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Evolving Clinical Practice Guidelines in the Management of Hypertension

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Abstract

Hypertension is the commonest cardiovascular disease. The prevalence in our country is around 20-22% of adult population. Most patients are treated by general physicians and only around 5-10% of patients need to be referred to specialised centres. Clinical practice guidelines are important so as to guide physicians regarding measurement techniques, clinical and laboratory evaluation and treatment strategies of these patients. Emphasis on non pharmacological life style modification needs to be placed. Since five-six class of drugs are available and a pertinent choice has to be made by the physician, drug pharmacology and interactions need to be known.

Definition and treatment of hypertension have been evolving over last 5-6 decades and various medical bodies have been updating the guidelines. The JNC guidelines (I-VII) have been the most followed ones. The British guidelines, European Society and WHO guidelines are also useful documents. Our own Indian guidelines have been published in 2000 and 2007. Hypertension is not only a disease due to genetic predisposition but psychosocial, environmental and dietary factors have important implications. Individuals from different races have variation in the pattern of disease. Thus, guidelines need to be evolved by various countries which are suitable for their physicians and countrymen.

Key Words : Hypertension, clinical practice guidelines, psychosocial and environmental factors, dietary factors

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Hypertension is the commonest cardiovascular disease in our country & world over. About 25% of world population above 30 years has hypertension. Hypertensive patients have increased risk of coronary heart disease (CHD), cerebrovascular accidents (hemorrhagic & occlusive), heart failure, atrial fibrillation, chronic renal failure, eye changes, aortic aneurysms, aortic dissections & peripheral arterial disease. Antihypertensive treatment brings back the risk to near normal although it does not reach the level of normotensive individuals. It is associated with a major reduction in the risk of fatal or non-fatal stroke (about 30–40%), but, coronary events are reduced to a lesser degree (20%). There is also a large reduction in the incidence of heart failure and other risks involved. Doctors from all fields especially primary care physicians are expected to treat most patients of hypertension & only 5-10% of patients need to be referred to specialists.

Clinical practice guidelines need to be evolved so as to provide simplistic guidelines to physicians regarding measurement, clinical evaluation, risk stratification, baseline investigations and pharmacotherapy. At present there are guidelines for management of hypertension from the British Hypertension Society (BHS) (1), World Health Organization - International Society of Hypertension (WHO-ISH) (2), European Society of Cardiology (3), the Joint National Committee (JNC VII) (4) guidelines from USA & also the Australian (5) & Japanese guidelines. These guidelines provide statistical data and practice suggestions according to the population of their countries. We have our own Indian hypertension guidelines I & II (6), which were released in the year 2000 and 2007 respectively. These are the joint guidelines of Association of Physicians of India, Indian Hypertension Society, Cardiological Society of India and Indian Medical Association.

With evolution of concepts in management of hypertension most bodies have been updating the guidelines, every 4-5 years to guide physicians (BHS 1989, 1993, 1999 and 2004). It is important to review all the guidelines so as to look at the interpretation of data by different experts.

In mid 90's the definition of hypertension was different in different

guidelines with WHO guidelines having 160/95 & JNC V having 140/90 as cut off levels. Now there is uniformity in the cut off levels in all guidelines which is 140/90. New terms like optimal BP <120/80 & normal BP 120-129/80-84 mm Hg have been introduced by most bodies. A category of high normal is included by Indian & BHS guidelines corresponding to 130-139/85-89 mm of Hg. The JNC VII has used the term pre hypertension for this category. This term however has not been picked up by other guidelines because even in the Framingham study although the risk of developing hypertension was higher in subjects with high normal (130–39/ 85–89mm Hg) than in those with normal blood pressure (120–129/80–84mm Hg) but for the layman, the term "prehypertension" may create anxiety and will result in unnecessary medical visits and examinations in many subjects.. The JNC VII recognizes stage I & II hypertension, while the Indian guidelines hold on to the stage I, II, & III of hypertension, as was the case in JNC VI.

