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Review Article

A Basic Review on Hypertension, its Non-Pharmacological and Pharmacological Treatment

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Abstract

Hypertension (HTN) Is Prevalent Leading Health Issue Around the World. It is significant cause for cardiovascular morbidity and mortality risk factors? The term "high blood pressure" refers to hypertension. It is long term condition in which the blood pressure in the arteries continuously increased. Distribution of HTN in developed nation, in obese, elderly, pregnancy and now a day's teenager is also affected. The pathological mechanisms involved in HTN are genetics, sympathetic nervous system over activity, gender differences, cardiac output and peripheral vascular resistance, obstructive sleep apnoea, racial and ethnic factors, and many others. it can be prevented by reducing salt intake, weight loss, exercise, smoking cessation. There are many drugs are available for the treatment of this and its combination therapy is more effective. The pathophysiology, diagnosis, and current state of the disease's management are covered in this study.

Keywords: Hypertension, cardiovascular morbidity, cardiac output, peripheral vascular resistance

Introduction

When blood pressure rises due to excessive salt intake, the kidneys excrete more water and sodium, which results in an increase in the amount of fluid and a restoration of blood pressure to normal in normotensive individuals. The maintenance of salt balance at the cost of an increase in arterial pressure is referred to as the pressure-natriuresis phenomenaA little increase in glomerular filtration and a decrease in the renal tubules' absorption capacity are the mechanisms involved. Patients with primary hypertension have been demonstrated to reset the pressure-sodium excretion curve, which prevents the blood pressure from returning to normal[1-8].

Sleep apnea with obstruction

Obstructive sleep apnea (OSA) and hypertension (neurogenic hypertension) are related. The most common cause of people's persistent neurogenic hypertension is obstructive sleep apnea. OSA is clinically identified by sleep disruption, frequent awakenings, loud snoring at night, and daytime drowsiness. OSA is characterised by hypoxic apnea episodes during sleep. The carotid body chemoreceptors become active in response to repeated hypoxia, which also raises blood pressure and reflexively increases sympathetic activity. Electroencephalography, or EEG, is indicative of disorganised brain activity. To find OSA, polysomnography (PSG) is performed. Various hypoxia levels are visible on PSG. Continuous positive airway pressure reduces both daytime and nighttime hypertension, and the fall in blood pressure frequently occurs in tandem with a decline in sympathetic activity[9-12].

Vasoactive substances

Endothelin is a potent vasoconstrictor and one of the primary molecules that keep vascular tone intact. The first finding was made in 1985 by Hickey et al. It is secreted by endothelial cells and acts on vascular smooth muscle cells in a paracrine or autocrine manner, helping to counteract the sedative effects of NO[13, 14].

When the heart's atria experience an increase in blood volume, the hormone atrial natriuretic peptide is released. Through inducing the kidneys to produce more water and salt, it acts as a natural diuretic. A malfunction in this system could lead to hypertension and fluid retention. Furthermore, it is

believed that sodium transfer across vascular smooth muscle cell membranes affects blood pressure through interaction with calcium transport[15].

Racial and ethnic factors

Hypertension is more common in the black community, but it also causes more damage to target organs, starts earlier, and is more severe. It has been suggested that increased renal sodium absorption accounts for the greater prevalence of hypertension among black people[15, 16].

Uric acid and hypertension

Hyperuricemia is strongly correlated with cardiovascular events, metabolic syndrome, chronic renal illness, and hypertension, according to a number of experimental and epidemiological studies. In a review study by C Borghi (2017). It has been demonstrated that, in addition to known risk factors, gout patients' chance of acquiring cardiometabolic disorders rises significantly, as does the likelihood of silent hyperuricemia. Intracellular uric acid stimulates NADPH oxidase and helps to develop and progress hypertension by raising oxidative stress in the kidney and vascular smooth muscle, changing the mitochondrial response, decreasing NO levels in endothelial cells, and activating the renin-angiotensin system. Due to UA, microvascular renal disease and hypertension gradually develop on their own[17-19].

