

Letter to the Editor

Clinical Trials in Hypertension: An Uncertain Impact on Physician Practice

MICHAEL A. WEBER, M.D.

Dear Sir:

Research in hypertension continues to explain more about the pathogenesis of this condition and the underlying changes in vascular biology that can lead to cardiovascular events. But despite this exciting work, two ongoing issues continue to be highly relevant: first, that effective control of high pressure should remain the cornerstone of management; and second, that many clinicians still are not sufficiently focused on adequately achieving treatment goals. The purpose of this letter is to draw attention to some recent developments in these areas.

Clinical trials in hypertension during the last 30 years have provided consistent evidence that blood-pressure-lowering treatment reduces the number of major clinical events and improves survival in hypertensive patients. This experience has included hypertension of differing degrees of severity, and has shown the benefit of treatment in systolic as well as diastolic hypertension, and in the elderly as well as in the younger patient (1, 2). Newer trials have shown that aggressively treating blood pressure to reach relatively low target goals — systolic blood pressures in the low 130s and diastolic blood pressure in the low 80s — appears to provide even greater protection against serious endpoints than when blood pressure is reduced to the more traditional goal of 140/90 mm Hg (3). Patients at heightened risk of

poor outcomes, including hypertensives with diabetes mellitus (4) or with renal insufficiency (5), seem to be particularly well served by reduction of blood pressure to optimal levels.

Published guidelines for managing hypertension, both in the United States (5) and internationally (6), have endorsed the desirability of tight blood pressure control in appropriate patients. But despite these widely disseminated recommendations, clinical practice appears to lag far behind. According to the National Health and Nutrition Examination Survey (7), only about half the hypertensive people in the United States are receiving treatment, and of these, fewer than half (approximately 24% of all hypertensives) have their blood pressures controlled to 140/90 mm Hg or below. In all likelihood, only about 10% of hypertensive individuals have blood pressures maintained at the even lower optimal levels. Who is to blame? Suggested explanations include poor patient compliance with treatment, problems with access to health care or affordability of treatment, and physician knowledge and attitude to treatment (8). To be fair, it is often genuinely difficult to treat hypertension aggressively enough to reach optimal blood pressures goals, and complex regimens of drugs in high doses are frequently required (3).

Two recent studies cast light on differing aspects of this issue. One study, carried out in a Veterans Affairs (VA) medical setting, emphasizes potential problems in how physicians approach hypertension therapy (9); the other, a report from the Framingham Heart Study, looks at the long-term benefits of hypertension treatment for a particular population (10). Of course, both the VA population and the Framingham population have special characteristics that may, to some extent, limit the generalizability of conclusions from these studies, but the findings are of interest nonetheless.

Department of Medicine, State University of New York, Health Science Center, Brooklyn, NY.

Address correspondence to Michael A. Weber, M.D., Chairman, Department of Medicine, The Brookdale University Hospital and Medical Center, One Brookdale Plaza, Brooklyn, NY 11212.

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A total of 800 hypertensive men (mean age: 65) were studied at five VA sites in New England during a 2-year period (9). A technique known as recursive partitioning, based on the probability that a variety of clinical and demographic variables in these patients would prompt an increase in treatment, was used to create a measure of "treatment intensity" in each patient, which in turn could then be associated with blood pressure control. At the outset, despite an average of six hypertension-related visits per year, 40% of the patients had blood pressures over 160/90 mm Hg. For clinic blood pressures of 155/90 mm Hg or higher, treatment was increased at 25.6% of visits; when systolic blood pressure was 165 mm Hg or higher (with diastolic blood pressure below 90 mm Hg), treatment was increased in only 21.6% of cases. Overall, changes in treatment occurred at 6.7% of visits, and generally were prompted by increases in blood pressure, the presence of coronary heart disease, and a previous record of changing treatment for that particular patient. Increases in therapy did not appear to be stimulated by the presence of other target organ changes or cardiovascular risk factors, or by patient demographics. Not surprisingly, patients with more intensive therapy for their hypertension achieved significantly lower blood pressure values.

