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A study of pathophysiological approach on hypertension and its comarbidities

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ABSTRACT

Hypertension is caused by increased blood pressure due to increased cardiac output and/or increased peripheral resistance. Hypertension is the leading cause of cardiovascular disease and premature death worldwide. Owing to the widespread use of antihypertensive medications, global mean blood pressure (BP) has remained constant or has decreased slightly over the past four decades. By contrast, the prevalence of hypertension has increased, especially in low- and middle-income countries.This article includes various types of hypertension,different pathological approaches such as based on autonomic nervous system and RAAS mechanism endothelial dysfunction,based on thrombophylia ,based on genetical cause.And it includes risks of getting hypertension and usual clinical manifestations were addressed , and also added diagnostic approaches and management of hypertension which includes both pharmacological and non pharmacological.

Keywords: Hypertension, Endothelial dysfunction, pharmacological approach

INTRODUCTION

Narrow blood vessels, also known as arteries create more resistance for blood flow. The narrower your arteries are, the more resistance there is, and the higher your blood pressure will be. Over the long term, the increased pressure can cause health issues, including heart disease.Hypertension is quite common. In fact, since the guidelines changed in 2017, nearly half of American adults could now be diagnosed with this condition.(1) Hypertension typically develops over the course of several years. Usually, you don't notice any symptoms. But even without symptoms, high blood pressure can cause damage to your blood vessels and organs, especially the brain, heart, eyes, and kidneys.Early detection is important. Regular blood pressure readings can help you and your doctor notice any changes. If your blood pressure is elevated, your doctor may have you check your blood pressure over a few weeks to see if the number stays elevated or falls back to normal levels.(2) Treatment for hypertension includes both prescription medication and healthy lifestyle changes. If the condition isn't treated, it could lead to health issues, including heart attack and stroke.(3)

TYPES OF HYPERSTENSION

Essential Hypertension

In as many as 95% of high blood pressure cases in the U.S., the underlying cause can't be found. This type of high blood pressure is called "essential hypertension."

Though essential hypertension remains somewhat mysterious, it has been linked to certain risk factors. High blood pressure tends to run in families and is more likely to affect men than women. Age and race also play a role. In the United States, blacks are twice as likely as whites to have high blood pressure, although the gap begins to narrow around age 44. After age 65, black women have the highest incidence of high blood pressure.(4)

Essential hypertension is also greatly influenced by diet and lifestyle. The link between salt and high blood pressure is especially compelling. People living on the northern islands of Japan eat more salt per capita than anyone else in the world and have the highest incidence of essential hypertension. Most people

with high blood pressure are "salt sensitive," meaning that anything more than the minimal bodily need for salt is too much for them and increases their blood pressure. Other factors that can raise the risk of having essential hypertension include obesity; diabetes; stress; insufficient intake of potassium, calcium, and magnesium; lack of physical activity; and chronic alcohol consumption.(5)

Secondary Hypertension

When a direct cause for high blood pressure can be identified, the condition is described as secondary hypertension. Among the known causes of secondary hypertension, kidney disease ranks highest. Hypertension can also be triggered by tumors or other abnormalities that cause the adrenal glands (small glands that sit atop the kidneys) to secrete excess amounts of the hormones that elevate blood pressure. Birth control pills -- specifically those containing estrogen -- and pregnancy can boost blood pressure, as can medications that constrict blood vessels.

RISK FACTORS

Age

Blood pressure tends to increase with age. Our blood vessels naturally thicken and stiffen over time. These changes increase the risk for high blood pressure.(6)

However, the risk of high blood pressure is increasing for children and teenagers, possibly because more children and teenagers are living with overweight or obesity.

Family history and genetics

High blood pressure often runs in families as hereditary . Many different genes are linked to a small increase in the risk high blood pressure. Research suggests that some DNA changes as an unborn baby grows in the womb may lead to high blood pressure later in life.

Gender

Middle age men are more likely to develop hypertension than women, but in older age ,women are more prone to develop hypertension.

One who develop high blood pressure during pregnancy are more likely to get hypertension in later period of their life

COMORBIDITIES

Other medical conditions change the way your body controls fluids, sodium, and hormones in your blood. Other conditions that can cause high blood pressure include:

Some of tumors

Metabolic disorders

Sleep disturbances

Abnormal in thyroid hormones

SOCIO - ECONOMIC FACTORS

According to some research , the factors like one's education, salary type, living area, based on job, might be risk of getting high blood pressure which results in hypertension.

Other factors include late night shifts leads to stress which in turn increase blood pressure.

RACE

During pregnancy, African women are more likely than white women to develop preeclampsia. Preeclampsia is a pregnancy disorder that causes sudden high blood pressure and problems with the kidneys and liver.(7)

MEDICINES

Some of the prescription and over-the-counter medications can make it more difficult for our body to control our blood pressure. Antidepressants like nortryptylline, decongestants such as oxymetazoline, hormonal birth control pills, and non-steroidal anti-inflammatory drugs such as aspirin or diclofenac or naproxen can all increase your blood pressure.