Vitamin D and hypertension

The frequency of vitamin D deficiency as shown by a 25-hydroxyvitamin D (25 [OH] D) level. The processes leading to hypertension may involve the interdependence of calcium-regulating hormones (vitamin D) and sodium-regulating hormones (the RAS) [20, 21].

Hypertension due to obesity

Weight gain raises sympathetic activity to burn fat, but studies have shown that this sympathetic hyperactivity leads to hypertension; the precise cues that trigger sympathetic outflow are unknown[22-24].

RAAS (renin angiotensin aldosterone system) over activity

According to a study Saxena et al 2014, there is a connection between diabetes and mental exhaustion, which is assessed by the perceived stress scale (EEG), or chronic stress. In addition, there was chronic stress, diabetes, and elevated basal sympathetic activity. Insulin can increase blood pressure through a variety of mechanisms, such as increased renal sodium reabsorption, sympathetic nervous system activation, modified transmembrane ion transport, and hypertrophy of resistance arteries. Hypertension can cause insulin resistance by affecting the body's ability to absorb glucose and modifying the amount of insulin that skeletal muscle cells receive. One possible common aetiology for both insulin resistance and hypertension is the activation of the sympathetic nervous system, which is most likely central in origin[25-29].

Environmental variables

Hypertension is linked to factors like stress, obesity, smoking, physical inactivity, excessive salt consumption, air pollution, and noise pollution.

Air pollution: A short period of exposure to air pollution significantly raises blood pressure in persons with normal blood pressure, particularly in the diastolic range. Exposed to fine particulate matter (PM2.5) having an aerodynamic diameter of less than 2.5 u, the lungs' afferents are stimulated, which naturally increases sympathetic activity. The systemic circulation can be reached by the smallest particles, which can lead to oxidative stress and vascular inflammation. A substantial risk of childhood hypertension exists for expectant mothers who breathe contaminated air and expose their foetus to a much polluted environment[30].

Noise pollution: Several solitary investigations and comprehensive reviews have demonstrated a positive association between noise pollution and high blood pressure. Furthermore, it is postulated that the relationship could be mediated through both direct and indirect pathways, with importance for physiological effects on the autonomic nervous system, sleep physiology, and endothelial function[31].

Smoking: Inflammation, lipids, endothelial function, and thrombosis can all be negatively impacted by tobacco use and e-cigarette use, which can raise blood pressure and speed up atherothrombotic processes[32].

Miscellaneous: In addition, the roles of potassium, magnesium, calcium, phosphorus, citrates, alcohol, coffee, cola, high altitude, toxic lead exposure, and macro- and micronutrients are taken into account.

Classification of hypertension[33]

Category	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
Normal	120-129	80-84
High normal	130-139	85-89

Hypertension

Stage 1 (mild)	140-159	90-99
Stage 2 (moderate)	160-179	100-109
Stage 3 (severe)	180-209	110-119

The dispersion of hypertension across populations

Hypertension in the Elderly: Particularly in the elderly, hypertension poses a serious risk for cardiovascular morbidity and mortality. Numerous studies have demonstrated that treating hypertension in older persons is safe and reduces their risk of heart attack, stroke, myocardial infarction, and overall mortality. Treatment for hypertension in elderly adults also decreases dementia and cognitive decline. One of the most important aspects of managing hypertension is living a healthy lifestyle. Although the data points to the potential benefits of several antihypertensive drug classes in reducing cardiovascular events, older adults with hypertension require more than one therapy to keep their blood pressure stable[34].

Hypertension during pregnancy: The use of antihypertensive drugs is fraught with controversy, especially when moderate hypertension is involved. PIH is a common health issue that can be detrimental to the foetus or baby as well as the mother. It is believed to be a complex health issue with a poorly known pathogenetic pathway[35].

