Preventing Cardiovascular Complications of Hypertension

JS Hiremath
Chief of Cardiology, Poona Hospital & Research Centre, Pune.

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ABSTRACT

Hypertension has reached pandemic proportions. Merely controlling the numbers of systolic & diastolic blood pressure is no longer the goal. Reducing the overall risk of the individual for cardiovascular events, preventing target organ dysfunction, yet maintaining quality of life & minimizing medication is aimed at. Multiple high power trials, JNC VII & European guidelines for management of hypertension indicate clearly that tighter control of blood pressure, choosing medications which improve endothelial dysfunction are means of achieving these goals. Conventional management of hypertension leaves patients with an unacceptably high risk of CV events due to failure to address coexisting risk factors. Lifestyle modifications in the form of DASH diet, weight reduction, aerobic activity, moderation in alcohol consumption form the basis of tight BP control in any stage of hypertension. Multiple medications in small dose combinations need to be applied as first line therapy. Thiazide like diuretic including Indepamide featuring in all combinations is second principle. ACE inhibitors especially Ramipril & Perindopril in appropriate dosages have important role to play. Regression of LV hypertrophy is documented with prolonged use of ACEI. Statins should be used liberally in hypertensive individuals even with marginally high lipids or with associated diabetes mellitus. Use of long acting Nifedipine/Amlodepin has surfaced again for their endothelial dysfunction improvement properties and probable anti-atherosclerotic effect. Quinapril as ACEI has evidence for improvement of endothelial dysfunction. The hypothetical "polypill" is likely to emerge for hypertension management especially for prevention of complications. In special subgroups like diabetics, chronic kidney disease, coronary artery disease, maintaining blood pressure of 120/80mm of Hg & below is clearly shown to be beneficial to prevent cardiovascular & global risk. Lifestyle modification, multiple small dose preventive drug combinations, tighter control of BP & biochemical parameters are the cornerstones of preventing CV complications of hypertension. Periodic checks for early detection and management of CV complications and health insurance for all, are additional points to note.

INTRODUCTION

Hypertension is growing in pandemic proportions. Control of hypertension has been inadequate all along even in developed countries. In the last few years, the focus has been shifting from merely controlling hypertension to controlling the overall risk of the hypertensive individual & especially in preventing cardiovascular complications.[1] This approach is not only important from the individual's point of view, but from reduction in the global risk of CV disorders & the financial implications thereof. Stringent control of hypertension, management of cross risk factors, early detection of CV disorders along with health insurance for all should be the targets. Hypertension presents as a tip of iceberg of a complex multidimensional problem (Fig. 1). Endothelial dysfunction & HTN can mutually worsen each other.[2] None of the major therapeutic trials has provided evidence that reducing blood pressure per say completely reverses risk of CV complications.[3] Hence every additional risk factor leads to an exponential rise in CV mortality & morbidity (Table 1).

WHAT LEADS TO CARDIOVASCULAR COMPLICATIONS IN HTN ?

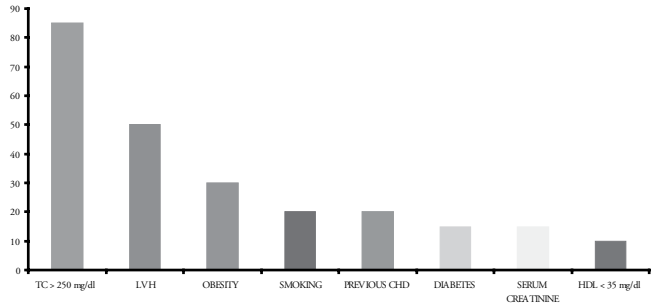
1. Uncontrolled hypertension.
2. LV hypertrophy.
3. Endothelial dysfunction.
4. Diabetes mellitus.
5. Hyperlipidimia.
6. Tobacco, drug effects.

Intensive management of these "cross" risk factors effectively prevents CV complications of HTN (Fig. 2).[4]

1. Uncontrolled Hypertension

The prevalence of hypertension in India is close to the tune of 11% of the population.[5] Diabetes & hypertension

Hypertension rarely occurs in isolation



Hypertension usually occurs in conjunction with other risk factors

Kannel WB, JAMA 1996;275: 1571
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Fig. 1 : Hypertension occurs in conjunction

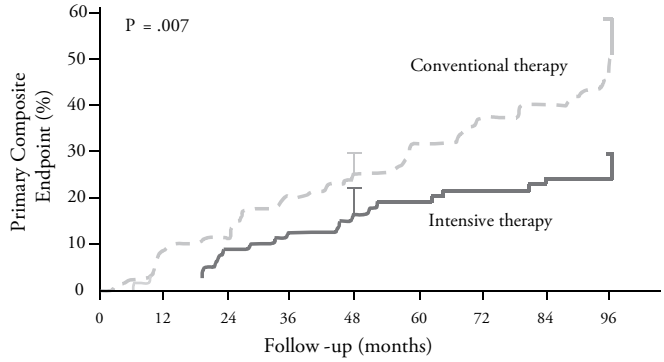
Table 1 : Exponential increase in CV risk in Hypertension

