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Review Article

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Review on Hypertension

T. Anantha lakshmi*, M. Ramesh, B. Mounika, K. Bhuvaneswari, Sreekanth Nama

Priyadarshini institute of pharmaceutical education & research (PIPER)
5th mile, Vatticherukuru (M), Guntur -523169
*E-mail: brahmaiahmph@gmail.com

Abstract

In this review the discussion was about the prevalence, awareness, diagnosis, treatment, and control of hypertension in a population-representative sample of adults. Hypertension is a major health problem throughout the world because of its high prevalence and its association with increased risk of cardiovascular disease. Advances in the diagnosis and treatment of hypertension have played a major role in recent dramatic declines in coronary heart disease and stroke mortality in industrialized countries. However, in many of these countries, the control rates for high blood pressure have actually slowed in the last few years. It is estimated that by 2010, 1.2 billion people will be suffering hypertension worldwide. In the Eastern Mediterranean Region, the prevalence of hypertension averages 26% and it affects approximately 125 million individuals. Of greater concern is that cardiovascular complications of high blood pressure are on the increase, including the incidence of stroke, end-stage renal disease and heart failure.

Key words: Hypertension, Angiotensin, Diagnosis, Risk factors, Treatment.

Introduction

High blood pressure (hypertension) is one of the most important preventable causes of premature morbidity and mortality in the UK (Cain AE *et al* 2002). Hypertension is a major risk factor for ischemic and hemorrhagic stroke, myocardial infarction, heart failure, chronic kidney disease, cognitive decline and premature death. Blood pressure is normally distributed in the population and there is no natural cut-off point above which 'hypertension' definitively exists and below which it does not. 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 ischemic heart disease and an 10% increased risk of mortality from stroke. Hypertension is remarkably common in the UK 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 [1]. The clinical management of hypertension is one of the most common interventions in primary care, accounting for approximately £1 billion in drug costs alone in 2006 [2].

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 motu cordis". The English clergyman Stephen Hales made the first published measurement of blood pressure in 1733.(Haynes WG 1998) Descriptions of hypertension as a disease came among others from Thomas Young in 1808 and especially Richard Bright in 1836. The first report of elevated blood pressure in a person without evidence of kidney disease was made by Frederick Akbar Mahomed (1849–1884).

The concept of essential hypertension ('hypertonie essential') was introduced in 1925 by the physiologist Otto Frank to describe elevated blood pressure for which no cause could be found. In 1928, the term malignant hypertension was coined by physicians from the Mayo Clinic to describe a syndrome of very high blood pressure, severe retinopathy and adequate kidney function which usually resulted in death within a year from strokes, heart failure or kidney failure [3] Consequently, hypertension was often classified into "malignant" and "benign". In 1931, John Hay, Professor of Medicine at Liverpool University, wrote that "there is some truth in the saying that the greatest danger to a man with a high blood pressure lies in its discovery, because then some fool is certain to try and reduce it" [4].This view was echoed by the eminent US cardiologist Paul Dudley White in 1937, who suggested that "hypertension may be an important compensatory mechanism which should not be tampered with, even where it certain that we could control it".Charles Friedberg's 1949 classic textbook "Diseases of the Heart", stated that "people with 'mild benign' hypertension ... [defined as blood pressures up to levels of 210/100 mm Hg] ... need not be treated".Subsequently the National Institutes of Health also sponsored other population studies, which additionally showed that African Americans had a higher burden of hypertension and its complications.

