Journal of the American Heart Association

EDITORIAL

Low Adherence to High Blood Pressure Treatments: Innovative Solutions Are Needed

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The combination of high prevalence and attributable risk makes high blood pressure (BP) the leading cause of cardiovascular disease.[1] Treatment is highly effective in lowering BP and preventing its consequences, but only about 1 in 5 individuals with hypertension has controlled BP.[2] Low adherence to treatment plays a significant role in these unacceptable control rates. The following summarizes the prevalence, consequences, strategies for diagnosing and improving adherence, and innovative approaches to achieving higher rates of control of high BP.

See Article by Lee et al.

PREVALENCE AND CONSEQUENCES OF INADEQUATE ADHERENCE TO TREATMENT OF HIGH BP

The low rate of control of high BP worldwide among individuals being treated for hypertension[2] could be secondary to the inadequacy of drug prescription or nonadherence to the prescription. There is evidence that the second condition is relevant. A meta-analysis involving 27 million patients found that the global prevalence of antihypertensive medication nonadherence ranges from 27% to 40%.[3] The occurrence of nonadherence in patients with resistant hypertension led to the coining of the diagnoses of apparent (secondary to the lack of adherence) and true resistant hypertension. The prevalence of true resistant and pseudo-resistant hypertension were 10.3% and 10.3%, respectively, in a meta-analysis with >3.2 million patients on antihypertensive drugs globally.[4]

The consequence of low adherence to treatment is a higher incidence of cardiovascular disease. In a cohort study of 2 health plans, 1.9% of patients developed resistant hypertension among 205 750 patients with incident hypertension. These patients had an incidence of cardiovascular disease almost 50% higher than their counterparts who did not develop resistance to treatment.[5] The risk for cardiovascular disease is associated with BP values, independently of being treated or treated without adherence to treatment.

Another consequence of low adherence to treatment was reported in this issue of the *Journal of the American Heart Association* (*JAHA*).[6] The database included claims for inpatient, emergency department, outpatient, and prescription drugs from enrollees and their dependents under commercial health insurance plans. The authors explored the association between adherence to BP-lowering treatment and several

Key Words: adherence ■ Editorials ■ hypertension ■ treatment

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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This manuscript was sent to Ajay K. Gupta, MD, MSc, PhD, FRCP, FESC, Senior Associate Editor, for editorial decision and final disposition.

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JAHA is available at: www.ahajournals.org/journal/jaha

outcomes. Among 379 503 individuals with hypertension, 54.4% adhered to antihypertensives. Treatment adherence was associated with significantly lower per-capita total medical, short-term, and long-term disability costs. In addition, medication adherence was linked to lower health care usage and fewer sick absence days. Due to the cross-sectional analysis, reverse causality cannot be mathematically excluded, but it is unlikely that the low adherence to treatment was secondary to the health conditions.

METHODS FOR DIAGNOSING ADHERENCE

The gold-standard method for assessing adherence to treatment is measuring the prescribed drugs in plasma or urine. Studies of other methods for measuring nonadherence and its risk factors have used this method as a reference. However, this method is infeasible in clinical practice in most countries and does not correlate blood and urine levels with the expected concentrations of medication doses.[7]

Patients' self-reports are inefficient for checking adherence. Structured questionnaires are more reliable than self-reports; however, they are time-consuming and may overestimate adherence compared with objective measurements.[8] Electronic drug monitors, digital sensors, and pharmacy fills may be effective[8]; however, they are unavailable in primary care for patients with hypertension worldwide.

Directly observed therapy, which involves observing the swallowing of pills and measuring BP afterward, may be a practical approach to confirming adherence.[9] This method has been used during the hospitalization of patients with suspected nonadherence to treatment. Alternatives include measuring BP for 2 hours in the ambulatory setting after pill ingestion or installing a 24-hour BP monitoring device.

STRATEGIES FOR IMPROVING ADHERENCE

Strategies to improve adherence are multifaceted and target patient, provider, and health care system levels. The efficacy of methods more frequently tested in randomized controlled trials is summarized below.

Combining Drugs Into a Single Pill

The rationale for combining BP-lowering drugs into a single pill is strong and has led to numerous combinations of medications done by the pharmaceutical industry. They have been prepared with the full doses of the drugs or the combination of low doses of 3 or 4 drugs. Studies have compared single-pill combinations with free-equivalent combinations, assessing the adherence, persistence, and systolic BP levels.

A meta-analysis of studies that compared single-pill combinations with free-equivalent combinations showed that single-pill combinations increased adherence and persistence and indicated a trend toward better BP control.[10] Studies have been criticized because patients randomized to usual care may not have received the component drugs.[8] A meta-analysis of 7 studies showed that a low-dose combination of 3 or 4 BP-lowering drugs was more effective in lowering BP than monotherapy, usual care, and placebo.[11] Patients prefer single-pill combinations, but these presentations are affordable only in some countries or regions globally. One potential limitation of poly-pills is insufficient adherence to them, which would lead to the suspension of all drugs in use by the patient.

