

An Overview of Management of Hypertension in Clinical Practice



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Abstract

Hypertension is an important risk factor for the development of cardiovascular morbidity and mortality. In 2002, 10.9% of all deaths in the developed countries were attributable to hypertension, making it the second major risk factor of overall death just below tobacco use (12.2%) but over high cholesterol (7.6%), alcohol use (9.2%) and obesity (7.4%). In addition, about half of all cardiovascular disease (mortality and morbidity combined) is attributable to high blood pressure. High blood pressure in early stages causes no symptoms, so it is easy to ignore. However, if left untreated it can damage vital organs over the years and eventually it can lead to serious complications. Fortunately, it is widely considered as one of the most preventable causes because of the availability of effective antihypertensive drugs. Many pharmacological agents are available for treatment; however, the choice depends on the patients' age, diagnosis, co-morbidities, appropriate strength-dosage scheme and patients' tolerability. Hypertension can affect all ages despite gender and ethnicity. This review gives a general overview about the management of hypertension.

Keywords: Hypertension; Lifestyle changes; Antihypertensive drugs; Tolerability; Diagnosis

Introduction

Hypertension is an important risk factor for the development of cardiovascular morbidity and mortality. In 2002, 10.9% of all deaths in the developed countries were attributable to hypertension, making it the second major risk factor of overall death just below tobacco use (12.2%) but over high cholesterol (7.6%), alcohol use (9.2%) and obesity (7.4%). In addition, about half of all cardiovascular disease (mortality and morbidity combined) is attributable to high blood pressure. Fortunately, it is widely considered as one of the most preventable causes because of the availability of effective antihypertensive drugs [1]. Arterial hypertension or high blood pressure is a chronic medical condition which is characterized by elevated blood pressure in the arteries and is an important risk factor for future development of cardiovascular disease.

Arterial hypertension belongs to asymptomatic diseases because it usually does not cause symptoms for years until a vital organ is damaged [2]. Hypertension is reported to be the fourth contributor to premature mortality in developed countries and the seventh in developing countries. Almost 12.8% (7.5 million) of the total deaths and around 3.7% of the total DALYS (disability adjusted life years) are due to raised blood pressure (BP) [3,4]. Recent epidemiological data suggest both an increase in the prevalence (urban: 25% and rural: 10-15%) and poor levels of control of hypertension in India [4,5].

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 [6]. 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. Elevated BP is an established risk factor for cardiovascular disease. The relationship between BP level and cardiovascular risk is continuous, therefore the distinction between normotension and hypertension is arbitrary [7,8].

Appropriate management of hypertension reduces the risk for cardiovascular disease, renal disease, cerebrovascular disease, and death [9-12]. However, determining the most appropriate BP targets, particularly for adults aged 60 years or older, has been controversial. Debate about the goal for systolic BP (SBP) among adults treated for hypertension has intensified, especially in light of recent recommendations [13].

Blood pressure is represented by two values. The higher value called systolic is the highest pressure in the arteries when the heart contracts (systole). The lower value is the lowest pressure in the arteries when the heart relaxes between beats (diastole). Arterial hypertension for adults, who don't suffer

from any other kind of diseases, is defined by an elevation of blood pressure to 140 / 90 mm Hg or to higher values [14,15]. On the table below there is a classification of arterial blood pressure according to European Society of Hypertension (ESH) [16] (Table 1 & Figure 1).

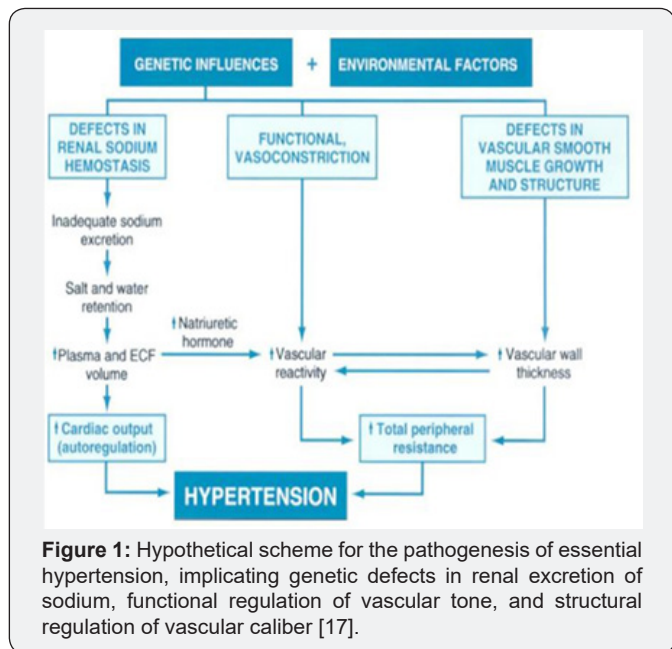


Figure 1: Hypothetical scheme for the pathogenesis of essential hypertension, implicating genetic defects in renal excretion of sodium, functional regulation of vascular tone, and structural regulation of vascular caliber [17].