Definition of Hypertension

Hypertension is defined as an abnormal elevation in diastolic pressure and/or systolic pressure; mean arterial pressure is also elevated in hypertension, but it is not usually measured in people. In past years, the diastolic value was emphasized in assessing hypertension. However, elevations in systolic pressure ("systolic hypertension") are also associated with increased incidence of coronary and cerebrovascular disease (e.g., stroke). Therefore, we now recognize that both systolic and diastolic pressure values are important to note. According to the latest U.S. national guideline [5], the following represents different stages of hypertension:

Classification	Systolic (mmHg)	Diastolic (mmHg)
Normal	<120	<80
Prehypertension	120-139	80-89
Stage 1	140-159	90-99
Stage 2	>160	

Symptoms of high blood pressure

Although patients with isolated hypertension are usually asymptomatic, occasionally they have symptoms such as Dizziness, Headache (especially pulsating headaches behind the eyes that occur early in the morning), Blurred vision, Facial flushing or tinnitus (ringing sound in the ears).Hypertension which is very severe with a systolic blood pressure (SBP) >240 mmHg or diastolic blood pressure (DBP) >120 mmHg is called accelerated hypertension. Accelerated hypertension is associated with confusion, visual disturbances, nausea and vomiting. When hypertension causes increased intracranial pressure (pressure exerted by the cranium on the brain tissue and brain fluid), it is called malignant hypertension or hypertensive crisis and is a medical emergency that requires immediate reduction of the blood pressure. This condition may present with end-organ damage.

Over time, untreated high blood pressure can damage organs such as the heart, kidneys or eyes leading to complications such as: Angina, heart attack or heart failure, Stroke, Kidney failure, Peripheral arterial disease, Retinopathy (eye damage)

Types of high blood pressure

There are two main types of high blood pressure:

Essential (primary) hypertension

a. The main form of high blood pressure – accounts for around 90–95% of cases
b. Has no single identifiable cause
c. Potential causes include genetic and environmental factor

Secondary hypertension

1. Rare forms of high blood pressure
2. Caused by another medical condition or treatment
3. Causes include kidney problems (renovascular hypertension), adrenal gland tumors, thyroid disease, and narrowing of the aorta (the main artery that takes blood from the heart to the rest of the body)
4. Other types of high blood pressure include:
5. Isolated systolic hypertension – the systolic pressure (top number) is raised but the diastolic pressure is normal
6. Isolated diastolic hypertension – the diastolic pressure (bottom number) is raised but the systolic pressure is normal
7. White coat hypertension – where the blood pressure is raised due to the stress of a visit to the doctor or nurse

Pathophysiology

Objectives

1. Understand the hemodynamic determinants of systemic hypertension.
2. Recognize primary and secondary forms of hypertension.
3. Understand the role of the kidney in systemic hypertension: innocent bystander or instigator.
4. Recognize the role of Angitension II, aldosterone, and the sympathetic nervous system in the pathogenesis of hypertension.

Hypertension is a chronic elevation of blood pressure that, in the long-term, causes end-organ damage and results in increased morbidity and mortality [6]. Blood pressure is the product of cardiac output and systemic vascular resistance vascular tone may be elevated because of increased α-adrenoceptor stimulation or increased release of peptides such as Angitension or endothelins. The final pathway is an increase in cytosolic calcium in vascular smooth muscle causing vasoconstriction. Several growth factors, including Angitension and endothelins, because an increase in vascular smooth muscle mass termed vascular remodeling [7] with ageing, stiffening of the aorta and elastic arteries increases the pulse pressure. 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.g. renovascular hypertension) and is suppressed in the presence of primary hyperaldosteronism. Elderly or black patients tend to have low-renin hypertension.

Diagnosis

Hypertension is diagnosed on the basis of a persistently high blood pressure. Traditionally, this requires three separate sphygmomanometer measurements at one monthly interval. Initial assessment of the hypertensive people should include a complete history and physical examination. With the availability of 24-hour ambulatory blood pressure monitors and home blood pressure machines, the importance of not wrongly diagnosing those who have white coat hypertension has led to a change in protocols. In the United Kingdom, current best practice is to follow up a single raised clinic reading with ambulatory measurement, or less ideally with home blood pressure monitoring over the course of 7 days.

Equipment [8]

Cuff size: The bladder size (six sizes are available) should encircle at least 80% of the arm circumference and cover two thirds of the arm length; if not, place the bladder over the brachial artery. If bladder is too small, spuriously high readings may result. The lower edge of the bladder should be within 2.5 cm of the antecubital fossa.

