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Treatment and Chemical compounds for hypertension. (Antihypertensive agents) : A Review

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ABSTRACT:

Hypertension is an important medical and public health issue all over the world. It is one of the most prevalent conditions seen today by clinicians in both developed and developing countries. Depending upon progression of systolic and diastolic blood pressure it is classified into stage 1, 2 and 3 hypertension. Life style modifications may be helpful in initial stage but pharmacological treatment is necessary when it became difficult to control it. In routine practice, pharmacological treatment is being selected from diuretics, β-blockers, calcium channel blockers and renin angiotensin system inhibitors either alone or in combination for both initial and maintenance therapy. Choice of drug depends upon favorable effects in specific clinical setting. Thiazide type diuretics are being preferred for most patients with uncomplicated hypertension whereas β-blockers show strong benefits in patients with a variety of cardiovascular complications. ACE-Inhibitors and ARBs are superior to other class in patients with multiple risk factors like obesity, insulin resistance or diabetes. Calcium channel blockers(CCB's) compared with other class of hypertensive drugs demonstrate similar blood pressure lowering effects and similar reductions in cardiovascular morbidity and mortality but higher incidence of heart failure and fatal myocardial in fraction in some patients. Despite the continued decrease in mortality and morbidity rate by these antihypertensive drugs, some documented increasing prevalence of cardiac failure and end stage renal disease remains to be explained.

Keywords: Hypertension, diuretics, β-blockers, angiotensin inhibitors, calcium channel blockers.

History of hypertension:

The modern history of hypertension begins with the understanding of the cardiovascular system with the work of physician William Harvey (1578–1657), who described the circulation of blood in his book "*De motucordis*". The English clergyman Stephen Hales made the first published measurement of blood pressure in 1733. Descriptions of hypertension as a disease came among others from Thomas Young in 1808 and especially Richard Bright in 1836.[1] The first report of elevated blood pressure in a person without evidence of kidney disease was made by Frederick Akbar Mahomet (1849–1884). However hypertension as a clinical entity came into being in 1896 with the invention of the cuff-based sphygmomanometer by Scipione Riva-Rocco in 1896. This allowed blood pressure to be measured in the clinic. The concept of essential hypertension ('hypertonic essential') was introduced in 1925 by the physiologist Otto Frank to describe elevated blood pressure for which no cause could be found.

Introduction

High blood pressure (hypertension) is one of the most important preventable causes of premature morbidity and mortality. Hypertension is a major risk factor for is chemical and hemorrhagic stroke, myocardial infarction, heart failure, chronic kidney disease, cognitive decline and premature death. Untreated hypertension is usually associated with a progressive rise in blood pressure. The risk associated with increasing blood pressure is continuous, with each 2 mmHg rise in systolic blood pressure associated with a 7% increased risk of mortality from is chemical heart disease and a 10% increased risk of mortality from stroke. Hypertension is remarkably common and the prevalence is strongly influenced by age. In any individual person, systolic and/or diastolic blood pressures may be elevated. Diastolic pressure is more commonly elevated in people younger than 50. With ageing, systolic hypertension becomes a more significant problem, as a result of progressive stiffening and loss of compliance of larger arteries. At least one quarter of adults (and more than half of those older than 60) have high blood pressure.

High blood pressure is defined as a systolic blood pressure (BP) 140 mm Hg and/or diastolic blood pressure 90 mm Hg obtained on two separate readings taken at least 1 week apart. The prevalence of hypertension is higher among minorities than whites, and it increases with age in all groups. There is increased morbidity and mortality associated with the following cardiovascular complications of hypertension:

- Aortic dissection
- Congestive heart failure
- Coronary artery disease with associated angina pectoris and myocardial infarction

- Left ventricular hypertrophy
- Peripheral vascular disease
- Renal insufficiency
- Stroke secondary to cerebral hemorrhage or thrombosis

Hypertension in pregnancy is associated with higher risk of complications including preeclampsia, placental abruption, fetal growth restriction, intrauterine fetal demise; worsening maternal cardiac function.

