HYPERTENSION - AN OVERVIEW

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INTRODUCTION

As the population grows older and more obese, the incidence of hypertension continues to increase, not only in the United States but in all developed and developing societies[1]. At the same time, despite the widely recognized dangers of uncontrolled hypertension, the disease remains inadequately treated in the majority of patients[2]. As a consequence, cardiovascular risk remains high among the majority of hypertensive patients, whether treated or not.

Clearly more attention is being directed towards hypertension, but adequate hypertension control remains elusive, in large part because of the asymptomatic nature of the disease for the first 15 to 20 years, even as it progressively damages the cardiovascular system. In view of these built in barriers to effective control of individual patient, population-wide application of preventive measures becomes inherently more attractive. Although the specific mechanism for most hypertension remains unknown, it is highly likely that the process could be slowed if not prevented by the prevention of obesity, moderate reduction to salt intake, higher levels of physical activities, and avoidance of excessive alcohol consumption[3]. Since hypertension will eventually develop in most people during their life time[4], the need for more wide spread adoption of potentially effective and totally safe preventive measures is obvious. In the mean time, better management of those already afflicted with hypertension must be practiced, starting with careful documentation of diagnosis.

DEFINITION

The definition of hypertension is somehow arbitrary and usually taken as the level of blood pressure associated with a doubling of long term risk. Perhaps the best operational definition is 'the level at which the benefits of action exceed the risk and cost of inaction.' Most recommendation currently regards as 'high blood pressure' any pressure up to 140mmHg systolic and / or 90mmHg diastolic.

ASYMPTATATIC NATURE OF HIGH BLOOD PRESSURE "THE SILENT KILLER"

Uncomplicated blood high pressure is largely without symptoms. Most symptoms are usually those of complications. This situation has given rise to the name 'silent killer' sometimes given to high blood pressure. Sufferers who are 'lucky' to have symptoms may have headache, dizziness, tinnitus, blurring of vision, palpitation or symptoms of specific complications.

PREVALENCE

Hypertension is of public health importance in Sub-Saharan Africa, particularly in urban areas, with evidence of considerable under diagnosis, treatment and control. There is urgent need to develop strategies to prevent, detect, treat and control hypertension effectively in the African region. The prevalence of hypertension is higher in urban than rural areas and also increases with increasing age. Less than 40% of people with blood pressure above the defined normal range had been previously detected as hypertensive. Of the people previously diagnosed, less than 30% are on drug treatment and less than 20% had blood pressure within the defined normal range[5]

Globally, more than a quarter of the world population is hypertensive. In 2000, 26.4% of the adult population had hypertension, 26.6% men and 26.1% women. By the 2025, the prevalence is projected at 29.2%.The estimated total number of adults with hypertension in 2000 was 927million. Of this figure, 333million were in economically developed countries and 639million in economically developing countries. The number of adults in 2025 is predicted to increase by about 60% to a total of 1.56billion[6]. Report from the Framingham Heart study suggested a 90% lifetime risk of developing hypertension in individual at age 55 years who has a normal blood pressure[7].

Studies in Nigeria gave a prevalence of 11.5% using the then recommended cut-off value of 160/95mmH.[8] By extrapolation, using the current WHO/ISH cut-off (140/90mmHg), the prevalence in Nigeria is projected to be about 20%.

SYMPTOMS AND SIGNS

Most people with hypertension have no symptoms even when blood pressure reading reaches dangerously high levels. Although a few people with early stage hypertension may have dull headaches, dizzy spells or a few more nose bleeds than normal, these symptoms and signs typically do not occur until hypertension has reached an advanced or even life-threatening stage.