Manometer

Mercury, aneroid or electronic devices used in measurement of blood pressure should be calibrated frequently and routinely against standards (typically every 6 months) to assure accuracy. Ensure that the equipment used is in working order: clean, calibrated, filled with non-leaking tubing and has a properly sized cuff.

ECG (Nazzareno Galie et al, 2004, Europian society of cardiology)

The ECG may provide suggestive or supportive evidence of Hypertension by demonstrating right ventricular hypertrophy and strain, and right atrial dilation. Right ventricular hypertrophy on ECG is present in 87% and right axis deviation in 79% of patients with hypertension. However, the ECG has inadequate sensitivity (55%) and specificity (70%) to be a screening tool for detecting significant hypertension. A normal ECG does not exclude the presence of severe PH.

Chest radiograph

In 90% of IPAH patients the chest radiograph is abnormal at the time of diagnosis. Findings include central pulmonary arterial dilatation which contrasts with 'pruning' (loss) of the peripheral blood vessels. Right atrial and ventricular enlargement may be seen and it progresses in more advanced cases. The chest radiograph allows associated moderate-to-severe lung disease or pulmonary venous hypertension due to left heart abnormalities to be reasonably excluded. However, a normal chest radiograph does not exclude mild post capillary pulmonary hypertension including left-heart disease or pulmonary veno-occlusive disease.

Transthoracic Doppler-echocardiography

Transthoracic Doppler-echocardiography (TTE) is an excellent non-invasive screening test for the patient with suspected pulmonary hypertension. TTE estimates pulmonary artery systolic pressure (PASP) and can provide additional information about the cause and consequences of PH. PASP is equivalent to right ventricular systolic pressure (RVSP) in the absence of pulmonary outflow obstruction. RVSP is estimated by measurement of the systolic regurgitant tricuspid flow velocity v and an estimate of right atrial pressure (RAP) applied in the formula: RVSP = 4v2 + RAP. RAP is either a standardised value, or estimated value from characteristics of the inferior vena cava51 or from jugular venous distension. Tricuspid regurgitant jets can be assessed in the majority (74%) of patients with PH.52 Most studies report a high correlation (0.57–0.93) between TTE and right heart catheterization (RHC) measurements of PASP.53 However, in order to minimise false positives. It is important to identify specific values for the definition of PH as assessed by TTE.

The range of RVSP among healthy controls has been well characterised. Among a broad population of male and female subjects ranging from 1 to 89 years old, RVSP was reported as 28 ± 5 mmHg (range 15–57 mmHg). RVSP increases with age and body mass index.55 According to these data mild PH can be defined as a PASP of approximately 36–50 mmHg or a resting tricuspid regurgitant velocity of 2.8–3.4 m/s (assuming a normal RAP of 5mmHg). It should be noted that also with this definition a number of false positive diagnoses can be anticipated especially in aged subjects and confirmation with RHC is required in symptomatic patients (NYHA class II–III). In asymptomatic subjects (NYHA class I) a concomitant CTD should be excluded and echocardiography should be repeated in six months.

In asymptomatic subjects (NYHA class I) a concomitant CTD should be excluded and echocardiography should be repeated in six months. It should be noted that defining the level for an elevated RVSP does not define the point at which an increased RVSP is clinically important, is predictive of future consequences and/or requires specific treatments. Also the possibility of false negative Doppler-echocardiographic results should be considered in case of high clinical suspicion. Additional echocardiographic and Doppler parameters are important for diagnosis confirmation and assessment of severity of PH including right and left ventricular dimensions and function, tricuspid, pulmonary and mitral valve abnormalities, right ventricular ejection and left ventricular filling characteristics, inferior vena cava dimensions and pericardial effusion size.