Table 1: Classification of arterial blood pressure according to European society of hypertension

Blood Pressure	Systolic		Diastolic
Category	(mm Hg)		(mm Hg)
Ideal	less than 120	and	less than 80
Normal	120-129	or/and	80-84
Prehypertension	130-139	or/and	85-89
Hypertension – Mild-Stage 1	140-159	or/and	90 - 99
Hypertension – Moderate-Stage 2	160-179	or/and	100-109
Hypertension – Severe-Stage 3	Higher or equal to 180	or/and	Higher or equal to 110
Isolated Systolic Hypertension	Higher or equal to 140	and	Less than 90

Management of Hypertension

All patients should be managed with non-pharmacologic interventions/therapeutic lifestyle modifications to lower BP. Patients with pre-hypertension should be followed up yearly to detect and treat HPT as early as possible. Decisions regarding pharmacological treatment should be based on the individual patient’s global cardiovascular risk. In subjects with MEDIUM RISK or HIGHER, the threshold for commencing HPT treatment should be lower. Therapeutic lifestyle changes should be recommended for all individuals with HPT and pre-HPT. It may be the only treatment necessary in Stage 1 HPT. A high degree of motivation is also needed to sustain the benefits of non-

pharmacological treatment. It is also important to remember that lifestyle modification requires a concerted effort and reinforcement on behalf of the practitioner. Lifestyle modification works better with concurrent behavioral intervention than just passive advice. This non-pharmacological management includes weight reduction, sodium restriction, avoidance of alcohol intake, regular physical exercise, healthy eating and cessation of smoking [18].

Weight reduction

Weight-reducing diets in overweight hypertensive persons can result in modest weight loss in the range of 3-9% of body weight [19] and are associated with blood pressure reduction of about 3-6 mmHg. It is advisable for overweight hypertensive patients to lose at least 5% of their weight.

Sodium intake

High salt intake is associated with significantly increased risk of stroke and total cardiovascular disease [20]. Evidence from published systematic review and meta analyses showed that restricting sodium intake in people with elevated blood pressure in the short term leads to reductions in blood pressure of up to 10.5 mmHg systolic and 2 mmHg diastolic [20-22]. An intake of <100 mmol of sodium or 6g of sodium chloride a day is recommended (equivalent to <1¼ teaspoonfuls of salt or 3 teaspoonfuls of monosodium glutamate) [23-26].

Avoidance of alcohol intake

Alcohol consumption elevates BP acutely. For those who consume alcohol, intake should be restricted to no more than 21 units for men and 14 units for women per week (1 unit is equivalent to one half-pint of beer or 100 ml of wine or 20 ml of “proof whisky”). Meta analyses have shown that, interventions to reduce alcohol consumption caused a small but significant reduction (3.3/2 mmHg) in both systolic and diastolic blood pressure respectively [27]. Hypertensives who are heavy drinkers are also more likely to have hypertension resistant to drug treatment. The only way to reduce these patients’ BP effectively is by reducing or stopping their alcohol intake [28].

Regular physical exercise

Aerobic exercise is more effective than resistance training (e.g., weight lifting) [29]. Exercise like walking-jogging can result in a reduction of 13/18 mmHg in SBP/DBP [30]. More recent evidence showed that resistant exercise is effective in lowering blood pressure among normotensives and pre-hypertensives but not among hypertensives [31]. However isometric resistant exercise can reduce BP by 10.4/6.7 mmHg as shown by a recent meta-analysis [32]. General advice on cardiovascular health would be for modest exercise, such as brisk walking for a total of at least 150 mins per week [33,34].

Healthy eating

A diet rich in fruits, vegetables and low-fat dairy products with reduced saturated and total fat can substantially lower BP

(11/6 mmHg in hypertensive patients and 4/2 mmHg in patients with high normal BP). 55 (Level I) More recently, diet high in L-Arginine has been shown to be able to reduce BP by 5.4/2.3 mmHg [35].

