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A Review: Pathophysiology of Hypertension

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ABSTRACT
Hypertension is mainly related to the heart and renal dysfunction. The main risk factor involved in hypertension i.e. cerebrovascular disease. Coronary artery disease & Congestive heart failure. Together with hypertension, other Cardio vascular risk factor, such as hyperlipidemia & diabetes along with vascular complications & sometimes patients death is observed. At that time we present on combination treatment & on fixed combinations of hypertension according to guidelines of ESH ,ESC& CSH from 2013. In most population the risk of CUS disease rises steeply with age. At most ages the risk of CUS disease is higher in men than in women.

At the time of treatment the most frequently recommended as dual combination include a blocker of the renin angiotensin system (ACE)& a CL+ channel blocker. It will also provide most of the data related to treatment in a collaborated form. The main purpose of this work is to comparatively study various drugs on hypertensin for their therapeutic dose potency & their side effed so that it will help in correct choice of medication to treat it.

Keywords: Hypertension, Antihypertensive drugs, Treatment, Combination therapy.

I. INTRODUCTION

o Defination:

Hypertension (HTN or HT), also known as high blood pressure (HBP), is a long term medical condition in which the blood pressure in the arteries is persistently elevated.The SBP will be more than or equal of 140 mmHg and DBP will be more than or equal of 90 mmHg.mmH

o Classification according to Blood Pressure

• Pre hypertention : SBP: 120-139 mmHg
DBP: 80-89 mmHg
• Hypertention stage I : SBP: 140-159 mmHg
DBP: 90-99 mmHg
• Hypertention stage II : SBP: more or equal to 160 mmHg
DBP: more or equal to 100 mmHg
• Pregnancy induced HTN: because of increased production of hormones and enzymes during pregnancy.

o Types of Hypertension

• Primary HTN: it is elevation in BP without an identified cause.
• Secondary HTN: it is elevation in BP with an exact cause.
This type is account for 5-10% of total eases.

The causes of Secondary HTN includes

i. Congenital narrowing of aorta.
ii. Renal disease
iii. Endocrine like Cushing's syndrome
iv. Neurological disorders like brain tumors and head injury
v. Sleep apnea
vi. Medication like oral contraceptive pills, NSAID, and Cocaine
vii. Cirrhosis of liver

o Risk Factor

a. Age chance of CAD after 50 yrs of age
b. Alcohol, smoking and DM
c. Excessive dietary intake of sodium
d. Gender
e. Family history
f. Obesity
g. Sedentary lifestyle
h. Traces

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Plans of Work

NEED'S & OBJECTIVE

- ✓ To compared the medication in different age groups for hypertension.
- ✓ To analyses interpreting drug's preferred for the hypertension.
- ✓ To assist identified patients with hypertension in achieving treatment goal.
- ✓ To study the pharmacology of Antihypertensive agent and to estimate awareness, Treatment, and adequacy of control of hypertension.
- ✓ To analyses dietary & nutritional intake in hypertensive patient

PATHOPHYSIOLOGY:

Hypertension is a chronic elevation of blood pressure that, in the long-Term, causes end-organ damage and results in increased morbidity and mortality. Blood pressure is the product of cardiac output and systemic vascular resistance. It Follows that patients with arterial hypertension may have an increase in cardiac Output, an increase in systemic vascular resistance, or both. In the younger age group, The cardiac output is often elevated, while in older patients increased systemic Vascular resistance and increased stiffness of the vasculature play a dominant role. Vascular tone may be elevated because of increased α-adrenoceptor stimulation or Increased release of peptides such as angiotensin or endothelin's. The final pathway Is an increase in cytosolic calcium in vascular smooth muscle causing Vasoconstriction. Several growth factors, including angiotensin and endothelin's, Cause an increase in vascular smooth muscle mass termed vascular remodeling. Both An increase in systemic vascular resistance and an increase in vascular stiffness Augment the load imposed on the left ventricle; this induces left ventricular Hypertrophy and left ventricular diastolic dysfunction.