Hypertension is classified as either primary (essential) hypertension or secondary hypertension; about 90–95% of cases are categorized as primary hypertension which means high blood pressure with no obvious underlying medical cause. The remaining 5–10% of cases categorized as secondary hypertension is caused by other conditions that affect the kidneys, arteries, heart or endocrine system. Dietary and lifestyle changes can improve blood pressure control and decrease the risk of health complications, although drug treatment is still often necessary in people for whom lifestyle changes are not enough or not effective. The treatment of moderately high arterial blood pressure (defined as >160/100 mmHg) with medications is associated with an improved life expectancy. The benefits of treatment of blood pressure that is between 140/90 mmHg and 160/100 mmHg are less clear, with some reviews finding no benefit and other reviews finding benefit.

Pathophysiology:

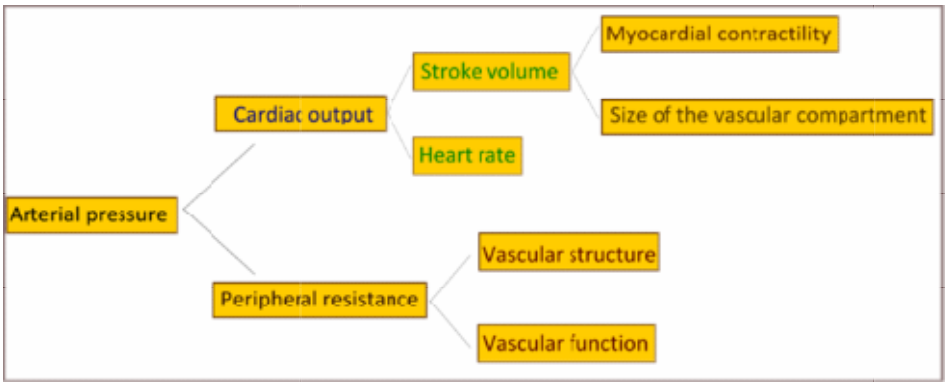


Fig.1. Pathophysiology of hypertension.

The **Pathophysiology of hypertension** is an area of active research, attempting to explain causes of hypertension, which is a chronic disease characterized by elevation of blood pressure. Hypertension can be classified as either essential or secondary. Essential hypertension indicates that no specific medical cause can be found to explain a patient's condition. About 90-95% of hypertension is essential hypertension. Secondary hypertension indicates that the high blood pressure is a result of another underlying condition, such as kidney disease or tambours (adrenal adenoma or pheochromocytoma). Persistent hypertension is one of the risk factors for strokes, heart attacks, heart failure and arterial aneurysm, and is a leading cause of chronic renal failure.

Most mechanisms leading to secondary hypertension are well understood. The pathophysiology of essential hypertension remains an area of active research, with many theories and different links to many risk factors.

Cardiac output and peripheral resistance are the two determinants of arterial pressure.[6] Cardiac output is determined by stroke volume and heart rate; stroke volume is related to myocardial contractility and to the size of the vascular compartment. Peripheral resistance is determined by functional and anatomic changes in small arteries and arterioles.

Signs and symptoms

Hypertension is rarely accompanied by any symptoms, and its identification is usually through screening, or when seeking healthcare for an unrelated problem. A proportion of people with high blood pressure report headaches (particularly at the back of the head and in the morning), as well as lightheadedness, vertigo, tinnitus (buzzing or hissing in the ears), altered vision or fainting episodes. These symptoms, however, might be related to associated anxiety rather than the high blood pressure itself.

On physical examination, hypertension may be suspected on the basis of the presence of hypertensive retinopathy detected by examination of the optic fundus found in the back of the eye using ophthalmoscopy. Classically, the severity of the hypertensive retinopathy changes is graded from grade I–IV, although the milder types may be difficult to distinguish from each other. Ophthalmoscopy findings may also give some indication as to how long a person has been hypertensive.

