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Case Studies in Primary Hypertension

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Case Studies in Primary Hypertension

Keith E. Wyche, MD, William J. Nicholson, MD, and A. Maziar Zafari, MD, PhD, FACC

I. INTRODUCTION

Several randomized clinical trials of blood pressure (BP)-lowering drugs have been published during the past 2 decades. The earlier trials established the benefits of multiple risk factor intervention as well as diuretic-based and β -blocker-based therapies. More recent trials have shown that angiotensin-converting enzyme (ACE) inhibitors or calcium channel blockers are equally effective. Select randomized clinical trials are described in this article, including the Multiple Risk Factor Intervention Trial (MRFIT), the Systolic Hypertension in the Elderly Program (SHEP) trial, the Hypertension Optimal Treatment (HOT) trial, the Losartan Intervention For Endpoint (LIFE) reduction in hypertension study, and the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT).

The initial choice of drug therapy should be individualized based on concomitant conditions and risk factors as previously discussed in the first half of this article (*see* "Diagnosis and Treatment of Primary Hypertension," in the *Hospital Physician Cardiology Board Review Manual*, Volume 8, Part 1). The case studies are designed to discuss various presentations of primary hypertension and to incorporate the knowledge gained from randomized clinical trials for hypertension management. Data from continuing trials of BP-lowering drugs may indicate differences in treatment regimens comparing either drug classes or differing intensities, which can be used to select the best regimen for individual patients.

II. CLINICAL TRIALS

Randomized clinical trials are the backbone of evidence-based medicine. Large epidemiologic studies (Framingham, National Health and Nutrition Examination Survey [NHANES]) and many clinical trials have provided the basis for diagnosis, treatment, and determination of risk and prognosis for patients with hypertension.

MRFIT

Investigators in MRFIT assessed whether a multi-risk factor modification program would decrease mortality from and prevent coronary heart disease (CHD). In the study, 12,866 high-risk men aged 35 to 57 years were randomly assigned to their usual form of primary care or to a special intervention program, consisting of stepped-care treatment of hypertension using thiazide diuretics, tobacco cessation counseling, and counseling on lowering cholesterol intake. After 7 years, no statistically significant differences were seen in either study group for cardiovascular morbidity or incidence of cardiovascular events. The intervention-group patients did show statistically significant improvements in risk-factor control. Subsequently, 16 years after randomization, an 11.4% decrease in cardiovascular mortality and a 20.4% reduction in the rate of myocardial infarction (MI) were observed in intervention patients compared with patients receiving "usual care."^{1,2}

HOT TRIAL

Conflicting evidence exists regarding the possibility of increased cardiovascular events with aggressive reductions in diastolic BP (DBP). A J-shaped curve has been demonstrated in trials showing a decline in cardiovascular events as the DBP is lowered from 100 to 85 mm Hg, with a subsequent increase in adverse events as the DBP is lowered further below 80 to 85 mm Hg.³ It is thought that occult coronary disease may be unmasked, as coronary filling occurs during diastole, thus accounting for the increased adverse events observed with more aggressive therapy.

The HOT trial randomly assigned 18,790 patients with diastolic hypertension between 100 and 115 mm Hg to 3 groups with target DBP goals (≤ 90 mm Hg, ≤ 85 mm Hg, and ≤ 80 mm Hg) to address the controversial existence of the J-curve. The antihypertensive treatment consisted of felodipine 5 mg per day. If the BP was not controlled, additional therapy was given. Unfortunately, the attained DBPs in the 3 target groups were 85.2 mm Hg, 83.2 mm Hg, and 81.1 mm Hg. This small separation of achieved DBP did not provide the power to detect differences in events between the 3 groups, leaving the controversy of the J-curve still unresolved.