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In youth, the pulse pressure generated by the left ventricle is relatively Low and the waves reflected by the peripheral vasculature occur mainly after the end Of systole, thus increasing pressure during the early part of diastole and improving Coronary perfusion. With ageing, stiffening of the aorta and elastic arteries increases The pulse pressure. Reflected waves move from early diastole to late systole. This Results in an increase in left ventricular afterload, and contributes to left ventricular Hypertrophy. The widening of the pulse pressure with ageing is a strong predictor of Coronary heart disease.

The autonomic nervous system plays an important role in the control of Blood pressure. In hypertensive patients, both increased release of, and enhanced Peripheral sensitivity to, norepinephrine can be found. In addition, there is increased Responsiveness to stressful stimuli. Another feature of arterial hypertension is a Resetting of the baroreflexes and decreased baroreceptor sensitivity. The renin–Angiotensin system is involved at least in some forms of hypertension (e.grenovascular hypertension) and is suppressed in the presence of primary Hyperaldosteronism. Elderly or black patients tend to have low-renin hypertension. Others have high-renin hypertension and these are more likely to develop myocardial Infarction and other cardiovascular complications.

In human essential hypertension, and experimental hypertension, volume Regulation and the relationship between blood pressure and sodium excretion (pressure natriuresis) are abnormal. Considerable evidence indicates that resetting of Pressure natriuresis plays a key role in causing hypertension. In patients with Essential hypertension, resetting of pressure natriuresis is characterized either by a Parallel shift to higher blood pressures and salt-insensitive hypertension, or by a Decreased slope of pressure natriuresis and salt-sensitive hypertension.

Consequences and complications of Hypertension

The cardiac consequences of hypertension are left ventricular Hypertrophy and coronary artery disease. Left ventricular hypertrophy is caused by Pressure overload and is concentric. There is an increase in muscle mass and wall Thickness but not ventricular volume. Left ventricular hypertrophy impairs diastolic Function, slowing ventricular relaxation and delaying filling. Left is an independent risk factor for cardiovascular disease, especially Sudden death. The consequences of hypertension are a function of its severity. There Is no threshold for complications to occur as elevation of blood pressure is associated With increased morbidity throughout the whole range of blood pressure.

Stages of hypertension

(Joint National Committee VI Guideline)

Stage	Systolic	Diastolic
Optimal	<120	<80
Normal	120-129	80-84
HT Stage 1	140-159	90-99
HT Stage 2	160-179	100-109
HT Stage 3	>180	>110

Coronary artery disease is associated with, and accelerated by, chronic arterial Hypertension, leading to myocardial ischemia and myocardial infarction. Indeed, Myocardial ischemia is much more frequent in untreated or poorly controlled Hypertensive patients than in normotensive patients. Two main factors contribute to Myocardial ischemia: a pressure related increase in oxygen demand and a decrease in Coronary oxygen supply resulting from associated atheromatous lesions. Hypertension Is a significant risk factor for death from coronary artery disease.Heart failure is

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a consequence of chronic pressure overload. It may start as diastolic Dysfunction and progresses to overt systolic failure with cardiac congestion. Strokes are Major complications of hypertension; they result from thrombosis, thrombo-embolism, Or intracranial hemorrhage. Renal disease, initially revealed by micro-albuminemia may Progress slowly and becomes evident in later years.