Causes of Hypertension

1. Age, history, physical examination, severity of hypertension, orinitial laboratory findings suggest such causes.
2. BP responds poorly to drug therapy.
3. BP begins to increase for uncertain reason after being well controlled.
4. Onset of hypertension is sudden.

Pheochromocytoma should be suspected in patients with labile hypertension or with paroxysms of hypertension accompanied by headache, palpitations, pallor, and perspiration. Decreased pressure in the lower extremities or delayed or absent femoral arterial pulses may indicate aortic obesity, glucose intolerance, and purple suggest Cushing syndrome. Examples of clues from the laboratory tests include unprovoked hypokalemia (primary aldosteronism), hyper calcemia (hyperparathyroidism), and elevated creatinine or abnormal urinalysis (renal parenchymal disease). Appropriate investigations should be conducted when there is a high index of suspicion of an identifiable cause.78–81 .The most common parenchymal kidney diseases associated with hypertension are chronic glomerulonephritis, polycystic kidney disease, and hypertensive nephrosclerosis. These can generally be distinguished by the clinical setting and additional testing. For example, a renal ultrasound is useful in diagnosing polycystic kidney disease.

Non-Pharmacological Treatment of hypertension:-

1. Reduction of salt intake-
   - It should be limited to a maximum of 6 g/day. In practice, individuals should avoid salted, cured, pickled, processed and smoked food and not add salt to food when or after cooking

.

2. Control of diabetes-
   - (Under medical surveillance).
3. Reduction of alcohol intake-
   - If alcohol is consumed, its intake should be limited to more than two drinks (each containing 10 g alcohol) per day, (20 g is approximately equivalent to 2 small glasses of wine, a pint of beer or 2 measures of spirits (whisky, brandy or vodka)).
4. Control of fat intake-
   - Fat intake should be limited to not more than 30% of daily energy and most saturated fats should be replaced with unsaturated vegetable oils or soft margarines.

5. Sufficient consumption of fruits and vegetables-
   - It is recommended to eat a varietyof fruits and vegetables several times per day (at least 400 g per day).

6. Regular physical activity-
   - Dynamic isotonic exercise (brisk walking, swimming, cycling, running, rowing, step climbing, hiking) is recommended on a regular basis (3–4 times a week; 30–45 min per day) depending on each individual and initial level of fitness.
   - Isometric exercise such as heavy weight lifting should be avoided.
   - Patients with health problems including individuals with years of sedentarism should first get advice from a doctor.
   - Verbal advice given on lifestyle modifications should be enforced by written information (e.g. leaflets, articles for the public, etc).

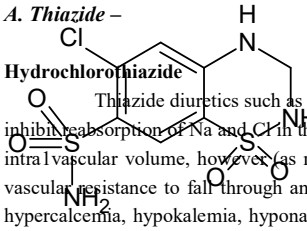
7. Smoking cessation.
   - This is perhaps the single most powerful lifestyle measure for the prevention of both cardiovascular and non-cardio vascular diseases in hypertensive patients. All hypertensive patients who smoke should receive appropriate counselling and assistance for smoking cessation and drug treatment when needed (nicotine replacement, bupropion)

Table no.1: Drug Treatment:

Sr. no.	Classification	examples
1	Diuretics.	Thiazides(Hydrochlorthiazide), Loop diuretics(furosemide), Potassium-sparing(spironolactone)
2	Beta adrenergic blockers.	Propanolol, atenolol, metoprolol
3	Calcium channel blockers	Verapamil, diltiazem, amlodipine
4	Angiotensin converting enzyme inhibitors	Captopril, enalapril, Lisinopril
5	Angiotensin receptor blockers	Losartan
6	Sympatholytics and adrenergic blockers.	Guanethidine, methyldopa
7	Vasodilators	minoxidil