1. Age	7. Diabetes
2. Obesity	8. LV hypertrophy
3. Lack of exercise	9. Lack of exercise
4. High LDL	10. Smoking
5. Low LDL	11. High CRP
6. Smoking	12. High small dense LDL

together runs as high as 23% of the population. Applying a US module of "controlled" hypertension, a large number of hypertensives remain uncontrolled. Uncontrolled hypertensions are considered as the rule of half. Only half of the hypertensives report or get diagnosed as hypertensive and of which under 50% remain under treatment. Of the 50% who are under treatment, 60% are uncontrolled and 40% are under control. Which means only 7.5% of the total hypertensive population is really under control. (These figures are likely to be worse in India). Just by stricter control of hypertension, one can expect prevention of cardiovascular complications.

Stricter control of hypertension can be achieved by many of the guidelines, which are offered by JNC VII and European Heart Association.[6,7] The Indian guidelines for control of hypertension also offer significant directions.[8] Population based strategies suggest that just an average reduction of systolic blood pressure by 5-7 mm of Hg, and shift in the bell shaped curve can lead to significant reduction in cardiovascular mortality (Fig.3). Intermittent use of ambulatory blood pressure monitoring has been found to be remarkably useful. Acceptance of the patient for such an investigation is also good. Round the clock control which is more effective in reducing CV complications can be documented by ambulatory 24-hour BP monitoring. For an uncomplicated hypertension without any risk factors, the aim should be to control at maximum of 130/85 mm of Hg round the clock. Incase of complications like diabetes, ischemic heart disease or chronic kidney disease, the aim of control should be below 120/80 mm of Hg. When

Steno-2 Study: Kaplan-Meier Estimates of Composite Endpoint



An intensive therapy reduces the risk of CVD and microvascular events by approx 50%

Gaede P et al. N Engl J Med. 2003;348:383-393. ©2003 Massachusetts Medical Society.

Fig. 2 : Intensive management of cross risk factors.

Population -Based Strategy

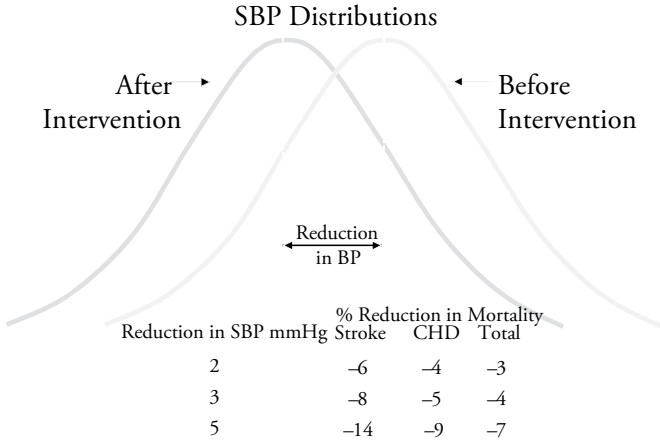
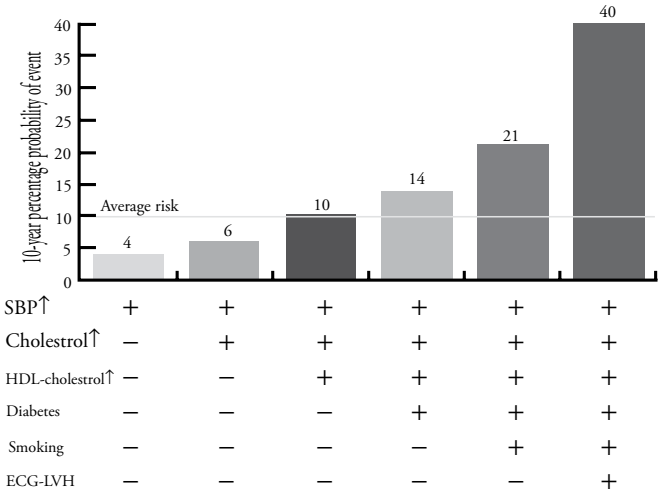


Fig. 3 : CV benefits of reduction of systolic blood pressure.

controlled to this level, cardiovascular complications will be prevented.

Lifestyle modification in the form of restricting dietary sodium, improvement in dietary potassium (DASH diet, which consists of predominance of raw food and uncooked vegetarian diet), reduction in alcohol consumption to moderation, control of weight, cessation of smoking, minimum of 30 min of aerobic exercise daily have been highly recommended.[6] When a strict lifestyle adherence has been achieved 20 points of systolic and 10 points of diastolic blood pressure can get reduced.

