HYPERTENSION: AN OVERVIEW

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Hypertension is a serious challenge worldwide. It is one of the most prevalent conditions seen today by researchers in both developed and underdeveloped countries. Depending upon progression of systolic and diastolic blood pressure it is classified into prehypertension, stage 1 and 2 hypertension. Modification in the lifestyle is an initial stage but pharmacological treatment is necessary when it become difficult to control it. In regular practice, drug therapy 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. This article is all about the reasons and treatments of hypertension. The article elaborates the common reasons which lead to raise the blood pressure in a normal individual. It also reviews the studies related to the effect of different factors of our daily life on the blood pressure.

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Introduction

The heart pumps blood through the blood vessels, the blood is pushed against the walls of the blood vessels. This creates a pressure, called as blood pressure. Body requires this pressure to move the blood throughout in itself. So that every part of body can get the oxygen it needs. Healthy arteries are elastic and they stretch to allow more blood to push through them. Their stretch depends on how hard the blood is pushed against the artery walls. It's important that the blood pressure be within a healthy range to remain healthy.

A device called sphygmomanometer is used to measure blood pressure. Blood pressure is recorded as two numbers. Systolic blood pressure ("upper" number) tells about the pressure exerted by blood against artery walls while the heart is pumping blood. The diastolic blood pressure (the "lower" number) tells about the pressure exerted by blood against artery walls while the heart is resting between beats. Blood pressure is measured in units of mm of Hg. For example, a blood pressure reading might be 120/80 mm Hg. A healthy blood pressure is under 120/80 mm Hg. A blood pressure reading of 120-139 systolic or 80-89 diastolic is defined as "prehypertension." This means that the blood pressure is not high enough to be called high blood pressure (hypertension), but that it is higher than normal. If systolic blood pressure is 140 or greater, or diastolic blood pressure is 90 or greater, it's high blood pressure (Table 1).

Factors affecting blood pressure

Hypertension has been emerged as a challenge worldwide irrespective of developing and developed nations.[1] It is responsible for the death of 1 billion individuals, and approximately 7.1 million per year.[2] Its recognition is for cardiovascular disease (CVD), cerebrovascular disease and end-stage renal disease. A significant relationship between hypertension and risk factors such as age, body mass index, smoking and physical inactivity are reported by many studies. Chronic disease conditions including hypertension include physical inactivity as a major factor.[3]

Hypertension is a different kind of medical condition. In almost 90 % of patients it results from unknown factors (essential or primary hypertension) and only 10 % of patients have a specific cause of their hypertension (secondary hypertension). While essential hypertension cannot be cured, it can be controlled. Although it has frequently been indicated that the causes of essential hypertension are not known, this is only partially true because we have little information on genetic variations or genes that are over-expressed or under-expressed as well as the intermediary phenotypes that they regulate to cause high BP.[4] A number of factors increase BP, including physical activity, obesity, insulin resistance, high alcohol intake, high salt intake, ageing, sedentary lifestyle, stress, low potassium intake and low calcium intake.[5,6]

Table 1. Threshold values.

Blood Pressure Category	Systolic (mm Hg)		Diastolic (mm Hg)
Normal	<120	and	< 80
Prehypertension	120-139	or	80-89
Hypertension (Stage 1)	140-159	or	90-99
Hypertension (Stage 2)	=>160	or	=>100
Hypertensive crisis (Emergency)	>180	or	>110

Physical activity

Lack of physical activity lead to many chronic conditions and hypertension is one of them.7 Commonly the people do not control blood pressure adequately, which contribute towards excessive cardiovascular mortality & morbidity. Risk of hypertention can be prevented and the best way to do this is life style modification. Hypertension can be controlled by doing physical activities. Many studies are finding the support in this way. An article (effect of exercise

on blood pressure control in hypertensive patients) reported that exercise can be a cornerstone therapy for the prevention, treatment, and control of hypertension.[8]

A review of 15 studies supported that exercise is an important practice to treat the moderate elevations in blood pressure.[9] An article used data of National Health and Nutritional Examination Survey III, found that patients who followed the advice to engage in physical activity to treat hypertension had systolic blood pressure that was on average of approximately equal to 3-4 mm Hg lower than those who did not follow them.[10]