Classification of antihypertensive drug with examples

1. ACE INHIBITORS

Example : Captopril, enalapril, lisinopril, perindopril, ramipril

2. ANGIOTENSIVE ANTAGONISTS

Example : Losartan, irbesartan, candesartan

3. CLACIUM CHANNEL BLOCKERS

Example : Verapamil, diltiazem, nifedipine, felodipine, amlodipine, lecideine

4. DIURETICS

Example: Thiazide = hydrochlorothiazide, chlorthalidone, indapamide High celling = furosemide Kasperwing = spironolac tone, amiloride

5. B = ADRENERGIC BLOCKERS

Example : propranolol, metoprolol, atenolol

6. A+β ADRENERGIC BLOCKERS

Example : Labetalol, carvedilol

7. A ADRENERGIC BLOCKERS

Example :Prazosin, terazosin, phentolamine

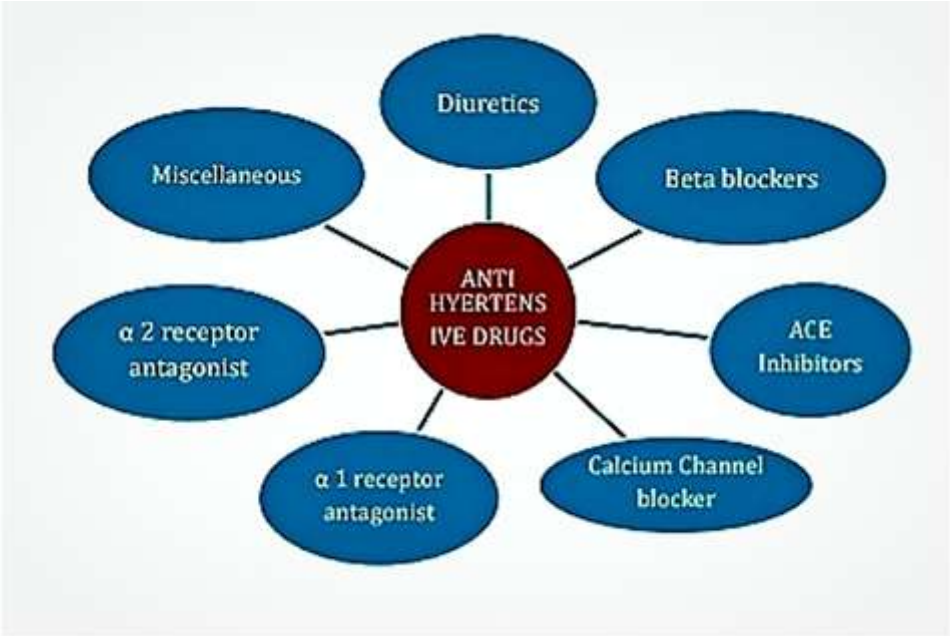
8. CENTRAL SYMPATHOLYTIC

Example : Clonidine, methyldopa

9. VASODILATORS

Example : Hydralazine, minoxidilsodium

PHARMACOLOGY OF ANTIHYPERTENSIVE DRUGS



Drug therapy

- Diuretics

Low-dose diuretic therapy is effective and reduces the risk of stroke, coronary heart disease, congestive heart failure, and total mortality. Whilst thiazides are most commonly used, loop diuretics are also used successfully and the association with a potassium sparing diuretic reduces the risk of both hypokalemia and hypomagnesaemia. Even in small doses diuretics potentiate other antihypertensive drugs. The risk of sudden death is reduced when potassium-sparing diuretics are used. In the long-term, spironolactone's reduce morbidity and mortality in patients with heart failure that is a typical complication of long-standing hypertension.

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- Beta-blockers

High sympathetic tone, angina, and previous myocardial infarction are good reasons for using β-blockers. As a low dose minimizes the risk of fatigue (an unpleasant effect of β-blockade) addition of a diuretic or a calcium channel blocker is often beneficial. However, β-blockade therapy is associated with symptoms of depression, fatigue, and sexual dysfunction. These side-effects have to be taken into consideration in the evaluation of the benefits of treatment.Over the past few years β-blockers have been used increasingly frequently in the management of heart failure, a known complication of arterial hypertension. They are effective but their introduction in the presence of heart failure has to be very cautious, starting with very low doses to avoid an initial worsening of heart failure.