1) Diuretics:

A. Thiazide –



Hydrochlorothiazide

Thiazide diuretics such as hydrochlorothiazide and chlorthalidone are among the most commonly used drugs for treating hypertension. They inhibit reabsorption of Na and Cl in the distal tubule and lose effectiveness when GFR is low. Their initial effects are said to be mediated by decreasing intravascular volume, however (as mentioned above) most untreated hypertensive have contracted intravascular volume. Diuretics cause peripheral vascular resistance to fall through an unknown mechanism. Unfortunately thiazide diuretics have a number of undesirable metabolic effects such as hypercalcemia, hypokalemia, hyponatremia, hyperglycemia, hyperlipidemia, and hyperuricemia. These side effects often dictate which drugs to use. When thiazide diuretics are used in low doses, their side effects seem to be minimized.

Hydrochlorothiazide

6-chloro-1,1-dioxo-3,4-dihydro-2H-1,2,4- benzothiadiazine-7-sulfonamide

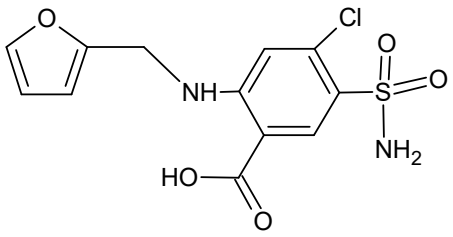
Mechanism of action

Hydrochlorothiazide belongs to thiazide class of diuretics. It reduces blood volume by acting on the kidneys to reduce sodium (Na) reabsorption in the distal convoluted tubule. The major site of action in the nephron appears on an electroneutral Na^+-Cl^- co-transporter by competing for the chloride site on the transporter. By impairing Na transport in the distal convoluted tubule, hydrochlorothiazide induces a natriuresis and concomitant water loss. Thiazides increase the reabsorption.

B. Loop diuretics–

Eg.Furosemide, Torsemide, Ethacrynic acid

- Loop diuretics such as furosemide inhibit the Na/K/Cl co-transporter in the ascending limb of the loop of Henle. They cause a very brisk diuresis, but their anti-hypertensive effects are actually not that strong. Acute intravenous administration of furosemide can cause veno-dilation by an unknown mechanism. Loop diuretics are often part of treatment for malignant hypertension and hypertension with hypervolemia (e.g., renal insufficiency). The metabolic derangements produced by these drugs (particularly hypokalemia, and hypocalcemia) can be profound. This class is not recommended as initial monotherapy for hypertension.



Furosemide

4-chloro-2-(furan-2-ylmethylamino)- 5-sulfamoylbenzoic acid

Mechanism of action-

Furosemide, like other loop diuretics, acts by inhibiting NKCC2, the luminal Na-K-2Cl symporter in the thick ascending limb of the loop of Henle. The action on the distal tubules is independent of any inhibitory effect on carbonic anhydrase or aldosterone; it also abolishes the cortico medullary osmotic gradient and blocks negative, as well as positive, free water clearance. Because of the large NaCl absorptive capacity of the loop of Henle, diuresis is not limited by development of acidosis, as it is with the carbonic anhydrase inhibitors.

By inhibiting the transporter, the loop diuretics reduce the reabsorption of NaCl and also diminish the lumen-positive potential that derives from K^+ recycling. This electrical potential normally drives divalent cation reabsorption in the loop, and by reducing this potential, loop diuretics cause a decrease in Mg^{2+} and Ca^{2+} reabsorption. Prolonged use can cause significant hypomagnesemia in some patients. Since Ca^{2+} is actively reabsorbed in the distal convoluted tubule, loop diuretics generally do not cause hypocalcemia.