Regular exercise reduces systolic blood pressure in prehypertensive as well as hypertensive people.[11] Systematic review of randomized controlled trials shows that blood pressure reductions were followed by weight loss, modification in diet and increased physical activity.[12]

Diet and exercise, alone or combination, were reported as an effective tool in reducing the blood pressure in subjects with moderate hypertension, with same effect of drug therapy in patients with higher BP level.[13] A research on Japanese-American people in Hawaii stated the beneficial outcomes of physical activity, body weight control, and reduction in salt intake in population-based control of high BP.[14]

The United States National High Blood Pressure Education Program Coordinating Committee has recommended weight loss, dietary sodium reduction, increased physical activity; potassium supplementation and modification of whole diets are six approaches which are efficient for the primary prevention of hypertension.[15].

Physical activity is required to lower blood pressure in hypertensive patients because it is natural, inexpensive, feasible, and effective means of control for hypertension and also a primary life style measure. The US Preventive Services Task Force (USPSTF) recommends the health care providers to counsel the patients for regular physical activity.[16] In the east part of New Zealand, a randomly controlled trial reported the reduction in BP by an average of 1-2 mm Hg over 12 months by counseling patients for general practice on exercise. The recommended that increasing physical activity and improving quality of life may reduce blood pressure by an average.[17] A meta-analysis including 69 studies demonstrated that, despite the relatively small effects, physically active subjects had better cardiovascular recovery than inactive ones.[18]

Stress

Stress can be defined according to the Medical Subject Headings (MeSH) as, a pathological process resulting from body response to external forces and abnormal states that tend to affect its homeostasis. It consists of daily events that enhance physiological activities and lead to somewhat psychological wear and tear.[19] Psychological stress is a condition when emotional stressors are prevailing. Events of the modernized life such as working conditions and family problems, withdrawal from society, financial planning and quarrels are some factors that can enhance stress.[20] Long term chronic exposure to psychological stress can cause increased blood pressure which can develop as hypertension.[21] A study of over 3,000 individuals[22] showed that urgency/impatience behavior, and hostility assessed during young adulthood along with depression and anxiety were the strong reasons for developing hypertension after 15 years. Financial strain lead to chronic stress has been reported to predict high blood pressure during three to seven years of follow-up.[23] Total 11,119 cases and 13,648 controls from 52 countries were studied[24] which reported attachment of myocardial infarction (cases) and more frequent periods of stress at home, more severe financial stress and more stressful life events compared with controls.

With reference to myocardial infarction risk, the effect of psychosocial stress was also as important as traditional cardiovascular disease risk factors such as smoking, obesity, diabetes and hypertension. A review of 23 treatment comparisons from 17 trials conducted in patients with raised BP, showed strong effects of meditations on lowering of blood pressure. Despite non-significant results, other anti-stress interventions such as biofeedback, progressive muscle relaxation and stress management training also reported clinically important reductions in blood pressure.[25] Therapies such as these may help patients to reduce the effects of stress by reducing physiologic arousal and restoring autonomic balance, thereby reducing blood pressure.[21] Stress reduction has often been regarded as an important component of the lifestyle changes that might be beneficial in reducing an elevated blood pressure in hypertensive patients.[26]