PATHOPHYSIOLOGY

1.BASED ON AUTONOMOUS NERVOUS SYSTEM AND RAAS MECHANISM

Sympathetic nervous system stimulation can cause both arteriolar constriction and arteriolar dilatation. Thus the autonomic nervous system has an important role in maintaining a normal blood pressure. It is also important in the mediation of short term changes in blood pressure in response to stress and physical exercise. There is, however, little evidence to suggest that epinephrine (adrenaline) and norepinephrine (noradrenaline) have any clear role in the aetiology of hypertension. Nevertheless, their effects are important, not least because drugs that block the sympathetic nervous system do lower blood pressure and have a well established therapeutic role.It is probable that hypertension is related to an interaction between the autonomic nervous system and the renin-angiotensin system, together with other factors, including sodium, circulating volume, and some of the more recently described hormones. (8)

2.BASED ON ENDOTHELIAL DYSFUNCTION

Vascular endothelial cells play a key role in cardiovascular regulation by producing a number of potent local vasoactive agents, including the vasodilator molecule nitric oxide and the vasoconstrictor peptide endothelin. Dysfunction of the endothelium has been implicated in human essential hypertension. Modulation of endothelial function is an attractive therapeutic option in attempting to minimise some of the important complications of hypertension. Clinically effective antihypertensive therapy appears to restore impaired production of nitric oxide, but does not seem to restore the impaired endothelium dependent vascular relaxation or vascular response to endothelial agonists. This indicates that such endothelial dysfunction is primary and becomes irreversible once the hypertensive proces has become established.

3.BASED ON THROMBOPHYLIA

Patients with hypertension demonstrate abnormalities of vessel wall (endothelial dysfunction or damage), the blood constituents (abnormal levels of haemostatic factors, platelet activation, and fibrinolysis), (9)and blood flow (rheology, viscosity, and flow reserve), suggesting that hypertension confers a prothrombotic or hypercoagulable state. These components appear to be related to target organ damage and long term prognosis, and some may be altered by antihypertensive treatment.

4.BASED ON GENETICAL CAUSE

Although separate genes and genetic factors have been linked to the development of essential hypertension, multiple genes are most likely contribute to the development of the disorder in a particular individual. It is therefore extremely difficult to

determine accurately the relative contributions of each of these genes. Nevertheless, hypertension is about twice as common in subjects who have one or two hypertensive parents, and many epidemiological studies suggest that genetic factors account for approximately 30% of the variation in blood pressure in various populations. This figure can be derived from comparisons of parents with their monozygotic and dizygotic twin children, as well as their other children, and with adopted children. Some familial concordance is, however, due to shared lifestyle (chiefly dietary) factors. Some specific genetic mutations can rarely cause hypertension. Experimental models of genetic hypertension have shown that the inherited tendency to hypertension resides primarily in the kidney. For example, animal and human studies show that a transplanted kidney from a hypertensive donor raises the blood pressure and increases the need for antihypertensive drugs in recipients coming from "normotensive" families. Conversely a kidney from a normotensive donor does not raise the blood pressure in the recipient.Increased plasma levels of angiotensinogen, the protein substrate acted on by renin to generate angiotensin I, have also been reported in hypertensive subjects and in children of hypertensive parents.(10) Hypertension is rarely found in rural or "tribal" areas of Africa, but it is very common in African cities and in black populations in Britain and the United States. Whereas the rural/urban differences in Africa are clearly due to lifestyle and dietary factors, the finding that hypertension is commoner in black people compared with white people may have some genetic basis. There is some evidence from salt loading studies in medical students that black Americans are more susceptible to a given salt load than white Americans, and may be more sensitive to the beneficial effects of salt restriction.

CLINICAL MANIFESTATIONS

If your blood pressure is extremely high, there may be certain symptoms to look out for, including:

- Nosebleed
- Fatigue or confusion
- Vision problems
- Chest pain
- Difficulty breathing
- Irregular heartbeat
- Blood in the urine
- Pounding in your chest, neck, or ears

DIAGNOSIS

- ***Electrocardiogram (EKG or ECG):*** A test that measures the electrical activity, rate, and rhythm of your heartbeat via electrodes attached to your arms, legs, and chest. The results are recorded on graph paper.
- ***Echocardiogram:*** This is a test that uses ultrasound waves to provide pictures of the heart's valves and chambers so the pumping action of the heart can be studied and measurement of the chambers and wall thickness of the heart can be made.