Cessation of smoking

Smoking can raise BP acutely. However, the effect of chronic smoking on BP is less clear. Nevertheless, smoking cessation is important in reducing overall cardiovascular risk.

Relaxation therapy

Relaxation interventions were shown to be associated with statistically significant reductions in systolic and diastolic blood pressure of about 3 mmHg [34]. However, another systematic review of studies on the effect of stress reduction on blood pressure found small and non-significant effect on blood pressure [36]. It is not recommended for routine provision in primary care.

Others

Table 2: Alternative treatments with level of evidence [42]

Alternative Treatments	Level of Evidence	Class of Recommendation
Behavioral therapies		
Transcendental meditation	B	IIB
Other meditation techniques	C	III ((no benefit)
Biofeedback approaches	B	IIB
Yoga	C	III (no benefit)
Other relaxation techniques	B	III (no benefit)
Noninvasive procedures or devices		
Acupuncture	B	III (no benefit)
Device-guided breathing	B	IIA

Classification of Antihypertensive Agents [2,16]

Table 3: α1-adrenoreceptors-blockers, centrally acting vasodilators and direct acting vasodilators

Antihypertensive agents - Groups	Indications	Major Side Effects	Contra-Indications
β-Blockers.	Post-myocardial infarction, angina, heart failure, atrial fibrillation, pregnancy.	Bradycardia, hypotension, fatigue, drowsiness, weight gain, glucose metabolism disturbances, arrhythmia, coldness of extremities.	COPD, asthma, atrioventricular block, combinations with non-dihydropyridines due to risk of bradycardia, heart failure, AV block.
Thiazide Diuretics.	Systolic hypertension in elderly, black patients, heart failure.	Hypokalemia, hyperuricemia, hyperglycemia, Hypercalcemia, orthostatic hypotension.	Pregnancy, gout, hypercalcaemia, Renal impairment, caution with b-blocker use due to metabolic effects.
Loop Diuretics.	Renal impairment, heart failure, hypertensive crisis, edematous states.	Hypokalemia, hyperuricemia, hyperglycemia, Hypercalcemia, orthostatic hypotension.	Pregnancy, gout.
Aldosterone antagonists.	Heart failure, post-myocardial infarction, primary-secondary hyperaldosteronism, resistant hypertension.	Hyperkalemia, gynecomastia.	Hyperkalemia, caution with use with ACE is, Sartans and other potassium sparing diuretics.

Exercise-based regimens		
Dynamic aerobic exercise	A	I
Dynamic resistance exercise	B	IIA
Isometric handgrip exercise	C	IIB

These include micronutrient alterations, caffeine reduction and dietary supplementation with fish oil, potassium, calcium, magnesium and fibre. However, the evidence for its beneficial effect is limited [37-40]. In summary while weight reducing diet, regular exercise, alcohol and salt restriction have been consistently shown to be beneficial in reducing BP in patients, the evidence thus far has not been consistent for relaxation therapies and supplementations with calcium, magnesium or potassium [41] (Table 2).

Pharmacotherapy

It has been proved by way of a large number of RCTs that by lowering the blood pressure values in hypertensive subjects the subsequent complications of HT can be reduced. Though some trials depict superiority of one class of antihypertensive drug over other types, meta-analyses from trials of larger sample size have failed to show clinically significant differences between drug classes and hence the beneficial effects of BP lowering are largely independent of the drugs employed [43,44]. Lifestyle modifications can be very effective but in real life patients usually need a combination of them with pharmacological therapy. Very often they need more than one type of anti-hypertensive medication or combination of more in order to achieve their blood pressure target goal.

Combination of lifestyle modifications and pharmacological medication may allow reduction of drugs doses, better therapeutic control, more effective treatment and prevention of other cardiovascular risks factors [2,16,45].