Working hours

Many disorders and diseases can be considered as an effect of working hours such as chronic fatigue,[27,28] musculoskeletal complaints,[29] mental stress or health,30-32 dissatisfaction with work,[33] depression,[34] and coronary heart disease.[35,36] As for the association between long working hours and blood pressure, the effect of long working hours on blood pressure is related to the activity of sympathetic nervous system and concentrations of hormones that accompanies psychological stress[37,38] and physical activity.[39] As overtime work is very often accompanied by such stress and physical activity, it is quite obvious to expect an association between long working hours and hypertension. Association of working hours per day with the risk for development of hypertension during five years in hypertension free subjects is shown in table 2.[40] During five years of follow up of 3940 person years were stuided, 336 men developed hypertension above the borderline level. The multivariate adjusted relative risk for hypertension above the borderline level, compared with those who worked < 8.0 hours per day, was 0.91 (95% confidence intervals (CI): 0.69, 1.21) for those who worked 8.0–8.9 hours per day, 0.79 (95% CI: 0.57, 1.08) for those who worked 9.0–9.9 hours per day, 0.63 (95% CI: 0.43, 0.91) for those who worked 10.0–10.9 hours per day, and 0.48 (95% CI: 0.31, 0.74) for those who worked > 11.0 hours per day (p for trend < 0.001). As for the incidence of definite hypertension, 88 men developed definite hypertension during five years of follow up (representing 4531 person years). The respective multivariate adjusted relative risks for definite hypertension, compared with those who worked < 8.0 hours per day, were 0.68 (95% CI: 0.39, 1.18), 0.93 (95% CI: 0.53, 1.65), 0.56 (95% CI: 0.27, 1.17), and 0.33 (95% CI: 0.11, 0.95) (p for trend = 0.045).[40]

Table 2. Correlation of working hours per day and the risk of hypertension.

	Working hours per day					
	<8.0	**8.0-8.9**	**9.0-9.9**	**10.0-10.9**	**>11.0**	**p for trend***
Hypertension above the borderline level						
Cases	113	92	61	41	29	
Person years	1022	969	695	645	610	
Rate per 1000 person years	110.6	94.9	87.8	63.6	47.6	
Age adjusted relative risk	1.00	0.86	0.81	0.60	0.45	<0.001
(95 % CI)	(Reference)	(0.66, 1.14)	(0.60, 1.11)	(0.42, 0.87)	(0.30, 0.68)	
Multivariate adjusted relative risk	1.00	0.91	0.79	0.63	0.48	<0.001
(95 % CI)	(Reference)	(0.69, 1.21)	(0.57, 1.08)	(0.43, 0.91)	(0.31, 0.74)	
Definite hypertension						
Cases	31	23	20	10	4	
Person years	1221	1160	782	711	658	
Rate per 1000 person years	25.4	19.8	25.6	14.1	6.1	
Age adjusted relative risk	1.00	0.78	1.03	0.57	0.25	0.010
(95% CI)	(Reference)	(0.45, 1.34)	(0.58, 1.81)	(0.28, 1.18)	(0.09, 0.70)	
Multivariate adjusted relative risk	1.00	0.68	0.93	0.56	0.33	0.045
(95% CI)	(Reference)	(0.39, 1.18)	(0.53, 1.65)	(0.27, 1.17)	(0.11, 0.95)	

Salt intake

It is well known that consumption of salt-rich diet lead to elevation of blood pressure in healthy individuals and is also responsible for making body vulnerable for cardiovascular events, intake of salt in food is generally not within the safe limit (5 g = 87 mmol per day) in developed as well as underdeveloped countries .[41] Even a moderate reduction in salt intake in the general population would be able to have an impact on health and it would reverse 8.5 million cardio-vascular related deaths in the world within a time interval of 10 years.[42] WHO have made a conclusion in a large meta analysis, that the management of cardiovascular diseases is having 11 % part in the total health expenditure in the world.[43]

The involvement of salt in developing hypertension is supported by the study of eight different randomized controlled trials of moderate dietary salt restriction, one observational review of a randomized controlled trial (TOHP Stage II) and one case-control study[44] including 2605 participants. The results gave evidence a reduction in systolic and diastolic blood pressure and urinary sodium excretion when the salt intake was reduced. The data in these 10 trials suggest that if we reduce consumption of salt in daily life, it will help us to maintain the blood pressure and help patients on anti-hypertensive therapy to leave or less use of medication without losing control on blood pressure. Other than blood pressure, studies also show the effects of low salt consumption on protein output of urine,[45] pulse wave velocity,[46] and other measures of vascular activities, namely aortic pulse wave velocity and augmentation index,[47] heart rate variability,[48] carotid artery compliance in the middle aged to older men and women,[49] and variability and consistency of individual systolic blood pressure responses.[50, 51]