There were insufficient data to assess the effect of patient compliance with therapy; unfortunately, pharmacy-dispensing records and comments in the patients' progress notes did not appear helpful in explaining the study findings. Moreover, in the VA setting, there is ready access to health care and drug therapy, usually at no cost to the patient. It is clear, however, that patients with higher blood pressures at a given visit tended to be brought back sooner than usual for a return visit, so it could be argued that many of the physicians involved, even when hesitant to adjust treatment, at least showed some sensitivity to the problem of poor blood pressure control. Despite this, the investigators concluded that "many physicians are not aggressive enough in their approach to hypertension."

The Framingham Study recently examined data on blood pressure, antihypertensive treatment and electrocardiographic (EKG) left ventricular hypertrophy during a 40-year period (1950–1989) in 10,333 people aged 45 to 74 (10). During this time, the prevalence of high blood pressure levels (systolic blood pressure of 160 mm Hg or higher or diastolic blood pressure of 100 mm Hg or higher) was reduced from 18.5% to 9.2% in men, and from 28% to 7.7% in women. At the same time, the use of antihyper-

tensive medications in this population increased from 2.3% to 24.6% in men and from 5.7 to 27.7% in women. Based on rigorous EKG criteria, the prevalence of left ventricular hypertrophy during this period was reduced from 4.5% to 2.5% in men, and from 3.6% to 1.1% in women. In considering these results, though, it should be remembered that the Framingham cohort, knowing that it was under continuing scientific scrutiny, might have behaved somewhat differently than populations elsewhere.

The authors have interpreted these clear trends as indicating that increased use of antihypertensive medications has decreased the prevalence of hypertension, thereby reducing the prevalence of left ventricular hypertrophy in this community. Since left ventricular hypertrophy is known to be a strong predictor of major cardiovascular endpoints (11), the authors have boldly gone on to conjecture that this sequence of trends can explain the progressive reduction in cardiovascular deaths observed in the general population since the late 1960s. In addition, the authors suggest that the benefit of treatment may result from decreasing blood pressures at the higher end of the hypertension spectrum; this may well be true, though recent prospective trials suggest that modest blood pressure decrements in the lower hypertensive ranges also appear to confer benefits (3).

These reports from New England point out two interesting facts about our management of hypertension. On the one hand, the observations in Framingham provide reassurance that antihypertensive therapy in the community appears to be reducing the prevalence of hypertension and the incidence of serious cardiovascular events. But the VA findings indicate that physicians are still not able to fully achieve optimal or even, in many cases, remotely acceptable blood pressure goals. Newer, more efficacious antihypertensive drugs, with minimal side effects, should prove helpful in improving blood pressure management. Evidence from recent randomized clinical trials should provide a further spur to the outcomes benefits of aggressive antihypertensive therapy.

References

1. Kannel WB, D'Agostino RB, Silberschatz H. Blood pressure and cardiovascular morbidity and mortality rates in the elderly. *Am Heart J* 1997; 134:758–763.
2. SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. *JAMA* 1991; 265:3255–3264.
3. Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low dose aspirin in patients with hypertension: Principal results of the Hypertension Optimal Treatment (HOT) randomised trial. *HOT Study Group. Lancet* 1998; 351:1755–1762.

4. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ* 1998; 317:703–713.
5. Joint National Committee. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med* 1977; 157:2413–2446.
6. Guidelines Subcommittee: 1999 World Health Organization — International Society of Hypertension Guidelines for the Management of Hypertension. *J Hypertens* 1999; 17:151–183.
7. Burt VL, Whelton P, Roccella EJ, et al. Prevalence of hypertension in the US adult population: Results from the Third National Health and Nutrition Examination Survey 1988–1991. *Hypertension* 1995; 25:305–313.
8. Weber MA. Strategies for improving blood pressure control. *Am J Hypertens* 1998; 11:897–899.
9. Berlowitz DR, Ash AS, Hickey EC, et al. Inadequate management of blood pressure in a hypertensive population. *N Engl J Med* 1998; 339:1957–1963.
10. Mosterd A, D'Agostino RB, Silbershatz H, et al. Trends in the prevalence of hypertension, antihypertensive therapy, and left ventricular hypertrophy from 1950 to 1989. *N Engl J Med* 1999; 340:1221–1227.
11. Levy D, Salomon M, D'Agostino RB, et al. Prognostic implications of baseline electrocardiographic features and their serial changes in subjects with left ventricular hypertrophy. *Circulation* 1994; 90:1786–1793.