CAUSES

Over 95% of subjects with hypertension are classified as having primary hypertension (previously commonly called essential hypertension). The cause is generally unknown although there are well known predisposing or risk factors such as:

i Genetic predisposition/hereditary- hypertension has been known to run in families. Hereditary and genetic expressions in hypertension are significantly influenced by multiple environmental factors.

ii Excessive salt consumption

iii Male sex- males have a higher predisposition for hypertension than pre-menopausal women. After menopause, sex prevalence appears to change significantly.

iv Age- blood pressure has been shown to increase

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with age. The prevalence of hypertension also increases significantly with age and becomes profound at ages >55 years for males and >65 years in females.

v Prolonged stress- chronic stress are known to affect blood pressure. Acute stress may transiently increase blood pressure but this usually would not be sustained. It is not fully appreciated how chronic stress affect blood pressure. Neuro-hormonal activity may be a factor here.

vi Significant tobacco use.

vii Excessive alcohol consumption affects blood pressure levels adversely and predisposes to the development of heart disease.

viii Obesity.

ix Physical inactivity is a recognized risk factor for hypertension. It also encourages increase in weight thereby providing an additional risk.

x Diets low in potassium, vegetables, fish, fruits; and rich in saturated fats are known to promote the development of high blood pressure.

Secondary hypertension constitutes <5% of all cases hypertension and is associated with the following conditions:

RENAL CAUSES

i Renal parenchyma diseases such as acute glomerulonephritis, chronic nephritis, polcystic disease and diabetic nephropathy.

ii Renovascular disorders such as renal artery stenosis, intra renal vasculitis

iii Other renal causes include: renin producing tumors, primary sodium retention (Liddle syndrome) and Gordon syndrome.

ENDOCRINE CAUSES

i Acromegaly

ii Hypothyroidism and hyperthyroidism

iii Hyperparathyroidism and hypercalcemia

iv Adrenal disorders such as Cushing's syndrome, primary hyperaldosteronism, congenital adrenal hyperplasia, phaeochromocytoma.

v Extra adrenal chromaffin tumors.

vi Apparent mineralocorticoid excess

vii Carcinoids

EXOGENOUS HORMONES

These include: oestrogen, glucocorticoids, mineralocorticoids, sympathomimetics and erythropoietin.

OTHER CAUSES

Tyramine containing foods and monoamine oxidase inhibitors

Coarctation of the aorta

Pregnancy induced hypertension

Increased intracranial pressure, sleep apnoea, quadriplegia, acute porphyria,

familial dysautonomia and Guillain Barre syndrome.

CLASSIFICATION OF HYPERTENSION

Two of the existing classifications are reproduced bellow: JNC-6 and JNC-7.

JNC-6 CLASSIFICATION OF BLOOD PRESSURE FOR ADULTS AGED 18 YEARS AND OLDER[9].

CATEGORY	SYSTOLIC BP (mmHg)		DIASTOLIC BP (mmHg)
Optimal BP	<120.	and	<80
Normal BP	<130	and	<85
High normal BP	130 – 139	or	85 – 89
Grade 1	140 – 159	or	90 – 99
Grade 2	160 – 179	r o	100–109
Grade 3	≥180	or	≤110

JNC-7 CLASSIFICATION[1]

BP CLSSIFICATION	SYSTOLIC BP (mmHg)		DIASTOLIC BP (mmHg)
Normal	<120	and	<80
Pre-hypertension	120 – 139	or	80 – 89
Stage 1	140 – 159	or	90 – 99
Stage 2	>160		>100

When systolic and diastolic blood pressures fall into different categories, the higher category should apply.

CARDIOVASCULAR RISK STRATEFICATION IN PATIENTS WITH HYPERTENSION

The risk factors, target organ damage, and associated clinical cardiovascular disease are used for stratifying the overall risk of any individual subject. This is useful in determining the need for and the nature of intervention for the individual.

MAJOR RISK FACTORS

Smoking
Dyslipidemia
Diabetes mellitus
Age > 60 years
Sex (men and post-menopausal women)
Family history of cardiovascular disease
Women > 65 years, men > 55 years.

TARGET ORGAN DAMAGE/ CLINICAL CARDIOVASCULAR DISEASE

Heart disease left ventricular hypertrophy
- angina or prior myocardial infarction
- heart failure
- prior coronary revascularization

Stroke or transient ischemic attack
Nephropathy
Peripheral arterial disease
Retinopathy.