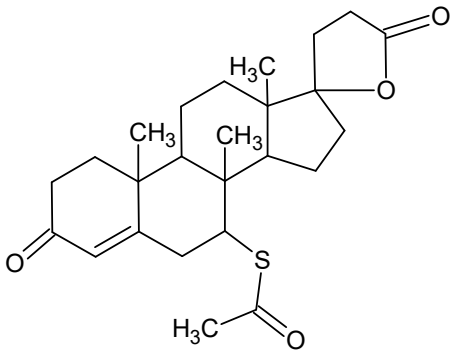
Additionally, furosemide is a noncompetitive subtype-specific blocker of GABA-A receptors. Furosemide has been reported to reversibly antagonize GABA-evoked currents of $\alpha_6\beta_2\gamma_2$ receptors at μM concentrations, but not $\alpha_1\beta_2\gamma_2$ receptors. During development, the $\alpha_6\beta_2\gamma_2$ receptor increases in expression in cerebellar granule neurons, corresponding to increased sensitivity to furosemide.

C. Potassium-sparing –

Eg. *Amiloride, Spironolactone, Triamterene*

Potassium-sparing diuretics such as spironolactone, amiloride, and triamterene are not as efficacious as thiazides or loop diuretics in reducing blood pressure, however, they do correct the potassium loss associated with thiazide and loop diuretics. Amiloride and triamterene inhibit the Na/proton exchanger in the distal and collecting tubules. Spironolactone inhibits the Na/K exchanger a0ffected by aldosterone, and it is particularly effective in the face of hyper aldosteronism. If potassium-sparing diuretics are given to patients on ACE inhibitors, particular care must be taken since both classes cause elevations in serum potassium.

Spironolactone



Spironolactone

7α-acetylthio-3-oxo-17α-pregn-4-ene-21,17-carbolactone

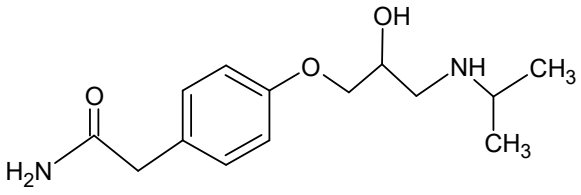
Side effect :

1. Metabolic effects (uncommon with small doses): hypokalemia, hypomagnesemia, hyponatremia, hyperuricemia, dyslipidemia (increased total and LDL cholesterol), impaired glucose tolerance, and hypercalcemia (with thiazides).
2. Postural hypotension.
3. Impotence in up to 22% of patients.

2. Beta adrenergic blockers:

Beta adrenergic blockers such as propranolol, metoprolol or atenolol are typical first-line agents for treating hypertension. They have negative chronotropic and negative inotropic effects. The acute effect of blocking beta-2 receptors is an increase in SVR , however chronic administration can decrease peripheral resistance, probably by decreasing plasma renin and angiotensin II. Unfortunately beta-blockers can elevate triglycerides and reduce HDL. In addition, they can produce glucose intolerance, impotence, and depression. In patients prone to bronchospasm (i,e., asthmatics), non-selective beta-blockers can theoretically worsen the problem, although the risks are somewhat overplayed. These side effects often dictate drug choices for the hypertensive patient. orption of calcium in this segment in a manner unrelated to sodium transport. Additionally, by other mechanisms, HCTZ is believed to lower peripheral vascular resistance.

Atenolol:



Atenolol

1-p-Carbamoylmethylphenoxy-3-isopropylamino-2-propanol

Mechanisms of Action:

Initial decrease in cardiac output, followed by reduction in peripheral vascular resistance. Other actions include decrease plasma renin activity, resetting of baroreceptors, release of vasodilator prostaglandins, and blockade of pre junctional beta-receptors.