Besides identification of PH, TTE also allows a differential diagnosis of possible causes and virtually starts the phases III and IV of the diagnostic process. TTE can recognize left heart valvular and myocardial diseases responsible for pulmonary venous hypertension (Clinical Class 2), and congenital heart diseases with systemicto-pulmonary shunts can be easily identified (Clinical Class 1.3.2). The venous injection of agitated saline as contrast medium can help the identification of patent foramen ovale or small sinus venosus type atrial septal defects that can be overlooked on the standard TTE examination. Trans-oesophageal echocardiography (TEE) is rarely required and is usually used to confirm the presence, and assess the exact size, of small atrial septal defects.

Prognostic parameters in patients with idiopathic pulmonary arterial hypertension Clinical parameters
NYHA functional classification
NYHA functional class on chronic epoprostenol treatment
History of right heart failure
Exercise capacity
6MWT distance, 6MWT distance on chronic epoprostenol treatment, Peak VO2
Echocardiographic parameters
Pericardial effusion, Right atrial size, Left ventricular eccentricity index, Doppler right ventricular (Tei) index
Haemodynamics
Right atrial pressure, Cardiac output, Mixed venous O2 saturation,Positive acute response to vasoreactivity tests, Fall in pulmonary vascular resistance <30% after 3 months of epoprostenol
Blood tests
Hyperuricaemia, Baseline Brain natriuretic peptide, Brain natriuretic peptide after 3 months therapy, Troponin–detectable, especially persistent leakage, Plasma norepinephrine, Plasma endothelin-1
Note: 6MWT: six-minute walk test; NYHA: New York Heart Association.
Causes of high blood pressure (Jun R. Chiong et al, 2008)
Essentially, Blood pressure is the outcome of cardiac output and peripheral vascular resistance (Blood pressure=cardiac output x peripheral vascular resistance). Therefore, maintenance of a normal blood pressure is dependent on the balance between the cardiac output and peripheral vascular resistance.
Essential Hypertension
The pathogenesis of essential hypertension is multifactorial and highly complex. Many factors (and risk factors) have been implicated in the genesis of essential hypertension, which include the following:

- Increased sympathetic nervous system activity.
- Increased production of sodium-retaining hormones and vasoconstrictors.
- Deficiencies of vasodilators such as prostacyclin and nitric oxide.
- Inappropriate or increased renin secretion, resulting in increased production of angiotensin II and aldosterone [9].
- Genetic predisposition.

Secondary hypertension
Ccommon identifiable causes of hypertension are the following [9]: (Jun R. Chiong et al, 2008)
Renal
Renal parenchymal disease, Renal vascular disease, Renin-producing tumors,Primary sodium retention (Liddle's syndrome), Increased intravascular volume
Endocrine
Acromegaly, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Adrenal cortical
Cushing syndrome, Primary aldosteronism, Apparent mineralocorticoid excess
Adrenal medulla
Pheochromocytoma, Carcinoid syndrome, Drugs and exogenous hormones, Neurological causes, Increase intracranial pressure, Quadriplegia, Guillain–Barre syndrome, Idiopathic, primary, or familial dysautonomia, Obstructive sleep apnea (OSA), Diseases of the aorta, Rigidity of the aorta, Coarctation of the aorta
Risk factors for high blood pressure
The risk factors associated with increase in the blood pressure include the following [10]:Long term increased sodium intake, Reduced dietary potassium, calcium and magnesium, Diabetes mellitus and insulin resistance,
Smoking, Excessive alcohol consumption, Lack of physical activity, Obesity, High stress levels
Treatment & Care
Treating high blood pressure can take a multi-pronged approach including diet changes, medication, and exercise. Learn about hypertension treatment options here.
Hypertension Treatment
Treatment for hypertension comes in many forms -- from lifestyle changes to medication. Learn more from this overview about how to lower blood pressure here.
High Blood Pressure and Smoking
Did you know that people who smoke are more likely to develop hypertension and heart disease? Learn more and get tips on quitting -- and avoiding a relapse.
Hypertension and Stress

Left unmanaged, stress can lead to emotional, psychological, and even physical problems, including coronary artery disease and high blood pressure. Get tips on the warning signs of dangerous stress and learn how to reduce it, while boosting a positive outlook.