- Calcium channel blockers

Calcium channel blockers can be divided into dihydropyridines (e.g. nifedipine, nimodipine, amlodipine) and non-dihydropyridines (verapamil, diltiazem). Both groups decrease peripheral vascular resistance but verapamil and diltiazem have negative inotropic and chronotropic effects. Short-acting dihydropyridines such as nifedipinecause reflex sympathetic activation and tachycardia, while long-acting drugs such as amlodipine and slow-release preparations of nifedipine cause less sympathetic activation. Short-acting dihydropyridines appear to increase the risk of sudden death. However, the systolic hypertension in Europe (SYST-EUR) trial which compared nitrendipine with placebo had to be stopped early because of significant benefits of active therapy.Calcium channel blockers are effective in the elderly and may be selected as monotherapy for patients with Raynaud's phenomenon, peripheral vascular disease, or asthma, as such patients do not tolerate β-blockers. Diltiazem and verapamil are contraindicated in heart failure. Nifedipine is effective in severe hypertension and can be used sublingually; there is need for caution because of the risk of excessive hypotension. Calcium channel blockers are often associated with β-blockers, diuretics and/or ACE inhibitors.

- Angiotensin converting enzyme inhibitors

ACE inhibitors are increasingly being used as first line therapy. They have relatively few side-effects and contraindications except bilateral renal artery stenoses. Though ACE inhibitors are effective in unilateral renovascular hypertension, there is risk of ischemicatrophy. Therefore, angioplasty or surgical renal artery reconstruction are preferable to long-term purely medical therapy. ACE inhibitors are first choice agents in diabetic hypertensive patients as they slow down the progression of renal dysfunction. In hypertension with heart failure, ACE inhibitors are also first choice drugs. The HOPE trial has shown that ramipril reduced the risk of cardiovascular events even in the absence of hypertension. Thus, this ACE inhibitor may exert a protective effect by mechanisms other than the reduction in blood pressure.

- Angiotensin II receptor blockers

As angiotensin II stimulates AT1-receptors that cause vasoconstriction, angiotensin AT1-receptor antagonists are effective antihypertensive drugs. Losartan, valsartan and candesartan are effective and cause less coughing than ACE inhibitors.The LIFE study is the most recent landmark trial in hypertension. More than 9000 Patients were randomized to receive either the angiotensin receptor antagonist losartan Or a β-blocker (atenolol). Patients in the losartan arm exhibited better reduction of Mortality and morbidity, owing to greater reduction in strokes. Losartan was also more Effective in reducing left ventricular hypertrophy, an independent powerful risk factor For adverse outcome. In patients with isolated systolic hypertension, the superiority of Losartan over atenolol was even more pronounced than in those with systolic and Diastolic hypertension. These favorable results led to an editorial entitled: 'Angiotensin Blockade in hypertension: a promise fulfilled'. It must be noted that the comparator in The LIFE study was a β-blocker, and that, in the past, β-blockers were found to be no Better than placebo in the elderly.

- α1-Adrenergic blockers

Free from metabolic side-effects, these drugs reduce blood cholesterol and reduce Peripheral vascular resistance. Prazosin is shorter acting than doxazosin, indolamineAnd terazosin. These drugs are highly selective for α1-adrenoceptors. Drowsiness, Postural hypotension, and occasionally tachycardia, can be troublesome. Fluid retention May require the addition of a diuretic. Phenoxybenzamine is a non-competitive α-Adrenoceptor agonist used (in association with a β-blocker) in the management ofPatients with

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phaeochromocytoma, though recently doxazosin has been used Successfully.

- Direct vasodilators

Hydralazine and minoxidil are directly acting vasodilators. Their usage has declined Because of the potential for serious side-effects (lupus syndrome with hydralazine, Hirsutism with minoxidil).