In blood pressure measurement electronic equipments that are semi automatic have been discouraged by most guidelines (BHS, Indian). The Mercury sphygmomanometer is considered the gold standard. Ambulatory BP monitoring is recommended in only some special situations and not as a routine. It is particularly considered when considerable variability of office BP is found over the same or different visits (marked discrepancy), resistance to drug treatment is suspected, hypotensive episodes are suspected usually in elderly and diabetic patients or elevated office BP is suspected in pregnant women and pre-eclampsia.

Initially the guidelines (early 90's) used primarily diastolic blood pressure for treatment decisions. More recently systolic BP is recognized as an equally or even more important factor after the release of the SHEP trial (7) and SYS-EUR trial results (8). In SHEP trial, individuals (aged= 60 years) with isolated systolic hypertension, antihypertensive treatment with low-dose chlorthalidone reduced the incidence of total stroke by 36%, with 5-year absolute benefit of 30 events per 1000 participants. Similarly major cardiovascular events were reduced, with 5-year absolute benefit of 55 events per 1000. In the Syst-Eur trial (Syst-Eur 1), 4695 ISH patients aged >

60 years were treated with nitrendipine 10-40 mg daily, with the possible addition of enalapril and hydrochlorothiazide. At a median follow-up of 2 years, the incidence of stroke was reduced by approximately 42% and cardiovascular endpoints by 31% in the active treatment group. Now the value of pulse pressure as prognostic factor is being realized.

Along with the, level of blood pressure, the overall risk of the individual is important for initiation of drugs and level of control to be achieved. The concomitant risk factors (diabetes, dyslipidemia, metabolic syndrome) and target organ damage need to be considered for these. The target BP is discussed in most guidelines and the level is 140/90 in most individuals. In diabetics & high risk individuals (stroke, renal dysfunction, proteinuria) the target blood pressure in most guidelines is < 130/80 mm of Hg. The beneficial effect (reduction in macro and microvascular complications) of a greater versus a smaller blood pressure reduction in type 2 diabetic patients was demonstrated by the HOT (9) and UKPDS trials and confirmed by the ABCD studies. HOT study (9) confirmed that there was no increase in cardiovascular risk in patients randomized to the lowest target blood pressure group. The earlier suggested "J" shaped curve by Cruickshank is not believed in any more.

There are expectedly some differences between the various guidelines. Indian guidelines emphasize the salt content of Indian food items, which is highly relevant to our country because of high usage of salt. Such charts are not available in any other guidelines. Similarly Indian guidelines state that alcohol abstinence is preferred. This is because of increased prevalence of problem drinking in India and lack of randomized data suggesting protective effects of alcohol. The Indian guidelines further highlight the metabolic syndrome according to our race since the criteria for central obesity as per waist circumference are different in different races.

The lifestyle measures that are widely agreed to lower blood pressure or cardiovascular risk, and that should be considered in all patients are: 1) smoking cessation, 2) Weight reduction in the overweight (JNC VII maintains target BMI <25 while Indian guidelines

suggest <23 Kg/m^2), 3) moderation of alcohol consumption, (according to ESC 2007 hypertensive individuals who drink alcohol should be advised to limit their consumption to no more than 20–30 g ethanol per day for men, and 10–20 g for women), 4) Physical activity (primarily endurance physical activity like walking, jogging, swimming), 5) Reduction of salt intake (The recommended adequate daily sodium intake has been recently reduced by ESC in 2007 from 100 to 65mmol/day corresponding to 3.8 g/day of sodium chloride, which may be currently difficult to achieve while both Indian and JNC VII maintain daily salt intake <100 mmol/day or < 6 g/day of sodium chloride), and 6) healthy diet such as increase in fruit and vegetable intake and decrease in saturated and total fat intake (fruits and vegetables 4–5 servings or 300 grams of vegetables per day), along with increase in fish and potassium intake.