Cornerstone in the management of achievement of strict hypertension control is the pharmacotherapy. JNC VII guideline recommends combination of multiple low dose drugs right from the beginning in order to effectively control blood pressure. This would also minimize the side effects of drugs. The pharmacotherapy has to be individualized in order to get a good blood pressure control. Beta-blockers are powerful and potent antihypertensive agents. Though one



Kannel WB. Am J Cardiol 2000;85:251-255

Fig. 4 : Cross risk factors in hypertension.

prefers ACE inhibitors or ARBs with diuretic as a first line antihypertensive for their preventive effect, blood pressure control may not be achieved very well with these agents. Addition of beta-blocker to ACE inhibitor and ARBs is not synergistic hence an additional Ca-channel blocker needs to be thought of. Alpha-blockers should be added only if adequate control is not achieved or if additional prostatic symptoms are seen. Diuretics combine very well with beta-blockers, ACE inhibitors, ARBs and alpha-blockers and probably will appear in most of the prescriptions. The dose of diuretic has to be small to avoid deleterious effects of the metabolic parameters. All and all with effective combination of pharmacotherapy, which will control the hypertension will be "the" important step to achieve strict control of hypertension.

Proper counselling of the patient about the nature of illness, about the importance of control of blood pressure, about the regularity of medication, about the adherence to lifestyle appear phenomenally important and they need to practiced much more vigorously for achieving good blood pressure control.

2. Left Ventricular Hypertrophy

Presence or appearance of left ventricular hypertrophy directly correlates with cardiovascular morbidity & mortality. For prevention of left ventricular hypertrophy or for regression by pharmacotherapy, ACE inhibitors are extremely well documented. Chronic use of good doses of ACE inhibitors will finally lead to left ventricular regression. In this regard, drug of choice would be perindopril and addition of indepamide also is shown to regress left ventricular hypertrophy significantly.

3. Endothelial Dysfunction

A vast research has gone into study of endothelial dysfunction and the entire cardiovascular mortality and morbidity rests on control of endothelial dysfunction. In hypertensive individuals, correction of endothelial dysfunction remains immensely important. The newer available tools like cardiovascular profilor can be utilized to study endothelial dysfunction. Whether it exists or not, choice of pharmacotherapy like ACE inhibitors should appear higher up in the list for endothelial dysfunction correction and prevention of cardiovascular complications. From the point of view of hypertension, the endothelial dysfunction can be prevented by good glycemic control, lowering of LDL, antithrombotic treatments like aspirin, overcoming insulin resistance by way of exercise and reduction of weight. As far as drugs related to hypertension, the best studied drug and most powerful drug for endothelial dysfunction correction is quinapril, but other ACE inhibitors and to some ARBs also appear in the list. Nebivolol, Folic acid supplements, Statins and Ca-channel blockers like long acting Nifedipine and Amlodipine also have been shown to improve endothelial dysfunction.[9,10] Combinations of all these drugs would be vital in order to prevent cardiovascular complications related to endothelial dysfunction.

There appears a strong link between inflammatory response, systolic BP & stroke. Hence drugs like statin with its pleotropic effects can be used to prevent stroke in HTN.[11]

4. Diabetes Mellitus

The co-existence of diabetes and hypertension especially in the form of metabolic syndrome is extremely well known. Tight glycemic controls in hypertensives prevent cardiovascular morbidity and mortality. Hypertension control needs to be adjusted to the level of 120/80 mm of Hg or less in the presence of diabetes mellitus. ACE inhibitors become the drug of choice. Combination of ACE inhibitor with ARB for diabetic nephropathy and when ischemic heart disease complicates, Beta-blockers would be important to control hypertension in diabetes mellitus.

5. Hyperlipidimia

The co-existence of hyperlipidimia and hypertension leads to significant amount of cardiovascular mortality in hypertensives. If there are additional risk factors like diabetes mellitus or kidney disease or recent CVA, irrespective of the lipid levels, statins have to be introduced to control the LDL levels to below 70mg%.[12] There are indicators about LDL control of below 70mg% irrespective of presence of risk factors.[13] We are slowly heading to a situation where all hypertensives will end up getting a statin in order to prevent their cardiovascular mortality and morbidity and obtaining a LDL value below 70mg%.

Prevention of cardiovascular complications of hypertension is now no longer restricted to control of blood pressure alone. Strict control of blood pressure no doubt is important in prevention LV hypertrophy and hypertension related complications. However managing the overall risk of the individuals, managing tight glycemic control, controlling LDL levels to 70mg%, managing endothelium rather than hypertension have emerged as important aspects, which reduce the cardiovascular mortality.

By this multipronged approach of lifestyle modification, control of cross risk factors, multiple low dose medication, one would be able to achieve cardiovascular risk reduction in that individual (Fig. 4). It also would be of paramount importance to reduce the global risk of cardiovascular mortality and morbidity and the phenomenal amount of financial implications thereof. We are heading to a polypill concept of atleast every hypertensive individual receiving multiple "preventive" drugs.[14]

TAKE HOME MESSAGE

1. Strict control of hypertension by lifestyle modification, multiple rational combination pharmacotherapy.
2. Strict control of cross risk factors like glycemic control and lipid control.
3. Prevention of LV hypertrophy and endothelial dysfunction by use of drugs, which work specifically on these aspects.
4. Period checks, early detection of cardiovascular events in order to prevent further complications.
5. Medical insurance for each and every healthy individual so that appropriate treatment can be offered for cardiovascular complications.

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