ACE is.	Heart failure left ventricular dysfunction, post-myocardial infarction, left ventricular hypertrophy, proteinuria, diabetic nephropathy.	Dry cough, hyperkalaemia, angioedema, renal failure, rash.	Pregnancy, combination with sartans and direct renin inhibitors in renal impairment and diabetes.
AT1-Receptor	Same as ACE is,	Same as ACE is except dry cough.	Same as ACE is.
Antagonists (Sartans).	In case of ACE is intolerance.	Same as ACE is except dry cough.	Same as ACE is.
Direct Renin Inhibitors (Aliskiren).	Hypertension, new in therapy, lack of experience.	Same as ACE is, diarrhea.	Same as ACE is.
CCBs (dihydropyridines).	Systolic hypertension in elderly, black patients, angina, pregnancy, metabolic syndrome.	Postural hypotension, edema around ankles, headache, flushing.	
CCBs (Non Dihydropyridines).	Angina, atrial fibrillation, pregnancy, ischemic disease of lower limb, ischemic heart disease.	Edema around ankles, hypotension, headache, dizziness, constipation, bradycardia.	Heart failure, AV block and bradycardia due to negative inotropic -chronotropic effect, combination with β -blockers.
α -Blockers.	Benign prostatic hypertrophy, pheochromocytoma.	Tachycardia, edema around ankles, sexual dysfunction, orthostatic hypotension, vertigo, diarrhea.	Syncope in elderly -start with low doses, urinary incontinence.
Centrally Acting.	Pregnancy (only methyldopa), resistant hypertension.	Bradycardia, depression, postural hypotension, rebound phenomenon.	

- a) Antagonists of β -adrenoreceptors (Beta-blockers).
- b) Diuretics (mainly thiazide, loop and potassium sparing).
- c) Calcium channel blockers (dihydropyridines – non dihydropyridines).
- d) Angiotensin converting enzyme inhibitors (ACEis).
- e) Angiotensin II receptors blockers (Sartans).
- f) Direct inhibitors of renin (Aliskiren-New in therapy, lack of experience) (Table 3).

For better pharmacological treatment outcomes, drugs should be chosen on the basis of efficacy, safety, convenience to the patient and cost. For assessment of efficacy evidence from large scale clinical trials should be used. Moreover, recognition of adverse effects is another important factor because is associated with patient adherence and effectiveness of treatment. In addition, the use of regimens (FDC) that is more convenient to the patient like once-daily regimens and also cost of treatment are other important factors because could help to improve the patient compliance [46] (Table 4).

Table 4: Evidence-based dosing for antihypertensive drugs [47].

Antihypertensive Medication	Initial Daily Dose (mg)	Target Dose in RCTs Reviewed (mg)	No. of Doses per Day
ACE inhibitors			
Captopril	50	150-200	2
Enalapril	5	20	2-Jan
Lisinopril	10	40	1
Angiotensin receptor blockers			
Eprosartan	400	600-800	2-Jan
Candesartan	4	Dec-32	1
Losartan	50	100	2-Jan
Valsartan	40-80	160-320	1
Irbesartan	75	300	1
β-Blockers			
Atenolol	25-50	100	1
Metoprolol	50	100-200	2-Jan
Calcium channel blockers			
Amlodipine	2.5	10	1
Diltiazem (ER)	120-180	360	1
Nitrendipine	10	20	2-Jan
Thiazide-type diuretics			
Bendroflumethiazide	5	10	1

Chlorthalidone	12.5	12.5-25	1
Hydrochlorothiazide	12.5-25	25-50	2-Jan
Indapamide	1.25	1.25-2.5	1

Conclusion

In conclusion arterial hypertension is an important risk factor for cardiovascular diseases and also contributes to increased morbidity and mortality. Hypertension is indeed a major public health problem accounting for drastic downward shifts in the economic progress of a country. That too in a country like India, the impact of this dreadful disease on the healthcare system as a whole is humongous. Figures portray that about Rs. 43 billion of the annual income among the adult working class in our country is spent for the management of HT. Suboptimal control of BP is the most common attributable risk for death worldwide. HT goals can be achieved and maintained only by a team-based approach with aid from all health personnel like general physicians, medical specialists, trained nurses, dieticians and pharmacists. Moreover, studies have shown the significance of multi-disciplinary approach in the management of HT. Emphasis should also be on strict lifestyle modifications which act as the cornerstone for prevention and treatment of HT.

Many pharmacological agents are available for treatment; however, the choice depends on the patients' age, diagnosis, comorbidities, appropriate strength-dosage scheme and patients' tolerability. Hypertension can affect all ages despite gender and ethnicity. Lifestyle modifications, including weight loss, reduction of dietary sodium intake, aerobic physical activity of at least 30 minutes a day at least three times a week, and a reduction in alcohol consumption, are a relatively cost-effective way to reduce high blood pressure. There is wide variability in the cost of antihypertensive medications; newer and more expensive agents have not been shown to be significantly safer or more effective than many older, well-established medications that are available in generic form. Fixed combinations of antihypertensive medications offer less dosing flexibility and are often substantially more expensive than prescribing the component medications independently. It is our goal to not just decrease the risk of CV diseases brought about by elevated BPs but to prolong their lives as well.

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