Side Effects:

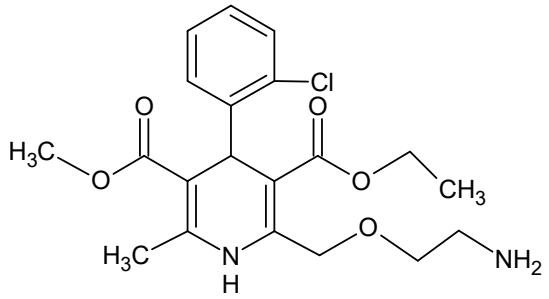
1. Bronchospasm and obstructive airway disease.
2. Bradycardia
3. Metabolic effects (raise triglycerides levels and decrease HDL cholesterol; may worsen insulin sensitivity and cause glucose intolerance). Increased incidence of diabetes mellitus.
4. Coldness of extremities.
5. Fatigue.
6. Mask symptoms of hypoglycemia.
7. Impotence.

3. Calcium channel blockers:

Eg. Nifedipine, Amlodipine, Felodipine, Diltiazem, Verapamil

Calcium channel blockers such as verapamil, diltiazem, nifedipine and amlodipine block L-type calcium channels and are effective arterial vasodilators. The dihydro pyridine agents nifedipine and amlodipine act primarily as vasodilators and have minimal direct effects on the heart. In contrast, verapamil and diltiazem act principally as negative inotropes and negative chronotropes, and thus decrease heart rate, contractility and cardiac conduction speed. In addition, they reduce vascular resistance. There is controversy over the use of short-acting dihydro pyridines in patients with angina because they can cause reflex sympathetic activation and worsen ischemia. When using verapamil or diltiazem one has to expect a reduction in LV systolic function as well as a reduction in cardiac conduction. Thus, in patients with congestive heart failure of the systolic type or in those with a significant conduction defect, these drugs should be avoided. Verapamil and diltiazem are synergistic with beta-blockers and the combination can cause severe bradycardia, heart block or pump dysfunction.

Amolodipine:



Amlodipine

(RS)-3-ethyl 5-methyl 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

Side Effects:

1. Cough (10 - 30%): a dry irritant cough with tickling sensation in the throat.
2. Skin rash (6%).
3. Postural hypotension in salt depleted or blood volume depleted patients.
4. Angioedema (0.2%) : life threatening.
5. Renal failure: rare, high risk with bilateral renal artery stenosis.
6. Hyperkalaemia
7. Teratogenicity.

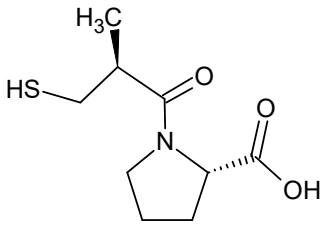
ACE inhibitors: –

Eg.Captopril, Enalapril , Enalaprilat, Lisinopril, *Benazepril*

ACE inhibitors like captopril, enalapril, and lisinopril decrease the conversion of angiotension I to angiotensin II (ATII). This reduces peripheral vascular resistance and promotes both natriuresis and hyperkalemia, since a reduction in ATII leads to a reduction in aldosterone. ACE also breaks down bradykinin, so inhibiting this enzyme can increase bradykinin levels and cause more vasodilation. ACE inhibitors have been shown to reduce morbidity (and possibly mortality – see below), and their relatively benign side-effect profile makes them frequent choices for first-line or monotherapy. Of note, ACE inhibitors are associated with a definite improvement in renal function in patients with diabetes and it has been shown that

renal injury due to long-standing diabetes is reduced. Diabetics who do not have a contraindication for this class of drugs should be taking them for renal protective purposes. ACE inhibitors are associated with a 5-10% incidence of dry cough, probably caused by the elevated bradykinin levels. For patients who have reduced renal perfusion pressure (e.g., renal artery stenosis), ACE inhibitors can cause renal dysfunction or renal failure. (Patients with bilateral renal artery stenosis have high levels of endogeneous angiotensin II which is used to maintain glomerular filtration and ACE inhibitors disrupt that compensatory process.) Finally, ACE inhibitors are associated with a rare, but potentially fatal, angioedema of the airway.