ASSESSMENT OF THE HYPERTENSIVE PATIENT

Detailed history is taken with emphasis on family history. Physical examination should be comprehensive and possible complications borne in mind. Diagnosis of hypertension is made if there is a persistent rise in blood pressure >140/ 90mmHg using appropriate cuff. Measurement is carried out in at least two positions, preferably lying and standing positions. This is mandatory in diabetics and elderly who are prone to postural hypotension.

Basic investigations should include urinalysis, packed cell volume, chest radiograph, electrocardiograph, serum urea, electrolyte, creatinine, uric acid and fasting lipid profile. Others will depend on clinical findings and the need to search for secondary causes in young subject. These include echocardiography, arteriography, 24hour urine vanyl mandelic acid, hormonal assay among others. Fundoscopy is important as retinal changes in hypertensive subjects have been closely related to the overall survival as well as degree of renal and cardiac affectation.

CARDIOVASCULAR RISK STRATIFICATION AND TREATMENT

BP stages	Risk group A	Risk group B	Risk group C
High normal	Life style modification	Life style modification	Drug therapy
Stage 1	Life style modification (up to 12 months)	Life style modification (up to 6 months)	Drug therapy
Stage 2	Drug therapy	Drug therapy	Drug therapy

Risk group A no risk factors, no target organ damage or clinical cardiovascular disease.

Risk group B at least one risk factor not including diabetes mellitus. No target organ damage or clinical cardiovascular disease

Risk group C target organ damage/ clinical cardiovascular disease and/or diabetes mellitus with or without other risk factors.

TREATMENT

LIFE STYLE MODIFICATION: This is recommended for all subjects with confirmed hypertension and includes:

i Weight reduction is recommended for individuals with body mass index > 25kg/m^2. Waist circumference has been found to be a better predictor of cardiovascular risk than other parameters.[10] This should be below 102 cm in men and 88cm in women. Up to about 5 20mmHg of reduction in systolic blood pressure have been recorded for every 10kg lost.

ii Physical inactivity is a cardiovascular risk factor independent of increase in body weight that results from it. Regular aerobic physical activity (for example brisk walking for at least 30minutes for a minimum of three times a week) has been found to result in blood pressure reduction of 4 9mmHg.[11]

iii Smoking or tobacco use smoking is a strong independent risk factor for cardiovascular disease. People that smoke show higher ambulatory blood pressure than non-smokers.[12] Quitting smoking is acknowledged to be one of the most effective lifestyle interventions for prevention of cardiovascular disease[12].

iv Excessive alcohol reduction in average daily alcohol drinking to two drinks (less than two bottles of beer) in men and less than one drink in women lowers blood pressure by 2- 4mmHg.[13]

v Excessive salt consumption there is a well recognized direct relationship between excessive salt intake and blood pressure elevation and prevention. When dietary salt is reduced to less than 6g of sodium chloride (equivalent to100mmoles of sodium) per day, blood pressure reduction of 2 - 8 mmHg could be achieved[14].

vi **DASH** - dietary approach to stop hypertension- recommends food rich in whole grain products, fish, poultry and nuts. While it is rich in potassium calcium, magnesium and fibre, it has reduced amount of red meat, sweets, sugar containing beverages, low saturated and total fat. This dietary approach is associated with blood pressure reduction of 8 - 14 mmHg.[15]

DRUG TREATMENT.

If the life-style modifications just described are not adequate to bring the blood pressure to goal (<140/90mmHg for most, <130/80mmHg for those with diabetes and chronic renal failure), drug therapy is indicated. Evidence suggests that reduction of blood pressure by 5-6mm Hg can reduce the risk of stroke by 40%, of coronary artery disease by 15-20% and also reduces the likelihood of dementia, heart failure and mortality from cardiovascular diseases. The fundamental goal of treatment should be the prevention of the important 'endpoints' of hypertension such as heart attack, stroke and heart failure. Drug therapy should be individualized. Several factors should be taken into consideration especially in a depressed economy.