There have been significant changes in the drug treatment of hypertension. The initial JNC I-IV had "stepped care approach" in which the treatment algorithm was compartmentalized & physicians were guided regarding step I and step II drugs. Recent guidelines likes JNC V-VII have emphasized on "individualized care approach" for drug therapy of hypertension. Five classes of agents have been included in the 1st step thus allowing greater discretion to physicians. Beta-blockers and diuretics are earlier drugs & most trials in 80's & 90's were evaluating these two groups. The agents are now grouped as conventional agents. The angiotensin converting enzyme inhibitors (ACEIs) and calcium channel blockers were added in 80's & are considered as newer agents. In the early 90's most guidelines included ACEIs, calcium channel blockers, beta-blockers and diuretics as 1st line agents. In the late 90's Alpha blockers were also added as 1st line agents. However, after the ALLHAT trial (10) alpha blockers have been withdrawn as 1st line agents. Recently angiotensin receptor blockers (ARBs) have been included as 1st line agents along with the four earlier mentioned groups. The most recent ONTARGET trial (11) proved that ARBs were equivalent to ACEIs in patient with vascular disease or high risk diabetes. The combination of ACE-inhibitors and ARBs was associated with the more adverse events without an increase in benefit when compared to either agent

used in full dose. As a result the concept of using complete RAAS blockade in treatment of hypertension is fading.

Even more recently, based on some reviews beta-blockers are being withdrawn as 1st line agents. LIFE study showed that losartan compared to beta-blocker (Atenolol) over 5 yrs of follow up had a significant, 13% reduction in major cardiovascular events (the primary end point) and a 25% difference in the incidence of stroke. This was considered strongly by BHS guidelines & now other bodies are following the same.

There is now realization of different hemodynamic profile of hypertensives according to the age. The young have high renin activity and more sympathetic drive and the old have low renin activity, stiffer vessels and more blood volume. So ACE I's & ARBs are preferred in the young & calcium channel blockers & diuretics are preferred in the elderly population. Beta blockers may still be used in young but should be avoided in elderly unless there are other compelling reasons like angina or heart failure. Drug treatment in elderly can be initiated with thiazide diuretics and /or calcium antagonists. Trials specifically addressing treatment of isolated systolic hypertension, a particular problem in elderly, have shown the benefit of thiazides and calcium antagonists but subanalysis of other trials also show efficacy of angiotensin receptor antagonists. Initial doses and subsequent dose titration should be more gradual because of a greater chance of undesirable effects, especially in very old and frail subjects. BP goal is the same as in younger patients, i.e. <140/90mm Hg or below, if tolerated. Many elderly patients need two or more drugs to control blood pressure and reductions to <140mm Hg systolic may be particularly difficult to obtain. Because of the increased risk of postural hypotension, BP should always be measured also in the erect posture. In subjects aged 80 years and over, evidence for benefits of antihypertensive treatment was inconclusive. However, recently the HYVET study (12) published in 2008 has provided evidence that antihypertensive treatment with indapamide (sustained release), with or without perindropril, in persons 80 years of age or older is beneficial with respect to fatal and nonfatal stroke, death from any cause, death from cardiovascular cause and rate of heart failure.

A significant change in the guidelines more recently is acceptance of fixed dose combination for treatment of hypertension. Drugs from different classes have synergistic effects and compliance is an important issue. The BHS and Indian guidelines both endorse combinations of drugs with synergistic effect. Most guidelines now provide data regarding good combinations (CCB's + ACE I's, ACE I's + diuretics, ARBs + CCB's) and bad combinations (ACE I's + ARBs, beta blockers + ACE I's, CCB's + diuretics). The blood pressure lowering arm of ASCOT trial (ASCOT-BPLA) showed that amlodipine combined with perindopril had better cardiovascular end points and total mortality compared to combination of atenolol and diuretic over 100,000 patient years of observation (stroke decreased by 23%, all cause death by 11%, cardiovascular events by 16% and new onset diabetes by 30%). Beta blockers especially in combination with a

