Impact of Nonadherence to Antihypertensive Therapy

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The benefits of antihypertensive therapy in reducing cardiovascular complications have been impressive. Several clinical trials in hypertension have shown that reduction of blood pressure is associated with significant decreases in the incidence of stroke, ischemic heart disease, congestive heart failure, and renal failure, irrespective of age, gender, race or ethnicity, type of antihypertensive used, or severity of hypertension. Nevertheless, control of hypertension remains unsatisfactory in the United States and throughout the world. Recent data from the National Health and Nutrition Examination Survey indicate that approximately 40% of hypertensive individuals are untreated, and 65% do not have their hypertension controlled to a blood pressure level of <140/90 mm Hg. Although control rates have improved in the past several years, the total number of patients with uncontrolled hypertension has actually increased because of the rise in hypertension prevalence during this period (Figure).

The capability currently exists to lower blood pressure to goal levels in most hypertensive individuals. As with the treatment of other chronic illnesses in which long-term treatment is required, adherence to prescribed medications for hypertension can be a problem. Studies have shown that about 50% of individuals discontinue antihypertensive medications within 6 to 12 months of their initiation. It has been assumed that inadequate adherence to antihypertensive medications and lack of persistence of therapy contribute to the development of cardiovascular complications, although little information has been available in persons without preexistent cardiovascular disease to support this concept. The article in this issue of Circulation by Massaglia and colleagues provides interesting new data on the influence of the level of treatment adherence on the incidence of cardiovascular events. The study is relevant to clinical practice in that it was carried out by 400 Italian primary care physicians and included >18,000 persons with newly diagnosed hypertension without cardiovascular disease who were included in an Italian general practice registry and were followed up for an average of 4.6 years. The registry contained extensive data on drug prescriptions, laboratory tests, hospital admissions, cardiovascular events, and mortality. The patients were divided into either high-, intermediate-, or low-adherence groups on the basis of either ≥80%, 40% to 79%, or ≤40% estimated adherence, respectively, to prescribed medications. Approximately 51% of patients initially were classified as low adherers, and only 8% were in the high-adherence group. The adherence level was not constant, with considerable switching of patients between groups during the study; at the study’s end, 49% of patients showed low adherence and 19% high adherence. The key finding of the study was that after appropriate risk adjustments, the high adherers had a significantly lower risk of cardiovascular events in comparison with the low adherers (hazard ratio 0.62; 95% confidence interval, 0.40–0.96).

The hypertensive patients in this study appeared to be at lower cardiovascular risk than those included in most hypertension treatment trials or in primary care practices in the United States. Only 27.5% had ≥1 other abnormal cardiovascular risk factors, ≥10% to 15% had diagnosed dyslipidemia, and only 10% were obese. Adherence was reportedly greater in men than women and in younger than older patients, which contrasts with previous reports indicating that young men are at highest risk for nonadherence. Also, adherence was highest in those receiving 5 or more medications, a finding that differs from other published data indicating lower adherence with increasing complexity of drug treatment regimens.

The benefits of high adherence to antihypertensive therapy in this study were said to be associated with only slight differences in blood pressures between adherence groups, although the actual data are not provided in the article. The differences between groups may have been minimized by the changing level of patient adherence to therapy during the study. Whatever the explanation, various clinical trials have shown that blood pressure differences of as little as 2–3/1–2 mm Hg are sufficient to cause significant changes in outcome. A recent study of nondiabetic hypertensive individuals compared the effects of lowering systolic blood pressure to goal levels of either <140 or <130 mm Hg. The more aggressively treated group that achieved blood pressure levels averaging 3.8/1.5 mm Hg lower than those in the less aggressively treated group had a 37% lower incidence of electrocardiographically diagnosed left ventricular hypertrophy and a 50% lower incidence of composite cardiovascular events.