Complementary and Alternative Treatment for Hypertension

There are many types of complementary and alternative treatments believed to be effective for treating hypertension. Get the facts on your options.

High Blood Pressure Drugs

Your doctor has hundreds of different high blood pressure drugs to choose from. These medications work in a variety of ways to lower blood pressure.

Calcium Channel Blockers

Calcium channel blockers are drugs used to lower blood pressure. They work by slowing the movement of calcium into the cells of the heart and blood vessel walls, which makes it easier for the heart to pump and widens blood vessels [11].

ACE Inhibitors

Angiotensin converting enzyme (ACE) inhibitors are high blood pressure drugs that widen or dilate your blood vessels to improve the amount of blood your heart pumps and lower blood pressure. Angiotensin

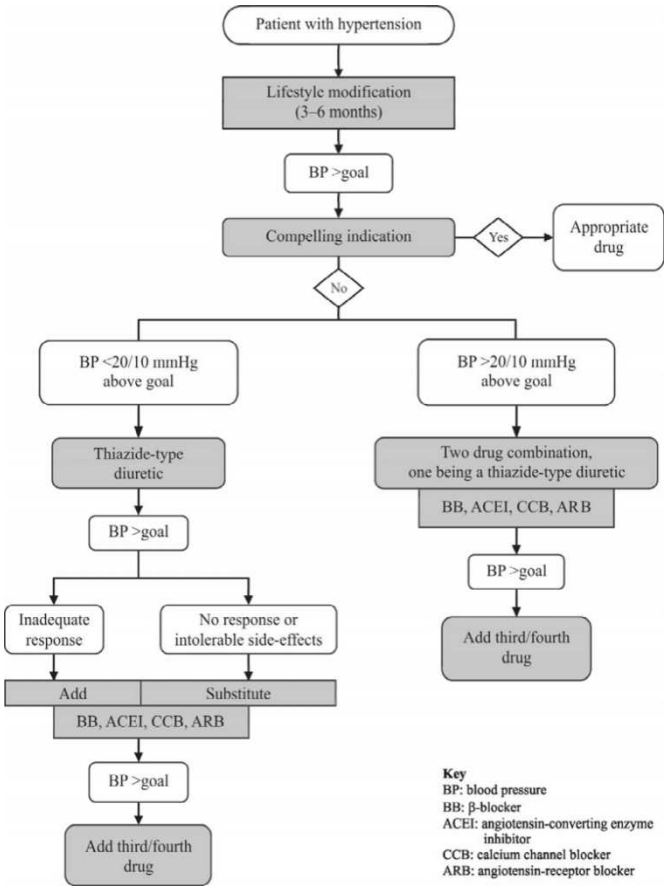
Diuretics (Water Pills)

For high blood pressure, diuretics, commonly known as "water pills," help your body get rid of unneeded water and salt through the urine. Getting rid of excess salt and fluid helps lower blood pressure and can make it easier for your heart to pump.

Beta-Blockers

Beta-blockers are drugs used to treat high blood pressure. They block the effects of the sympathetic nervous system on the heart.Omega-3 Fish Oil SupplementsIn the past 10 years, many Americans have turned to omega-3 fish oil supplements. Dietary fish a fish oil supplements have benefits for healthy people and also those with heart disease [12].

Life Style Modification [13]



Care for High Blood Pressure

- The most important element in managing high blood pressure is follow-up care. Here are six tips to keep in mind about follow-up care [14].
- Hypertension Management: In-Home Blood Pressure Monitoring
- Monitoring your own blood pressure is a good way to keep on top of hypertension. Get tips on how to prepare, and step-by-step instructions for taking your own blood pressure readings.
- High Blood Pressure Medication Guidelines: What You Want to Know If your doctor has prescribed medication to lower your blood pressure, here are twelve things to keep in mind about your treatment protocol.