Hypertension in Developing Countries: As one of the main causes of death and disability in developing nations, hypertension is a serious public health concern. By 2025, it is expected that 29% of adults worldwide would have hypertension, an increase from the current quarter. By 2025, it is anticipated that 1.15 billion individuals worldwide would suffer from hypertension in emerging nations. There have been many factors linked to this diversity, such as racial and

ethnic disparities, urbanisation and related lifestyle changes, nutritional status, and birth weight. Lack of awareness and insufficient care for people who have it exacerbate the disease's substantial burden[36].

Hypertension in the obese: Obesity is a major risk factor for important hypertension, diabetes, and other morbidities that contribute to the development of kidney disease because it primarily promotes tubular resorption to aggravate pressure natriuresis and promote volume expansion via the activation of the SNS and the RAS. Consuming foods rich in omega-3 fatty acids, fibre, antioxidants, plant and animal proteins, low in fat and sugar, vitamins, and fibre on a regular basis aids in the body's nutritional signalling pathways' adaptation to reference levels[37].

Hypertension in teenagers: Childhood hypertension has been related to cardiovascular disease risk factors, such as LVH and thicker arterial walls[38-44]. With a prevalence of 14% to 26%, LVH is the most commonly described kind of end organ damage in children and adolescents with hypertension[45]. Even after accounting for age, sex, and BMI, children with hypertension still have an elevated left ventricular mass index, which is linked to a higher risk of cardiovascular death. Mass index, which is linked to a higher risk of cardiovascular death.

Diagnosis of Hypertension

First line treatment

Establishing baseline blood pressure, assessing the degree of target organ damage and concurrent CVD, looking for specific causes of secondary hypertension that may be treated, identifying hypertensinogenic factors and other CVD risk factors, and characterising the patient will help with treatment decisions (particularly drug selection) and prognostic determination[46].

BP measurement

The most important part of the patient's diagnostic evaluation and follow-up is taking their blood pressure using the cuff technique, which is an effective and precise technique that should be done in a uniform manner using equipment that has been approved and calibrated .

Every visit ought to incorporate a couple of measures, with a minimum of two minutes separated among each measurement. An alternative to a mercury sphygmomanometer is a freshly calibrated aneroid manometer or an authorised electronic instrument coupled to an arm cuff. The systolic reading is collected at the level when sounds stop. Each excursion should involve two or three measures, with a minimum of two minutes elapsed between each measurement. The mercury sphygmomanometer can be substituted with a newly calibrated aneroid manometer or an approved electronic device fastened to an arm cuff. The systolic reading is obtained at the point at which sounds cease[33, 47, 48].

Laboratory tests and other diagnostic procedures

The only tests that are regarded as routine are urinalysis, a 12-lead ECG, a complete blood count, blood chemistry (potassium, salt, creatinine, fasting glucose, total and high-density lipoprotein, or HDL cholesterol), and a blood sample. Optional tests for the diagnosis of secondary hypertension and/or comorbid conditions are recommended in some patients. These tests include creatinine clearance, 24-hour urine protein, and measurement of microalbuminuria, uric acid, calcium, glycosylated haemoglobin, fasting triglycerides, limited echocardiography, 34, and plasma renin activity and aldosterone measurement[49].

Medical history and physical examination

A careful, complete history should be obtained and a physical examination performed in all patients before beginning treatment.

Some are-

The length of time and type of hypertension
Family background
Signs that could point to a hypertensive cause
CVD history of the patient
Elements related to lifestyle
Both past and present prescription drugs physical assessment
Two or more blood pressure measures, including one while standing
Confirmation in the opposite arm
Dimensions: height, weight, and waist size
A funduscopic examination for retinopathy caused by hypertension
Keep an eye out for symptoms of damage to the target organs in the abdomen, heart, lungs, neck, and extremities.

It should help detect other co-morbid conditions or CVD that may affect diagnosis or therapy, as well as known, treatable causes of high blood pressure and whether or not injury to the target organ and CVD are present.

Primary prevention of hypertension

In order to accomplish the main goal of treating all blood pressure-related illnesses in society at large, preventative strategies must be implemented in alongside the identification and management of hypertension[33].

