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How can One Reduce Cardiovascular Mortality in Patients with Hypertension?

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Cardiovascular disease (CVD) including coronary heart disease (CHD) is the commonest cause of death in hypertensive patients. In elderly hypertensives, notably the diuretic-treated group in the Medical Research Council (MRC) elderly trial and in two trials of isolated systolic hypertension (SHEP and SYST-EUR), there was significant reduction (30%) in coronary disease events with reduction of blood pressure (BP). There is no doubt that it is essential to reduce the level of systolic and diastolic BP to prevent cardiovascular (CV) mortality, but there are many pros and cons. These are: when to intervene- at any particular level of BP or in presence of any particular clinical feature?

WHAT ASSOCIATED RISK FACTORS NEED SPECIAL ATTENTION?

How to intervene, when first detected? By pharmacological agents or by nonpharmacological means? Which agents are most helpful? Attempts have been made to find out the most effective drug treatment strategies. Systolic and diastolic thresholds of 160 and 100 mmHg, respectively are clear indicators of drug treatment. Systolic pressure in the range of 140-159 mmHg and diastolic pressure in the range of 90-99 mmHg indicate treatment under certain situations. It is remarkable from different observational studies that international guidelines are inconsistent in their recommendations on thresholds for intervention to prevent CHD and CVD. In recent years; however, the following recommendations have been made:

- When there is evidence of end-organ damage, like left ventricular hypertrophy (LVH).
- When coexistent clinical situation, like diabetes, may increase the risk of CV mortality.
- When dyslipidemia adds to the risk factor; premature mortality from hypertension among first-degree relatives.
- In elderly hypertensives: Most elderly people exceed the threshold for intervention both on BP and lipid-lowering. In contrast, younger people, notably women, may have high levels of BP or cholesterol which, when projected through their life time, would reduce life expectancy, but under current guidelines, would not warrant therapeutic intervention.
- An estimated 10-year coronary risk of 15% (equivalent to a CVD risk of 20%).

PHARMACOLOGICAL AGENTS USED VARY IN THEIR ABILITY TO PREVENT CV MORTALITY

Antihypertensive agents, which achieve similar reduction of level of BP, differ in their ability to prevent CV mortality, due to the differences of their mechanism of action or their effect on central or peripheral pulse pressure. It is found that central pulse pressure i.e., mean aortic pressure, which is the chief determinant of arterial wall stiffness, is the predictor of all-cause mortality including CV mortality. Very stiff arteries cause increase in circumferential arterial wall stress, and this is likely to cause breakdown of medial elastic tissue and it increases possibility of endothelial damage and development of atherosclerosis. So, antihypertensive drugs need to be effective not only in reducing brachial artery BP but also in reducing central arterial wall stiffness.

Calcium channel blockers, though may have very little effect on large central elastic arteries, through their effect on peripheral muscular arteries, they reduce wave reflection amplitude and markedly lower systolic and pulse pressure, hence ventricular afterload. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) study failed to identify any treatment benefit attributable to a particular class of agent, but the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) study shows BP reduction with β-blockers and diuretics as the best recorded intervention for prevention of CV mortality.

The Losartan Intervention For Endpoint reduction (LIFE) in Hypertension study and Perindopril pROtection aGainst REcurrent Stroke Study (PROGRESS) clearly

showed that angiotensin-converting enzyme (ACE) inhibitors prevent CV mortality more than β-blockers for a similar reduction of BP.

'Pressure-independent' effect of ACE inhibitors and receptor blockers may be explained by their optimal effects on arterial stiffness, augmentation of aortic pressure, left ventricular wasted energy, all of which should be reduced to lowest possible level to prevent CV mortality.

LIPID-LOWERING DRUGS

These drugs, formerly set at a higher threshold for global risk of intervention, are brought down by the joint British guidelines. With introduction of statin, the West of Scotland Coronary Prevention Study (WOSCOPS) and ASCOT-Lipid-Lowering Arm (ASCOT-LLA) studies showed that a 20% reduction in cholesterol was associated with a 30-40% reduction of the incidence of CHD. The issue relating to treatment of patients with lower levels of cholesterol becomes an economic argument rather than one demanding an evidence base.

ANTIOXIDANTS

In hypertensives, endothelial dependent dilatation is impaired. This dilatation is mediated largely by release of nitric oxide (NO), which plays an important role in maintaining vascular integrity by modulating vascular tone, inhibiting thrombosis and leukocyte adhesion and influencing smooth muscle proliferation. So, reduced endothelial NO may contribute to vascular injury and hence increase CV mortality. Despite the plausibility for antioxidant therapy in CVD risk reduction, there is lack of evidence of benefit in prospective placebo-controlled trials.

LIFESTYLE MODIFICATIONS

Lifestyle modifications produce important effect in lowering BP and prevention of CV mortality. In obese patients, a 10 kg loss of weight might well normalize the BP. Short-term studies of physical exercise program demonstrated a 10% fall in mean arterial pressure, a 25% fall in total peripheral resistance and a 20% rise in cardiac index. Epidemiological studies demonstrated that potassium intake, given as potassium chloride tablets, brings about a significant fall in BP. Potassium intake, as potassium chloride tablet, is not recommended but intake may be increased as fruits and vegetables. A major American study, Dietary Approaches to Stop Hypertension (DASH) done to investigate the effects of diet on hypertension has recommended:

- A diet with decreased content of dairy produce
- A diet with increased fruit and vegetable content
- A diet avoiding salty and processed food
- A diet rich in starchy food (which promotes weight loss by flat glycemic response, reduces BP and protects against atherosclerosis by providing phytoestrogens, helpful for raising high-density lipoprotein [HDL]: total cholesterol ratio).

SALT RESTRICTION

Studies on salt restriction show that a reduction in salt intake by 76 mmol/day (4.6 g/day) results in 5.0 mmHg and 2.7 mmHg falls in systolic and diastolic BP, respectively. There is evidence of additive effect of salt restriction in hypertensive patients when used in conjunction with drugs which block the renin-angiotensin-aldosterone system (RAAS).

SMOKING CESSATION

Smoking cessation may reduce CHD by about 25%.

MODERATION OF ALCOHOL INTAKE

Moderation in alcohol intake shows a significant fall in both systolic and diastolic BP, though relationship of alcohol intake and CHD is more complex due to beneficial effect of alcohol on HDL cholesterol. Therefore, preventive strategies for CV mortality in essential hypertension include:

- Early detection
- Lifestyle modification
- Timely therapeutic intervention
- Appropriate choice of therapeutic agents
- Adoption of preventive program not only at personal and clinical level, but also at national level.

SUGGESTED READING

1. Hanson L, Hedner T, Lund-Johnasen P, Kjeld SE, Lindholm LH, Syvertsen Jo, et al. Lancet. 2000;356(9227):359-65.
2. Yusuf S, Sleight P, Pogue J, Bosch J, Davies K, Dagenais G. N Engl J Med. 2000;342(3):145-53.
3. du Cailar G, Ribstein J, Mimran A. Am J Hypertens. 2002;15(3):222-9.
4. Frolich ED, Varagic J. Nat Clin Pract Cardiovasc Med. 2004;1:24-30.
5. He FJ, MacGregor GA. BMJ. 2001;323(7311):497-501.