There are many strong evidences which support the role of salt intake in causing hypertension. The normal salt ingestion in most countries lies between 9 and 12 g day^{-1}.[52] In Latin American and the Caribbean countries, after year 2000, its value exceeds 9 g day^{-1}.[53] It is about 40 times higher than the amount our ancestors consumed during several million years of their development. This high increase in salt ingestion is relatively recent in evolutionary terms. Physiological systems also face challenge when this amount of salt is excreted through kidneys which causes a gradual rise in BP[54,55] and body become vulnerable to CVD and kidney diseases. An update on the evidences related to the role of salt intake to BP and cardiovascular diseases has been published. The report also provides a brief update on salt reduction programs being carried out in several countries, particularly in the Americas.[56]

Treatment

As recommended by Joint National Committee 7 of WHO, a practical approach regarding this is to continue to involve lifestyle modifications (non pharmacological treatment). If it does not give the expected results, then pharmacological therapy should be introduced.[57] These therapies work only in the case of sustained hypertension, they are not meant for resistant hypertension.

Non-pharmacological

Modification in the lifestyle is the key process to prevent the onset of hypertension and is necessary therapy for those who are suffering from hypertension.[58] Lifestyle modifications should be introduced, whenever appropriate, in all patients, including those who require drug treatment. The main goal is to lower BP, to control cardiovascular risk factors and to reduce the number or the doses of antihypertensive drugs to a minimum level.[59]

These modifications include weight reduction in overweight or obese patients, physical activity, controlled sodium intake, the adoption of the Dietary Approaches to Stop Hypertension (DASH) diet, controlled alcohol consumption, and reduction in smoking. According to these guidelines, patients whose SBP (Systolic BP) and DBP (Diastolic BP) falls between 130 and 139 mmHg and 80 and 89 mmHg, respectively, should modify their lifestyle to control BP but the effect of this therapy should be observed for maximum of 3 months. If it is not working then the patient should move towards pharmacological treatment.[57]

Dietary modification

DASH-trial proved reductions in BP of 11.4/5.5 mmHg in persons having hypertension on a diet rich in fruits, vegetables, and low-fat dairy products, compared with those people who were on a so-called "usual American diet". Dietary salt intake and weight were kept constant.[60] Another two clinical trials, one with a comprehensive food plan that supplied the recommended dietary allowances of all major nutrients and the other with a diet rich in fruits, vegetables, and low-fat dairy products and reduction in saturated and total fat produced reductions in BP comparable to or greater than those usually seen with monotherapy for stage 1 hypertension.[61, 62] Dietary salt intake has a linear association with blood pressure. Reduced sodium intake to approximately 100 mmol day^{-1} can prevent the development of hypertension.[63]

Weight loss and physical activity

Overweight (body mass index >25 kg/m^2) has been seen in epidemiologic studies to be an important risk factor for higher blood pressure, and there seems to be a linear relation between body weight and blood pressure.[64] Clinical trials have shown that weight loss, specially when combined with dietary sodium restriction, lowers blood pressure in hypertensive and also in normotensive patients. The Hypertension Prevention Trial showed that a 4 % reduction in body weight over 3 years was associated with a 2.4 mmHg reduction in SBP and a 1.8 mmHg reduction in DBP.[63] Increasing aerobic physical activity such as brisk walking, jogging, swimming or bicycling has been shown to lower BP. A meta-analysis of 54 randomized controlled trials showed a net reduction of 3.8 mmHg in SBP and 2.6 mmHg in DBP in individuals performing aerobic exercises, compared to controls.[65]

Pharmacological treatment

As blood pressure increases, it become more difficult to control it at the target level through life style modifications alone and treatment with antihypertensive drugs becomes necessary. WHO guidelines also recommend the use of antihypertensive drugs in patients with grade 1 hypertension at low or moderate cardiovascular risk, that is, when BP is between 140 and 159 mmHg SBP and/or 90 and 99 mmHg DBP, provided nonpharmacological treatment has proved unsuccessful. So, in these conditions the patient should move towards pharmacological treatment.