Weight loss: Cross-sectional and longitudinal research has repeatedly found a link between obesity and hypertension, regardless of age[50]. Furthermore, several scientific trials have shown that losing weight may lower blood pressure[33, 51]. Men and women with high normal blood pressure participated in the Trials of Hypertension Prevention (TOHP), Phase I, and were given weight loss counselling. Their blood pressure dropped by -2.3 mm Hg in the diastolic phase and -2.9 mm Hg in the systolic phase (all K.01). As a result, people shed an average of -3.9 kg. Furthermore, weight loss treatments reduced the prevalence of hypertension by 34% (95% CI, 6% to 54%)[52].

Dietary sodium: Numerous research have demonstrated a connection between dietary sodium and blood pressure, including animal tests, observational epidemiological studies, migration studies, and randomised controlled trials[53]. Results from observational epidemiologic studies as well as randomised controlled trials have shown a dose-response relationship between dietary sodium and blood pressure in humanity. Within-population analyses in the cross-sectional INTERSALT study, which included 10,074 participants from 52 populations in 32 countries after correcting for regression dilution bias and adjusting for age and sex, revealed a relationship between a 100 mmol higher 24-hour urinary sodium and a 4.3 mm Hg increase in systolic and 1.8 mm Hg increase in diastolic blood pressure[54].

Potassium supplementation: Randomized controlled trials that were published between 1981 and 1995 were the subject of a meta-analysis by Whelton and colleagues. The average systolic blood pressure decreased by 3.1 (95% CI, -1.9 to -4.3) mm Hg, while the average diastolic blood pressure decreased by 2.0 (95% CI, -0.5 to -3.4) mm Hg with potassium supplementation[55].

Stress management: According to research from the Framingham Heart Study, anxiety levels among middle-aged

men were a strong predictor of the later incidence of hypertension[56].

Moderation in consumption of caffeine: A meta-analysis of 23 controlled clinical trials looking at the impact of coffee drinking on blood pressure was done by Jee and colleagues. Most of the trials were brief, and the majority of the subjects were normotensive. The average daily consumption of 3.3 cups of coffee was linked to a 2.4 (95% CI, 1.0 to 3.7) mm Hg rise in systolic blood pressure and a 1.2 (959'0 CI, 0.4 to 2.1) mm Hg rise in diastolic blood pressure among the 11 trials that lasted longer than two weeks[57].

Cross-sectional and prospective studies have demonstrated an inverse relation between dietary fiber intake and blood pressure[58, 59].

According to cross-sectional and prospective studies, blood pressure and dietary fiber intake are inversely correlated. The impact of fibre supplementation on blood pressure has been studied in at least 47 trials over the past few decades. He and colleagues conducted a meta-analysis of fibre supplementation in 12 randomised trials and found that there was an overall decrease in blood pressure of 1.2 (95% CI, -0.1 to -2.4) mm Hg for the systolic and 1.8 (950/, CI, -0.7 to -2.8) mm Hg for the diastolic, both P .05. The median dose of dietary fibre supplementation used during the trials was 14 g/day. Trial lengths ranged from 3 weeks to 1 year[53].

Fish oil supplementation: Clinical trials account for the majority of the data indicating that adding omega-3 polyunsaturated fatty acids, also known as fish oils, to the diet may lower blood pressure. Appel and colleagues observed an average decrease in systolic blood pressure of 1.5 (95% CI, -0.6 to -2.4) mm Hg and in diastolic blood pressure of 1.0 (95% CI, -0.4 to -1.6) mm Hg in a meta-analysis of 17 controlled trials (n = 1019) of fish oil intake[33].

Magnesium supplementation: Observational studies on the relationship between dietary magnesium consumption and blood pressure were examined by Mizushima and colleagues[60]. Twenty-seven of the 88 published observational studies on magnesium supplementation have been shown to have a negligible effect on hypertension patients' blood pressure in randomised controlled trials[33]. In TOHP-I, oral magnesium supplementation (340 mg/day) only slightly lowered systolic and diastolic blood pressure by -0.2 and -0.1 mm Hg, respectively[52].