Captopril:



Captopril

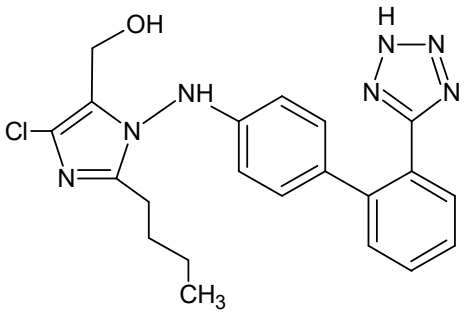
(*2S*)-1-[(*2S*)-2-methyl-3-sulfanylpropanoyl]
pyrrolidine-2-carboxylic acid

Angiotensin receptor blockers (ARB's)

Eg. Losartan, valsartan.

Drugs like losartan and valsartan cause arteriolar vasodilation by blocking the effects of angiotensin II at the angiotensin Type I receptor. Since the mechanism is essentially the same as for the ACE inhibitors, the indications and contraindications are the same. The blockade is downstream, so bradykinin is not elevated, and this class of drugs is not associated with a cough.

Losartan:



Losartan

(2-butyl-4-chloro-1-{[2'-(1*H*-tetrazol-5-yl)biphenyl-4-yl]methyl}-1*H*-imidazol-5-yl)methanol

Mechanism of action:

Losartan is a selective, competitive angiotensin II receptor type 1 (AT_1) receptor antagonist, reducing the end organ responses to angiotensin II. Losartan administration results in a decrease in total peripheral resistance (afterload) and cardiac venous return (preload). All of the physiological effects of angiotensin II, including release of aldosterone, are antagonized in the presence of losartan. Reduction in blood pressure occurs independently of the status of the renin-angiotensin system. As a result of losartan dosing, plasma renin activity increases due to removal of the angiotensin II feedback.

Side effect

The most common side effects for losartan are upper respiratory infections or stuffy nose, dizziness, and back pain.

Sympathoplegic agents:

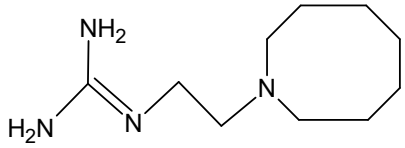
Adrenergic synthesis / release blockers-

Eg. Eserpine, Guanethidine

Beta adrenergic blocker ssuch as propranolol, metoprolol or atenolol are typical first-line agents for treating hypertension. They have negative chronotropic and negative inotropic effects. The acute effect of blocking beta-2 receptors is an increase in SVR, however chronic administration can

decrease peripheral resistance, probably by decreasing plasma renin and angiotensin II. Unfortunately beta-blockers can elevate triglycerides and reduce HDL. In addition, they can produce glucose intolerance, impotence, and depression. In patients prone to bronchospasm (i,e., asthmatics), non-selective beta-blockers can theoretically worsen the problem, although the risks are somewhat overplayed. These side effects often dictate drug choices for the hypertensive patient. orption of calcium in this segment in a manner unrelated to sodium transport. Additionally, by other mechanisms, HCTZ is believed to lower peripheral vascular resistance.

Guanitidine:



Guanitidine

2-[2-(azocan-1-yl)ethyl]guanidine.

Mechanism of action-

Guanethidine is transported by uptake 1 into the presynaptic terminal transported by Norepinephrine transporter (NET). (In this it competes with norepinephrine so can potentiate exogenously applied norepinephrine.) It becomes concentrated in norepinephrine transmitter vesicles, replacing norepinephrine in these vesicles. This leads to a gradual depletion of norepinephrine stores in the nerve endings. Once inside the terminal it blocks the release of norepinephrine in response to arrival of an action potential. Guanethidine was once a mainstay for hypertension resistant to other agents, and was often used safely during pregnancy, but it is no longer used in the US due to lack of availability. It is still licensed in some countries, e.g., UK, for the rapid control of blood pressure in a hypertensive emergency.