	Indian HTN Guidelines II	ESC 2007	BHS IV	JNC VII	AUSTRALIAN GUIDELINES 2008
1. Classification					
<120/80	Optimal	Optimal	Optimal	Normal	Normal
102-129/80-84	Normal	Normal	Normal	Prehypertasion	High Normal
130-139/85-89	High Normal	High Normal	High Normal		
140-159/90-99	Stage I	Stage I	Stage I	Stage I	Grade I (mild)
160-179/100-109	Stage II	Stage II	Stage II	Stage II	Grade II (mod)
≥ 180/110	Stage III	Stage III	Stage III		Grade III (severe)
ISH G – I	SBP 140-159 DBP < 90	SBP >140 DBP < 90	SBP 140-159 DBP < 90	SBP > 140 DBP < 90	SBP ≥ 140 DBP < 90
ISH G – II	SBP ≥ 160 DBP < 90		SBP ≥ 160 DBP < 90		SBP ≥ 160 DPB < 70
2. Lifestyle Changes					
Wt reduction	Targat BM I <23 kg/ m²	Wt stabalisation	Target BM I 20 -25 kg/ m²	Target 18.5–24.9 kg/m²	<25 kg/m²
Sodium restriction	<100 mmol/day	<65 mmol/day	<100 mmol/day	<100 mmol/day	<65 mmol/day
Alcohol consumption	≤ 60ml/day in men ≤ 30ml/day in women Abstinence preferred	20 – 30g /day in men 10 – 20 g/day in women	<3 units/day in men <2 /day in women	<2 drink/day in men <1 drink/day in women	<2 drink/day in men <1 drink/day in women

	Indian HTN Guidelines II	ESC 2007	BHS IV	JNC VII	AUSTRALIAN GUIDELINES 2008
3. Goals of Treatment					
	Young < 130/85 Elders < 140/90 Stroke < 130/85	All pt.<140/90	Optimally treated < 140/85 Audit standard < 150/90	All pt. < 140/90	All pt. < 140/90 or lower if tolerated proteinuria >1g/day <125/75
	Diabetes < 130/80	**Diabetes or high risk** < 130/80	**Diabetes** : optimally treated <130/80 audit standard < 140/80	**Diabetes or renal disease** < 130/80	**Diabetes or high risk** <130/80
4. 1st line Drug					
	Low dose diuretic In case of compelling indications – CCBs, ACEIs, ARBs, Beta Blockers	Five classes :– thiazides, CCBs, ACEIs, ARBs, Beta Blockers	<55 yr ACEIs or Beta Blockers >55 yr CCBs or diuretic	Thiazides	Three classes :- ACEIs, ARBs, CCBs
5. Treatment of Elderly					
	Low dose diuretic or CCBs	Thiazides CCBs, ARBs, ACEIs, Beta Blockers	Low dose diuretic or CCB's	Low dose diuretic	Four classes :- ACEIs, ARBs, CCBs, Thiazides
6. Hypertension in Pregnancy					
Treatment threshold	—	≥ 140/90	>150-160/100-110	>150-160/100-110	
Drugs of choice	Methyl dopa (1st line) CCB's, beta blockers, labetelol, alpha blockers	Methyl dopa, CCBs, beta blockers, labetelol	Methyl dopa, CCBs (nifedipine)	Methyl dopa, CCBs, beta blockers, labetelol, clonidine	

thiazide diuretic should not be used in patients with the metabolic syndrome or at high risk of incident diabetes.

Research in hypertension is an ongoing process. We are still looking at the ideal drug & drug combination. The target level of BP is likely to come down since there is a continuous relationship between the level of blood pressure and the risk of complications. Starting at 115/75 mm Hg cardiovascular disease risk doubles with each increment of 20/10 mm Hg throughout the blood pressure range. Newer agents like renin antagonist (aliskiren) are likely to be used clinically. The benefits of some combinations over others will be delineated. Some high risk individuals requiring better blood pressure control will be defined. Consequently with our greater understanding of mechanism of

hypertension and translation of risk reduction trials into practice guidelines we can expect ongoing changes in various guidelines.

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