
- j) Nebivolol
- k) Oxprenolol
- l) Penbutolol
- m) Pindolol
- n) Propranolol
- o) Timolol

2) Alpha Blockers

- a) Doxazosin
- b) Phentolamine
- c) Indoramin
- d) Phenoxybenzamine
- e) Prazosin
- f) Terazosin
- g) Tolazoline

3) Mixed Alpha + Beta Blockers

- a) Bucindolol
- b) Carvedilol
- c) Labetalol

Although beta blockers lower blood pressure, they do not have a positive benefit on endpoints as some other antihypertensives.^[7] In particular, beta-blockers are no longer recommended as first-line treatment due to relative adverse risk of stroke and new-onset of type 2 diabetes when compared to other medications,^[3] while certain specific beta-blockers such as atenolol appear to be less useful in overall treatment of hypertension than several other agents.^[8]

Despite lowering blood pressure, alpha blockers have significantly poorer endpoint outcomes than other antihypertensives, and are no longer recommended as a first-line choice in the treatment of

hypertension.^[9] However, they may be useful for some men with symptoms of prostate disease.

Vasodilators

Vasodilators act directly on the smooth muscle of arteries to relax their walls so blood can move more easily through them; they are only used in hypertensive emergencies or when other drugs have failed, and even so are rarely given alone. Sodium nitroprusside, a very potent, short-acting vasodilator, is most commonly used for the quick, temporary reduction of blood pressure in emergencies (such as malignant hypertension or aortic dissection). Hydralazine and its derivatives are also used in the treatment of severe hypertension, although they should be avoided in emergencies. They are no longer indicated as first-line therapy for high blood pressure due to side effects and safety concerns, but hydralazine remains a drug of choice in gestational hypertension.^[10]

Renin Inhibitors

Renin comes one level higher than angiotensin converting enzyme (ACE) in the renin-angiotensin system. Renin inhibitors can therefore effectively reduce hypertension. Aliskiren (developed by Novartis) is a renin inhibitor which has been approved by the U.S. FDA for the treatment of hypertension.^[11]

Aldosterone Receptor Antagonist

Aldosterone receptor antagonists

- 1) Eplerenone
- 2) Spironolactone

Aldosterone receptor antagonists are not recommended as first-line agents for blood pressure,^[6] but spironolactone and eplerenone are both used in the treatment of heart failure and resistant hypertension.

Alpha-2 Adrenergic Receptor Agonists

Central alpha agonists lower blood pressure by stimulating alpha-receptors in the brain which open peripheral arteries easing blood flow. These alpha 2 receptors are known as autoreceptors which provide a negative feedback in neurotransmission (in this case, the vasoconstriction effects of adrenaline). Central alpha agonists, such as clonidine, are usually prescribed when all other anti-hypertensive medications have failed. For treating hypertension, these drugs are usually administered in combination with a diuretic.^[10-11]

- 1) Clonidine
- 2) Guanabenz
- 3) Guanfacine
- 4) Methyldopa
- 5) Moxonidine

Adverse effects of this class of drugs include sedation, drying of the nasal mucosa and rebound hypertension.

Some indirect anti-adrenergics are rarely used in treatment-resistant hypertension

- 1) Guanethidine - Replaces Norepinephrine In Vesicles, Decreasing Its Tonic Release

- 2) Mecamylamine - Antinicotinic And Ganglion Blocker

- 3) Reserpine - Indirect Via Irreversible Vmat Inhibition For the most resistant and severe disease, oral minoxidil (Loniten) in combination with diuretic and β -blocker or other sympathetic nervous system suppressant may be used.

Endothelium Receptor Blockers

Bosentan belongs to a new class of drug and works by blocking endothelin receptors. It is specifically indicated only for the treatment of pulmonary artery hypertension in patients with moderate to severe heart failure.^[10-11]

CONCLUSION

The streamline challenges within the management of hypertension still need special attention and proper treatment. Numerous national and international guidelines and protocols for the management of hypertension are published highlighting mono- or combination therapy consistent with the BP levels and associated comorbidity. Globally, hypertension treatment strategies have varied widely over time in terms of initial drug of choice from the above stated classification and from monotherapy to low dose combination single pill therapy. National health policy makers should consider evaluation and better treatment of hypertension as a right in public health system for better outcomes in terms of morbidity and mortality from hypertension. In developing countries like India, more systematic studies are required on the evaluation of prescribing patterns and guideline-based antihypertensive medications' use, which can be tailored to suit the patients' requirements.

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