Diuretics

The steady introduction of newer agents and their heavy promotion by the industry made physicians switch away from use of diuretics as first line agents in the treatment of mild to moderate hypertension but then also thiazide type of diuretics offer better reduction of blood pressure with lesser incidence of coronary revascularization and heart failure as compared to other drugs like CCB, ACEI or ARB.[66] The evidence from the SHEP study emphasizes the value of a low-dose thiazide-type drug as initial therapy for isolated systolic hypertension in older patients.[67] Clinical trial data also indicate that diuretics are generally well tolerated.[66-68]

β-Blockers

These drugs decrease cardiac output and the slowing of heart rate and was originally thought to be of clinical importance, particularly in hypertensive patients with tachycardia. But, at the same time, peripheral resistance is increased slightly and sodium reabsorption by the kidney is increased. The ability of β-blockers to inhibit activity of the RAS by reducing the release of renin from the juxtaglomerular cells of the kidney may contribute to their blood pressure lowering effects, especially in patients with medium or high levels of plasma renin activity.[69] Over time, they became widely accepted for the treatment of hypertension, and one of the reasons for the acceptance of this drug class by clinicians was that these agents appeared to be better tolerated than many of the drugs previously available for treating hypertension.[70]

Angiotensin-converting enzyme Inhibitors, angiotensin receptor antagonists and renin inhibitors

Inhibitors of the renin-angiotensin system (RAS), including ACE-inhibitors, ARBs and now direct rennin inhibitor (DRI) are commonly used in the treatment of hypertension.[71] ACE-inhibitors modulate blood pressure by inhibiting ACE mediated conversion of angiotensin I to angiotensin II. ARBs modulate blood pressure by inhibiting the activation of the AT1 receptor by angiotensin II.[72] Aliskiren, a direct renin inhibitor, is the first of a new class of antihypertensive drugs that block the RAS further upstream. Its antihypertensive effect, safety, and tolerability are comparable with ARBs and ACE inhibitors, however, its long-term data is awaited.[73]

Calcium channel blockers

CCBs which include both dihydropyridines (DHPs) e.g., nifedipine and amlodipine and non-dihydropyridines, like verapamil and diltiazem, are among the most widely prescribed agents for the management of essential hypertension. Several large outcome risk trials and comprehensive meta-analyses have found that CCBs reduce the cardiovascular morbidity and mortality associated with uncontrolled hypertension, including stroke.[74] Conditions favoring the choice of a DHP CCB for hypertension include: advanced age, isolated systolic hypertension, angina pectoris, peripheral vascular disease, carotid atherosclerosis, and pregnancy. Diltiazem or verapamil is considered for use in patients with angina pectoris or supraventricular tachycardia.

Alpha-1 receptor antagonist

A1-adrenergic blocking drugs are effective in reducing blood pressure and do so in a fashion comparable to most other antihypertensive drug classes.[75] Initially, for many years α1-adrenergic antagonists had been considered suitable initial drugs for uncomplicated early-stage hypertension. But guidelines including the European Society of Hypertension/European Society of Cardiology and the authors of the JNC 7 no longer include α1-adrenergic antagonists as initial agents for the treatment of hypertension.[57,59,76]

TRPV1 antagonists

Transient Receptor Potential Vanilloid Receptor type 1 is the latest site for the antihypertensive action. The endocannabinoid, anandamide, can have depressor effects and its production is upregulated in certain pathophysiological states.[77] TRPV1 receptor has been implicated in the hypotensive effects of anandamide.[78-80] Oleamide (*cis*-9 10 octadecenoamide) is a fatty acid primary amide, which was originally derived from sleep-deprived cats and shares structural similarities with anandamide.[81]

Conclusion

After reviewing the literature, it is concluded that hypertension is one of the biggest challenge in the present scenario. Each and every country of the world is in the grip of the disease irrespective of the status of its development. The disease is having prevalent in every kind of population. Now there is a need to make people aware regarding the enormity of the disease and the ways to prevent it. Patient should be given first the nonpharmacological treatment and then they should move towards the pharmacological treatment, if necessary. Life style of the people is the main cause of hypertension and it need to be modified. The world is developing, everything is going in a forward direction so we need to move our health in a forward direction.

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