Digital Health

This term encompasses mobile health and telehealth. Mobile health involves using mobile devices and technologies to support health services and information, such as mobile applications, wearable sensors, and text messages, among others. Telehealth includes virtual visits, remote monitoring, and electronic health records integration, among others. The diversity of methods precludes estimating the effectiveness of specific interventions. A meta-analysis of 74 trials assessed the efficacy of mobile health and telehealth separately.[12] The interventions increased adherence. Both interventions had a placebo-discounted systolic BP–lowering effect of about 4 mm Hg. Only mobile health increased the rate of BP control.

Many other strategies to improve adherence have been proposed: home BP measurement, pharmaceutical care, behavioral counseling, motivational interviewing, health care system changes, multicomponent programs, and financial incentives, among others. Their effects are, at best, similar to those commented on above. The possibility of publication bias exists, and negative results may be reported only as abstracts.[13] A randomized controlled trial with high quality, with 2101 participants and 6 months of follow-up, showed that a protocol of enhanced self-measurement BP, paired with a connected smartphone application, had a null effect on BP.[14] Even if these strategies or their combination reduce systolic BP by 5 mm Hg, the magnitude of benefit would be small and obtained at a high cost effectiveness.

INNOVATIVE STRATEGIES FOR IMPROVING ADHERENCE

The low rate of controlling BP globally and its overwhelming consequences show that what we have

done so far needs improvement. It seems necessary to think outside the box. Below are examples.

Convergence of Guidelines

The thresholds for the diagnosis of hypertension established in guidelines are benchmarks for distinguishing health from disease. Most guidelines still recommend 140/90 mm Hg as the threshold for diagnosis and goal of treatment. The evidence that these values can be lower than 140/90 mm Hg, such as 130/80 mm Hg, proposed by the 2017 American Heart Association/American College of Cardiology guidelines,[15] is progressively more robust. The predicted benefit size of BP reduction corresponds closely to the observed benefit demonstrated in randomized controlled trials, providing mathematical (Cartesian) evidence of causality.[1]

The convergence of guidelines in establishing simplified and lower thresholds for diagnosis and treatment can reduce BP globally. The recent European Society of Cardiology guidelines moved a bit in the direction of the values of the American Heart Association/American College of Cardiology guidelines and withdrew the additional classification of BP in patients with hypertension.[16] The numbers, however, became more complex, with 120/70 mm Hg as the limit of normal and abnormal, 140/90 mm Hg for the diagnosis, and 130/80 or 140/90 mm Hg as the goals for treatment, depending on the cardiovascular risk of patients.

Patients have a dichotomic view of health and disease. For >60 years, doctors have been convincing asymptomatic individuals that they are sick on the basis of 2 numbers that they barely understand. Lowering BP levels for the diagnosis of hypertension would increase the proportion of patients with uncontrolled BP. However, the mean BP of populations would become lower, reducing the burden of high BP.

Another simplification in the diagnosis could be to consider using only systolic BP for the diagnosis and goal of treatment. Until the publication of the Systolic Hypertension in the Elderly Program,[17] the diagnosis of hypertension was based only on the values of diastolic BP. Maintaining a diastolic criterion for the diagnosis considers increasing diastolic BP before increasing systolic BP. If a stricter criterion for the diagnosis is based on systolic BP, say 120 mm Hg (or 100 mm Hg in the future), the corresponding diastolic BP would also be lower.

The global use of lower BP goals and only systolic BP for diagnosis may not influence personal adherence to treatment. Still, doctors and patients would be involved in more intensive treatment of high BP, making it easier for patients to understand the diagnosis. The left shift of the BP distribution curve would increase the number of individuals with controlled BP values.

Population-Based Interventions

The World Health Organization HEARTS (Hypertension, Equity, Awareness, Response, Treatment, and Systems) initiative was developed to use a simple but structured, evidence-based, practical approach to hypertension diagnosis and treatment tailored to each country's needs. Governmental agencies, foundations, and professional societies support the HEARTS program, which uses clinically validated BP measurement devices and access to antihypertensive medications, including single-pill combination antihypertensive therapies. Initial reports suggest success.[18]

Cluster-randomized trials conducted in China explored 2 strategies offering perspectives on enhancing BP control at the community level. Replacing 25% sodium chloride in meal preparation with potassium chloride resulted in a notable 14% reduction in stroke incidence.[19] Another promising approach involved a hypertension management program led by nonphysician professionals under the guidance of community health care providers. The intervention yielded a 23.1 mm Hg reduction in systolic BP, leading to a reduction of a composite cardiovascular outcome (myocardial infarction, stroke, heart failure, and cardiovascular disease death) of 33%.[20]

Population-based strategies have the potential to overcome the problem of adherence because all individuals consume a sodium-reduced diet or take their pills under the strict control of a health care team. These strategies would also reduce the need to understand the risks of high BP and the importance of using the drugs prescribed correctly. However, the feasibility of these strategies may pose challenges in adapting them to other societies.

The efficacious control of high BP is the top priority for preventing noncommunicable diseases globally. Progress has been made, yet more is needed. Lack of treatment adherence is a crucial aspect that should be addressed with innovative solutions. Converging guidelines to recommend lower BP levels for diagnosing and treating hypertension and simplifying diagnosis may be a global and efficient strategy.

ARTICLE INFORMATION

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Disclosures

None.

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