Exercise in hypertension: By increasing physical activity, cardiovascular illnesses caused by hypertension may be averted. Vigorous activities, such as long-distance running, may have an even stronger preventive or pressure-lowering effect than less vigorous ones; however, this has not always been observed. (COX et al., 2001).Arroll and Beaglehole examined 22 published clinical trials that looked at the impact of exercise on blood pressure[61].

A serious study found that some type of design flaw or flaws were present in almost all of these trials. Both hypertensive and normotensive people who exercised saw a reduction in their blood pressure overall. A consistent and long-lasting reduction in both systolic and diastolic BP at rest and during activity is achieved in hypertensive individuals by engaging in a moderately frequent aerobic exercise program. Regular exercise may have a similar positive impact on hypertension treatment as pharmacological therapy[62].

Smoking: Smoking cessation for one week reduces blood pressure by 3-5 mmHg in chronic smokers[63].

Alcohol consumption: 2-4 mmHg drops with fewer than 2 drinks of alcohol per day for men and less than 1 drink per day for women[64].

Pharmacological Treatments for HTN

Choices of drugs for HTN are influenced by age, comorbidities, ethnicity, pregnancy and other parameters necessitating individual specific treatment regimens therefore only major drug classes are discussed in this review.

ACE inhibitors: Operate in two distinct ways. They lessen the metabolism of the active RAAS vasoconstrictor angiotensin II and increase the availability of the RAAS vasodilator bradykinin. These medications can be taken alone or in conjunction with calcium channel blockers (CCB) and diuretics, with the former being more advantageous in Caucasians, perhaps because the RAAS is less apparent in the black population. In patients with heart failure, chronic renal disease, left ventricular systolic dysfunction, and post-myocardial infarction, these medications have been shown to improve clinical outcomes, according to several studies[65,66].

Angiotensin receptor blockers (ARB's): Similar to ACE inhibitors, angiotensin receptor blockers (ARBs) work by inhibiting the AT1 receptor, which is in charge of the angiotensin II receptor's downstream actions, to target the RAAS? Due to comparable methods of action, patients using these medications enjoy the same advantages as those receiving the ACE inhibitors discussed before. As an added bonus, these medications do not result in an unwanted cough[67].

Direct renin inhibitors: Which, in contrast to ACE inhibitors and ARBs, target a different portion of the RAAS, are another treatment option for individuals who are resistant to first-line antihypertensive medications as an add-on or monotherapy[68].

Calcium channel blockers: In order to stop the contraction of smooth muscle cells and cardiac myocytes, calcium channel blockers (CCBs) attach to the L channels of vascular smooth muscle cells. Dihydropyridine Non-dihydropyridines work by reducing both heart rate and the force of myocardial contraction, unlike CCBs, which lower blood pressure primarily through direct vasodilation and lowering systemic vascular resistance. There is ample proof that CCBs lower the risk of stroke and improve overall mortality in people with HTN[69].

Beta-blockers: When treating hypertensive patients with a history of myocardial infarction and heart failure, beta-blockers are the medication of choice. When starting therapy in the setting of heart failure, it is important to anticipate that heart failure will initially get worse as a result of these medications' reductions in cardiac output and renal renin secretion.

Diuretics: Increased renal salt and water excretion is how diuretics work. Diuretics have a proven track record of enhancing cardiovascular health and lowering stroke risk[65,66,70,71]. Studies have shown that the use of spironolactone reduces the risk of morbidity and mortality in hypertensive individuals with heart failure, which is a long-term consequence of HTN[72].

Aldosterone antagonist: Spironolactone, an aldosterone antagonist that is a member of the mineralocorticoid receptor antagonist family, merits special attention because of the benefits it provides when used with ACE inhibitors, ARBs, CCBs, and diuretics, particularly in patients with heart failure. However, in patients who can tolerate it, it has been demonstrated that its use as an antihypertensive is excellent[72-74].