Age should be given due consideration in drug management of hypertension.

CHOICE OF ANTIHYPERTENSIVES

Current management of hypertension hinges on the issue of compelling indications for specific drugs based on evidence from randomized clinical trials. Cost effectiveness is also of uttermost importance. This is determined by assessing benefits derived form the medication and the expenditure. In a depressed economy setting, however, an otherwise cost effective drug may not be affordable. In that situation, consideration is given to the cheapest drug (e.g. diuretics) in each class of the compelling indications. Other drugs that would offer additional benefits could be added as circumstances improve. In the United States, the JNC-7 recommends starting with thiazide diuretic if a single therapy is being initiated.[1] If blood pressure is more than 20/10 mmHg above goal blood pressure, consideration should be given to initiating therapy with two agents, one of which should be a thiazide-type diuretic. Most patients with hypertension will require two or more antihypertensive medications to achieve goal blood pressure.

The compelling indication for some particular antihypertensive drug, in some common clinical conditions and evidence for inclusion is shown below.

TABLE 1: Clinical trial basis for compelling indications for individual drug classes

COMPELLING INDICATIONS	RECOMMENDED DRUGS	CLINICAL TRIAL BASIS
Diabetes	ACEI,ARB, Diuretics, CCB	ALLHAT[16] UKPDS[17]
Heart failure	Diuretics, ACEI, ARB, -blockers, aldosterone antagonist (AA)	MERIT-HF[18] SOLVD[19] TRACE[20] RALES[21]
Left ventricular hypertrophy (without evidence of heart failure)	-blockers, CCB, ACEI, ARB, Diuretics	SOLVD[19] LIFE[22]
Ischaemic heart disease	-blockers, ACEI, AA	HOPE[23] SAVE[24] EPHESUS[25]
Cerebrovasculr disease (stroke)	Diuretics, ACEI	PROGRESS[26]
Chronic kidney disease	ACEI, ARB	IDNT[27] REIN[28]

ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial;
UKPDS, United Kingdom Prospective Diabetes Study;
MERIT-HF, Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure;
SOLVD, Studies of Left Ventricular Dysfunction;
TRACE, Trandolapril Cardiac Evaluation Study
RALES, Randomized Aldactone Evaluation Study;
LIFE, Losartan Intervention for Endpoint Reduction in Hypertension Study
HOPE, Heart Outcomes Prevention Evaluation Study
SAVE, Survival and Ventricular Enlargement Study;
EPHESUS, Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study;
PROGRESS, Peridopril Protection against Recurrent Stroke Study;
REIN, Ramipril Efficacy in Nephropathy Study
IDNT, Irbesartan Diabetic Nephropathy Trial;

CLASSES OF ANTIHYPERTENSIVE DRUGS

DIURETICS
Diuretics act at different segments of the nephron to promote salt and water excretion with a resultant fall in blood volume, stroke volume, cardiac output and with prolonged use, fall in peripheral resistance. There are three classes of diuretics of clinical importance in the treatment of hypertension: thiazide/thiazide-like diuretics, loop diuretics, and potassium sparing diuretics. Thiazides are the most commonly used in hypertension.

CALCIUM CHANNEL BLOCKERS
Calcium channel blockers bind to the L-type calcium channels on vascular, cardiac muscle and conducting cells and block the influx of calcium with resultant vascular smooth muscle relaxation, reduced cardiac inotropy and chronotropy depending on the cell type. Additionally, they possess natriuretic and diuretic properties and are very effective in the treatment of hypertension in blacks and elderly. There are three classes of calcium channel blockers: dihydropyridines, phenylalkylamine sand benzothiazepines, with the dihydropyridines (nifedipine, amlodipine etc) possessing the greatest vascular selectivity and therefore blood pressure reducing properties. Side effects of dihydropyridine include headaches, flushing, tachycardia and peripheral oedema.