Table 1; Main side-effects of antihypertensive drugs[15]

Drug	Main side-effects
Diuretics	
Thiazides	Hypokalaemia, hypomagnesaemia, hyperuricaemia
Loop diuretics	Hypocalcaemia and ototoxcity may occur
K-sparing diuretics	Hyperkalaemia
Adrenergic inhibitors	
Acting within neurons	
reserpine	Nasal congestion, lethargy, sexual dysfunction, depression
guanethidine	Postural hypotension
α-agonists	
Methyldopa	Sedation, dry mouth, impotence, galactorrhea
clonidine	Inflammatory side effects, withdrawal syndrome
α-adrenergic receptor	First-dose hypotension, dizziness, weakness
β-adrenergic receptor	Bradycardia, fatigue, insomnia, bizarre dreams
α-/β- blockers	Nausea, fatigue, postural hypotension, hepatotoxicty
Direct vasodilators	
hydralazine	Tachycardia, flushing, headache, angina,
minoxidil	Hirsutism, pericardial effusion, ascites
Calcium antagonists	
deltiazem	First-degree AV block, bradycardia,
verapamil	Constipation
dihydropyridines	Ankle oedema, flushing, tachycardia
ACE inhibitors	Cough, rash, hyperkalaemia, angioedema

Researchers Uncover Genetic Clues to Blood Pressure

An international research team has identified a number of unsuspected genetic variants associated with systolic blood pressure (SBP), diastolic blood pressure (DBP), and hypertension (high blood pressure), suggesting potent of investigation for the prevention or treatment of hypertension. The research was funded in part by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health and by several other NIH institutes and centers [16]. The analysis of over 29,000 participants is being presented at the American Society of Hypertension, Inc. scientific meeting on May 8, 2009, and is published online in the journal Nature Genetics on May 10, 2009.

"This study provides important new insights into the biology of blood pressure regulation and, with continued research, may lead to the development of novel therapeutic approaches to combat hypertension and its complications," said NHLBI Director Elizabeth G. Nabel, M.D. About 1 in 3 adults (approximately 72 million people) in the United States has high blood pressure. Hypertension can lead to coronary heart disease, heart failure, stroke, kidney failure, and other health problems, and causes over 7 million deaths worldwide each year [17]. Blood pressure has a substantial genetic component and hypertension runs in families. Previous attempts to identify genes associated with blood pressure, however, have met with limited success.

Future Directions

This represents the second iteration of these guidelines. There are many aspects of diagnosis, evaluation and treatment that must be further clarified. However, some aspects of care clearly supported by the literature are $MgSO_4$ for severe preeclampsia, and antenatal corticosteroids for women with preeclampsia before 34 weeks. The following have been identified as priorities: the role of self-measurement of BP, accuracy of the ratios of urinary protein to creatinine and albumin to creatinine for diagnosis of proteinuria, multivariable mprediction of preeclampsia, prediction of complications in women with preeclampsia, the role of bed rest in the prevention or treatment of preeclampsia, the BP goal that optimizes perinatal and maternal outcomes in women with non-severe hypertension and use postpartum follow-up and interventions related to future pregnancy and cardiovascular risk. Forth- coming iterations are planned, no less frequently than ever [18].

Conclusion

Hypertension is prevalent worldwide and aging of the population means that there are more and more people with hypertension. Therefore, the scale of the problem of diagnosing, treating and controlling hypertension is immense. Current efforts are channelled towards the detection and treatment of hypertension in middle and old age. The linear rise in the prevalence of hypertension with age means that measures to prevent hypertension, such as a healthy diet and regular physical activity, should start early in life. For those who have already developed hypertension, early diagnosis and treatment is important. Existing antihypertensive drugs are not ideal individually and so a combination of drugs is needed in a large proportion of patients. The choice of such drugs should be rational and evidence-based.

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