PHARMACOLOGICAL TREATMENT

Drug therapy is needed if lifestyle modifications cannot adequately bring BP to goal. First-line medications used in the treatment of hypertension include diuretics, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), beta-blockers, and calcium channel blockers (CCBs). Some patients will require 2 or more antihypertensive medications to achieve their BP target. In newly diagnosed patients with BP >20/10 mm Hg above goal, 2 antihypertensives or a combination hypertensive may be added immediately.1 To minimize side effects, a second drug with a complementary mechanism of action should be added before the initial drug is used in the maximum recommended dosing;

Drug	Dose range, mg/d	Common side effects
Eplerenone (planep)	50–100	Dizziness, fatigue, GI disturbances, hyperkalemia, hypertriglyceridemia
Spironolactone (spirocris)	25–50	CNS effects (drowsiness, lethargy, headache, fatigue), GI disturbances, hyperkalemia, menstrual irregularities, gynecomastia, mastodynia
Doxazosin (doxacard)	1–16	Dizziness, headache, lack of energy, nausea, palpitations, orthostatic hypotension
Prazosin (minipress)	2–20	
Terazosin (hytrin)	1–20	
Clonidine tablets (arkamin)	0.1–0.8	Dry mouth, dizziness, drowsiness, constipation
Methyldopa (aldomett)	250–1000	Drowsiness, decrease in mental acuity, orthostatic hypotension, nasal congestion, sexual difficulty, bradycardia
Benazepril (benace)	10–40	Hypotension, cough, hyperkalemia, dizziness, headache, diarrhea, nausea, rash (primarily captopril), alteration or loss of taste perception (primarily captopril)
Captopril (capotaz)	25–100	
Enalapril (enam)	2.5–40	
Fosinopril (fovas)	10–40	
Lisinopril (lispro)	5–40	
Moexipril (cardiotendin)	7.5–30	
Perindopril (coversyl)	4–16	
Quinapril (accupril)	10–80	

Drug	Dose range, mg/d	Common side effects
Ramipril (ramistar)	1.25–20	
Trandolapril (gopten)	1–4	
Candesartan (candosa)	8–32	Hypotension, hyperkalemia, dizziness, fatigue, diarrhea
Eprosartan (teveten)	400–800	
Irbesartan (irovel)	75–300	
Losartan (losar)	25–100	
Olmesartan (olmesar)	20–40	
Telmisartan (telma)	20–80	
Valsartan (valzaar)	80–320	
Atenolol (aten)	25–100	Bradycardia, hypotension, GI disturbances, dizziness, fatigue, insomnia, heart failure, reduced peripheral circulation, impotence, depression, nightmares, bronchospasm in patients with asthma, masks symptoms of or potentiates hypoglycemia in patients with diabetes, hypertriglyceridemia
Bisoprolol (concor)	2.5–10	
Carvedilol (cardivas)	12.5–50	
Labetalol (labetamac)	200–800	
Metoprolol tartrate (metolar)		
Metoprolol succinate (met xl)	50–100	
Nadolol (corgard)	40–120	
Propranolol (provanol)	40–160	
Amlodipine (amlodac)	2.5–10	Peripheral edema, palpitations, headache, dizziness, fatigue, nausea
Felodipine (felogard)	2.5–20	
Nicardipine (nicardelex)	60–120	
Nifedipine (nicardia retard)	30–60	
Diltiazem (dilzem)	120–420	Dizziness, headache, bradycardia, hypotension, constipation, nausea, weakness, gingival hyperplasia, edema, AV block
Verapamil sustained-release capsule (calaptin sr)	120–480	
Verapamil sustained-release tablet (calaptin sr)		
Bumetanide (Bumex)	0.5–2	Hyperuricemia, hypokalemia, hyperglycemia, hypocalcemia, increased urination at onset of therapy, dizziness, weakness, muscle cramps, photosensitivity, hypotension
Furosemide (lasix)	20–80	
Torsemide (dytor)	2.5–10	
Chlorthalidone	12.5–25	Similar electrolyte abnormalities as loop diuretics except for hypercalcemia, increased urination at onset of therapy, dizziness, weakness, muscle cramps, photosensitivity, hypotension
Hydrochlorothiazide (Microzide, HydroDiuril)	12.5–50	
Indapamide (Lozol)	1.25–2.5	
Metolazone (Zaroxolyn)	1.25–5	
Amiloride (Midamor)	5–10	Hyperkalemia, GI disturbances, muscle cramps, weakness, headache, dizziness
Triamterene (Dyrenium)	50–100	
Aliskiren (Tekturna)	150–300	Diarrhea, headache, dizziness, fatigue, cough
Hydralazine (Apresoline)	25–100	Tachycardia, palpitations, GI disturbances, headache
Minoxidil (Loniten)	2.5–80	Tachycardia, hypertrichosis, sodium and water retention

NON PHARAMACOLOGICAL TREATMENT

- Reduction in salt intake
- Quit smoking
- Reduce weight and avoid obesity
- Be careful with complementary, alternative or traditional medicine
- Reduce alcohol intake
- Monitor the blood pressure in stress conditions

- Avoid fatty foods

CONCLUSION

Here we conclude, Hypertension is preventable and reversible if uncontrolled will lead to chronic disease. The initial approach to hypertension should start with ruling out,secondary causes detecting and treating other cardiovascular risk factors and looking for target organ damage. Hypertension continues to be an important public health challenge throughout the world. It effects more than a billions adults worldwide. Most of the risk factors for hypertension is modifiable and can be prevented which in turn reduces cardiovascular diseases and strokes. Therefore this decreases the burden of hypertension and cardiovascular diseases worldwide.

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