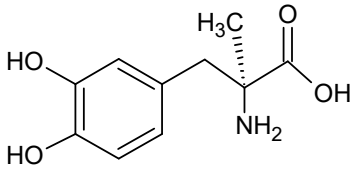
Central -adrenergic agonists –

Eg- Methyl-dopa, Clonidine

Central sympatholytics such as clonidine stimulate central alpha-2 receptors and thereby reduce sympathetic outflow. These drugs are effective in decreasing heart rate, contractility and vasomotor tone, however, they cause sedation and are usually not first line therapies.

- **Alpha-1 adrenergic blockers** such as prazosin, terazosin and doxazosin are effective at reducing sympathetic vasoconstriction and thereby reducing vascular resistance. These drugs are also useful for men who have benign prostatic hypertrophy because they can reduce bladder outlet obstruction. Unlike the beta blockers and thiazide diuretics, the alpha blockers have not been shown to decrease mortality. In fact, doxazosin caused an increase in
- **Mixed alpha and beta antagonists** such as labetalol. And carvedilol block both alpha receptors and beta receptors, so the reduction in blood pressure is usually not associated with reflex tachycardia. Labetalol is a very effective intravenous antihypertensive, but it is less frequently used chronically in its oral form. Carvedilol has had its primary use in the treatment of chronic congestive heart failure.

Methyldopa:



Methyldopa

(*S*)-2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid

Side Effects:

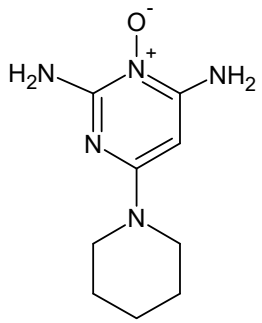
1. Prazocin: postural hypotension, diarrhea, occasional tachycardia, and tolerance (due to fluid retention).
2. Methyldopa: sedation, hepatotoxicity, hemolytic anemia, and tolerance.
3. Reserpine: depression, lethargy, weight loss, peptic ulcer, diarrhea, and impotence.
4. Clonidine: dry mouth, sedation, bradycardia, impotence, and rebound hypertension if stopped suddenly.

Vasodilator:

Eg. Minoxidil, hydralazine.

Arterial vasodilators such as minoxidil and hydralazine have relatively limited use. Neither has much effect on venous tone. The mechanism of action of hydralazine is not known. Minoxidil appears to increase potassium conductance in vascular smooth muscle, and the resultant hyperpolarization reduces calcium entry. Both drugs can cause reflex tachycardia (particularly minoxidil) and fluid retention. These side effects can be managed with the addition of a beta-blocker and/or a diuretic. Neither drug is effective for sustained periods. They are usually reserved for the short-term treatment of refractory hypertension, especially in patients with renal failure. Each of these drugs has a unique side effect: hydralazine can cause a lupus-like syndrome (cf. Drug Allergy case), and minoxidil can produce hair growth.

Minoxidil:



Minodixil

6-Piperidin-1-ylpyrimidine-2,4-diamine 3-oxide

Mechanism of action:

Minoxidil is also a vasodilator Hypothetically, by widening blood vessels and opening potassium channels, it allows more oxygen, blood, and nutrients to the follicle.

Side effects:

Chest pain, dizziness, fainting, tachycardia (rapid heartbeat), sudden and unexplained weight gain, or swelling of the hands and feet.

CONCLUSION:

The high cardiovascular risk in these patients requires an integrated therapeutic intervention that apart from effective antihypertensive therapy should include optimal achievement of goals for glycemic and lipid control, as well as inhibition of platelet aggregation .All patients with should be treated with a statin and, if needed, complimentary lipid-lowering drugs to reduce low-density lipoprotein cholesterol to <70 mg⁄dL, triglycerides to <150 mg⁄dL, and to raise high-density lipoprotein cholesterol to >40 mg⁄dL in men and >45 mg⁄dL in women.

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