ANGIOTENSIN CONVERTING ENZYME INHIBITORS (ACEIs)
Angiotensin converting enzyme inhibitors block the formation of angiotensin II (a potent vasoconstrictor, inhibit kininase leading to accumulation of bradykinin (vasorelaxant) with the net result of vascular relaxation. By inhibiting the stimulation of aldosterone release, they also prevent aldosterone-mediated sodium and water retention. They are more efficacious in high rennin states and are therefore less effective as monotherapy in hypertensive patients with low renin, such as majority of blacks and elderly. Side effects include a dry cough, angiooedema, hypotension and hyperkalemia. They are contraindicated in pregnancy and bilateral renal artery stenosis. Some commonly used ones include: captopril, lisinopril, enalapril, ramipril etc.

ANGIOTENSIN RECEPTOR BLOCKERS (ARBs)
Angiotensin receptor blockers act on the renin-angiotensin system and produce similar effect as angiotensin converting enzyme inhibitors,but act by blocking type-I angiotensin II receptors. Kiniase is not inhibited, bradykinin accumulation does not occur and so cough, and perhaps angooedema are not likely problems. Some examples of ARBs include: losartan, vasartan, olmesartan, candesartan etc.

RENIN INHIBITORS
These act by inhibiting the conversion angiotensinogen to angiotensin I and produce effect on blood pressure similar to those of ACEIs and ARBs. The side effects are generally similar to those of ACEIs but milder. Aliskirin has been approved for use.

ALPHA-BLOCKERS
Alpha-blockers , especially α_1-blockers, act on the vascular smooth muscle to block the post-synaptic action of noradrenaline, leading to vascular relaxation. They appear to be more effective in state of heightened sympathetic tone. Side effects include: dizziness, nasal congestion, headaches, reflex tachycardia, orthostatic hypotension and fluid retention. Commonly available ones include prazocin and doxazocin.

BETA-BLOCKERS
Beta-blockers act by competitively binding to beta-receptors in the nodal, conductive and muscle cells of the heart causing reduced heart rate, contractility, conduction velocity and, ultimately reduced cardiac output. Commonly available beta- blockers include: propranolol, atenolol, metoprolol, carvedilol and bisoprolol. They are particularly useful in patients with tachy-arrhythmias, thyrotoxicosis and migraine and should be avoided in patients with bronchial asthma, second or third degree heart block. Use of beta blockers in heart failure should be left for specialist and referral centers where careful use is guaranteed and test of cardiac function could be carried out.

CENTRALLY ACTING DRUGS
These drugs bind to activate α_2-adrenoceptors in the medulla leading to a reduction in sympathetic stimulation to the heart, reduced heart rate and contractility and, ultimately reduced cardiac output and blood pressure. Alpha-methyl dopa and reserpine are commonly available and are particularly useful in low income setting. Notable side effects include: dizziness, dry mouth, sexual dysfunction, depression and orthostatic hypotension.

DIRECT VASODILATORS
These drugs act directly on the vessel wall in ways that are not completely understood but may involve the opening of potassium channels and inhibition of calcium. They cause reflex tachycardia, headaches and flushing. Hydalazine is commonly available and minoxidil though one of the most effective antihypertensives, causes severe fluid retention and increased hair loss.

PREVENTION OF HYPERTENSION
The rising prevalence of hypertension worldwide calls for intensification of prevention measures. Preventive measures should therefore include:

i Proper patient education- concept of hypertension should be explained to the patient and patient made to participate in the management. It must be emphasized that treatment is lifelong.

ii Screening for hypertension- due to the asymptomatic nature of the disease, screening for apparently normal individuals become very important.

iii Primordial prevention- deals with addressing socio-

economic factor in the community that encourages the development of hypertension.

iv Primary prevention- addresses the risk factor that favour the development of hypertension.

v Secondary prevention- this refers to the proper management of complications.

vi Creating awareness- in order to effectively prevent hypertension, significant level of awareness must be created among the populace.

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