Alpha blockers: Since its inception more than ten years ago, the use of alpha-blockers in the treatment of HTN has developed further. In patients with uncontrolled HTN or those who have poor tolerance to other first-line treatments, this

drug, which reduces vascular sympathetic tone by blocking postganglionic 1-receptors, is typically used as an add-on therapy.

Additional HTN treatments include direct vasodilators and centrally acting adrenergic inhibitors, but due to their unfavourable side effects, clinical use of these drugs has been curtailed, and they are currently only used as add-on therapy for a select group of patients. The prospective applications of two more potential targets, endothelin receptor antagonists and vasopeptidase inhibitors, have not yet been established[75].

Resistant hypertension (rHTN) and treatment options An estimated 10–20% of the general hypertensive population experiences resistant hypertension, which is defined as blood pressure that remains above 140/90 mmHg despite treatment with at least three antihypertensive medications, including a diuretic, at optimal doses. (DA Calhoun and others, 2008) People with rHTN have 50% higher cardiovascular risks than those with controlled HTN, according to a US study[76].

Combination therapy for blood pressure reduction

RAAS Inhibitor + Diuretic When an ACE inhibitor, ARB, or direct renin inhibitor is used with a low-dose thiazide-type diuretic; a fully additive drop in blood pressure is achieved[77-80].

RAAS Inhibitor + CCB: Fully additive BP lowering occurs when an ACE inhibitor or ARB is used with a CCB[81-83].

Renin Inhibitor + ARBS: Together, a renin inhibitor and an ARB cause a well-tolerated, mostly additive drop in blood pressure. In a trial employing the highest permitted doses of both valsartan and aliskiren, the BP response was 30% larger than with either medication administered alone[84].

CCBs + Diuretics: Blood pressure is partially additively decreased when diuretics and CCBs are used simultaneously[85, 86].

Thiazide Diuretics + Potassium-Sparing Diuretics: Hypokalemia is an extremely serious dose-related side effect of thiazide diuretics. When used with a potassium-sparing diuretic like triamterene, amiloride, or spironolactone, which lowers hypokalemia, the safety profile of HCTZ is improved[87].

b-Blockers + Diuretics: Despite decreasing CV endpoints in placebo-controlled studies, beta-blockers are less effective than diuretics, ACE inhibitors, ARBs, and CCBs, according to meta-analyses (based mostly on atenolol's performance) [88-90].

RAAS Inhibitors + b-Blockers: Since both of these drug classes are cardioprotective, they are frequently given together to patients with coronary artery disease or heart failure. However, when compared to either of these medications taken alone, the combination of these medications does not significantly lower blood pressure[91].

CCBs + b-Blockers: The combined pharmacologic effects of these two pharmaceutical groups lower blood pressure in an additive way. In one trial, a low-dose combination of metoprolol extended-release (ER) and felodipine extended-release (ER), with a similar incidence of oedema as a placebo, reduced blood pressure to a level comparable to the maximum doses of each medication[92,93].

b-Blockers + Centrally Acting Agents: B-blockers and medications with a central action (such as clonidine and a-methyldopa) affect the sympathetic nervous system. How much of an additive BP-lowering effect they will have is uncertain. When they are combined, they may result in severe bradycardia or heart block. Patients using these drugs together run the risk of experiencing substantial rebound hypertension if abruptly stopped[94].

Conclusion

Hypertension is a very dangerous and most prominent disorder nowadays. It is the strongest or one of the strongest risk factors for almost all different cardiovascular diseases acquired during life, cerebral stroke and renal failure. It can be caused due to obesity, genetically reason, pregnancy, vitamin D deficiency many more reasons as well. We have many ways to diagnose hypertension. In market there is many drugs and their combination of drugs are available in market. Many natural products is also available in market But still many were dyeing due to suffering of hypertension. After reviewing we conclude that death rate due to hypertension is because of ignorance of symptoms of disease and due to unhealthy habits so, Pharmaceutical therapy of Hypertension is quintessential, life style interventions are equally important in conquering this preventable and easily diagnosed pathology.

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