Blood pressure goals have been revised progressively downward as clinical trial data have demonstrated improved outcomes at lower levels. Although a blood pressure target of ≤140/90 mm Hg had been advocated for many years, goals of ≤130/80 mm Hg are now recommended for patients with chronic renal disease, diabetes mellitus, angina, unstable angina, and congestive heart failure. Long-term adherence to and persistence of therapy are clearly required to achieve such goals.
Multiple factors can influence treatment adherence and persistence. Some are patient related, and others are related to clinicians or aspects of the health care delivery system itself.\textsuperscript{1,6,10} Positive interactions between clinician and patient and demonstration of empathy for the patient will promote trust and respect and enhance motivation of patients to take medications.\textsuperscript{1} Patients need to be educated about hypertension and the goals of treatment and be brought into the decision-making process. Management strategies should be tailored to patient needs. Race, ethnicity, and income status can influence hypertension control when these factors affect access to quality care or availability of health insurance or when they lead to cultural and attitudinal differences between patients and their clinicians.\textsuperscript{11}

Inadequate adherence to therapy is particularly prominent in persons with newly diagnosed hypertension, young men, Hispanic individuals, the uninsured, heavy drinkers, and those with depression or other significant psychiatric illnesses.\textsuperscript{12} Physicians generally overestimate the level of adherence to therapy.\textsuperscript{13} Poor adherence should be suspected in those whose blood pressure appears resistant to medications. Monitoring prescription refills and pill-counting are of value when nonadherence is suspected but can be unreliable in patients who wish to avoid admitting their failure to adhere to prescribed regimens.\textsuperscript{13}

Patients should be made aware of their blood pressure level at each clinic visit and be provided specific written instructions on the treatment program and its goals. In addition, home monitoring of blood pressure can help promote adherence. With the large array of effective and well-tolerated antihypertensive drugs, side effects of medications should not be accepted. Although cost of medications can affect adherence, cost is less an issue now than in the past because representatives of each of the major antihypertensive drug classes are either currently available in generic form or, in the case of angiotensin receptor blockers, will soon become so. Several 2-drug, fixed-dose combinations are also available that can facilitate treatment, reduce cost, and promote adherence.\textsuperscript{1,14} Recently, even a 3-drug preparation that includes a thiazide diuretic, calcium antagonist, and angiotensin receptor blocker has been approved for use.

The low rates of blood pressure control can be due to “therapeutic inertia” or failure of clinicians to increase medications when blood pressure goals have not been met. In a recent large study, antihypertensive therapy was increased in only 13% of patient visits when blood pressure levels exceeded 140/90 mm Hg.\textsuperscript{15} The physicians’ reluctance to treat elevated blood pressure was greater with elderly patients, those with systolic hypertension, and those with such comorbid conditions as diabetes mellitus, heart failure, and clinically significant cardiovascular disease.

The care delivery system should be designed to provide minimal waiting times for patients, appointment reminders, and rapid responses to missed appointments. The increasing use of information technology and electronic medical records in clinical settings should make it easier to monitor patients and provide timely feedback to them. Health Plan Employer Data and Information Set guidelines are being used in several conditions, including hypertension, to assess the quality of care provided by physicians. Some insurers have begun to tie reimbursement levels of physicians to their ability to achieve such quality-related goals as blood pressure control. The threat of income loss may motivate clinicians to reduce clinical inertia and deal more effectively with adherence issues in their patients.

Use of treatment algorithms, guidelines, or both in the primary care setting can facilitate therapy.\textsuperscript{16} These and other educational materials on healthy lifestyles and drug therapies are available through the National Heart, Lung and Blood Institute (http://www.nhlbi.nih.gov), the American Heart Association (http://www.americanheart.org), and other organizations. Not only physicians but also other healthcare professionals including nurse clinicians, physician assistants, dieticians, nutritionists, and pharmacists have an important role in the education and monitoring of hypertensive patients. Hypertension currently is responsible for more office visits to primary care physicians than any other medical condition,\textsuperscript{17} and the continued increase in its prevalence resulting from the increasing age of the population and the rise in obesity prevalence will only enhance the need to use ancillary health personnel in hypertension management.

The Healthy People 2000 goal of achieving 50% control rates for hypertension was not met, nor will the same stated goal be attained for Healthy People 2010.\textsuperscript{18} Although some progress has been made, more than one fourth of hypertensive patients are still unaware of their illness, and approximately two thirds are not at goal blood pressure levels.\textsuperscript{7} We must do better if the relatively modest goal of 50% control is to be reached by even 2020!

Disclosures

None.

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