- Central adrenergic inhibitors

Methyldopa is both a false neurotransmitter and α2-adrenoceptor agonist. Clonidine andDexmedetomidine are agonists at centrally located α2-adrenoceptors. The selectivity for A2- vs α1- adrenoceptors is greatest for dexmedetomidine (1620:1), followed by Clonidine (220:1), and least for α-methyldopa (10:1). Both clonidine anddexmedetomidine make the circulation more stable, reduce the release of catecholamines in response to stress, and cause sedation such that dexmedetomidine is now used for sedation in intensive care units.Monoxide is representative of a new class of antihypertensive agents acting on imidazoline1 receptors (I1). Monoxide reduces sympathetic activity by acting on centersin the rostral ventral lateral medulla, thereby reducing peripheral vascular resistance.

- Natriuretic peptides

Natriuretic peptides play a role in the control of vascular tone and interact with the renin–angiotensin–aldosterone system. By inhibiting their degradation, peptidase inhibitors make these naturally occurring peptides more effective, thereby reducing vascular resistance. However, there are only small scale trials of their efficacy. Overall, recent studies have failed to demonstrate the superiority of modern agents over the more traditional drugs, except in special circumstances, as demonstrated in a meta-analysis based on 15 trials and 75 000 patients. In many patients, effective treatment is achieved by the association of two or more agents, with gain in efficacy and reduction of side-effects.

Causes and Treatment

There are two types of Causes:

1) Primary or essential hypertension

• Term applied to95% of cases in which no cause for hypertension can be Identified.
• The pathogenesis of essential hypertension is multifactorial
• Genetic factors paly a important role.
• Increased salt intake and obesity have long been incriminated.
• Environmental factors also are significant.

2) Secondary hypertension

Approximately 5% of patients with hypertension have specific causesWhen we suspect secondary hypertension

• In patients who develop hypertension at an early age with or without a Positive family history
• Those who first exhibit hypertension when over age 50 years.
• Those previously well controlled now become refractory to treatment

Treatment

1) Long-term treatment of hypertension

All anti-hypertensive drugs must act by decreasing the cardiac output, the peripheral vascular resistance, or both. The classes of drugs most commonly used include the thiazide diuretics, β-blockers, ACE inhibitors, angiotensin II receptors antagonists, calcium channel blockers, α-adrenoceptor blockers, combined α- and β-blockers, direct vasodilators, and some centrally acting drugs such as α2-adrenoceptor agonists and imidazoline I1 receptor agonists.

2) Self care-

• Lose weight if overweight
• Limit alcohol intake to no more than 1 oz(30ml) of ethanol ie 24oz (720ml) of beer, 10oz of wine
• Increase aerobic activity (30-45 min on most of days)
• Reduce sodium intake to no more than 100 mmol/day (6gm/day)
• Maintain adequate intake of potassium (approx. 90 mmol/day)
• Maintain adequate dietary intake of calcium and magnesium
• Stop smoking and reduce intake of dietary saturated fat and cholesterol for overall cardiovascular heal

II. SUMMERY & CONCLUSION

From the above study of regarding causes, treatment methods and combination therapy of Hypertension we, can conclude that, Hypertension can cause due to gene transfer.Patients withDiabetes Mellitus(DM) & Chronic Kidney Disease (CKD) require more aggressive Blood Pressure control. Most patients with hypertension will require two or more antihypertensive medications to control blood pressure. The use of

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combination therapy is appropriate as initial treatment. Due to Increased level of sodium in body, hence risk of Hypertension is High.Including standard diet plan patient may lead to Reducing in blood pressure. Like they change the lifestyle to reduce amount of salt, daily exercises can be reduced risk of Hypertension.Also, they regulate seasonal blood pressure variation. Pharmacological treatment like diuretics is most used in treatment of Hypertension also ACE inhibitors are used in patients with diabetes. Combination Therapy more effective for Hypertension in CKD, Hypertension in thyroid Disorders and Hypertension in Diabetes.

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