Worldwide Trends and Shortcomings in the Treatment of Hypertension

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Despite advances in the availability and quality of antihypertensive medications and the institution of national programs to educate people about the seriousness of hypertension, much remains to be done. The percentages of people who are aware of their disease, are being treated for it, and are achieving adequate control of their blood pressure (BP) are disconcertingly low worldwide; surveys in numerous countries have consistently shown that fewer than 60% of affected people are being treated for hypertension and fewer than 30% have their BP adequately controlled. Reluctance on the part of many physicians to use antihypertensive therapy aggressively may be an impediment to improving these numbers. Further clinical trials are needed to assess the extent to which BP could be lowered safely and effectively with both single-agent and combination therapies.

Treatment of more than 90% of patients with chronically high blood pressure (BP) will remain empiric until the precise etiology (or etiologies) of primary or essential hypertension is (are) identified. Nevertheless, the quality of treatment for hypertension has improved considerably over the last four decades, becoming increasingly specific as scientists have probed its pathophysiologic mechanisms and have provided clinicians an expanding repertoire of antihypertensive compounds.

Clinical trials conducted in the 1950s, when the number of available pharmacologic agents was limited, yielded mixed results and a high risk of adverse drug reactions. A turning point was reached in the 1960s, when it became evident that administering relatively safe pharmacologic agents such as diuretics could lower high BP. This became the rationale for the Veterans Administration’s controlled clinical trials, which demonstrated by 1970 that lowering BP could translate into reduced morbidity. Investigations conducted in the 1980s demonstrated that antihypertensive therapy could benefit not only hypertensive male veterans, but also women, the elderly, diabetic patients, and blacks with hypertension. In the 1990s, attention turned to gaining a more complete understanding of the neurohormonal, vascular, renal, and other mechanisms that underlie this multifaceted disease and to developing antihypertensive drugs that are tailored to address these functional derangements.

Now, as we enter the 21st century, it is appropriate to ask whether the gains in control of high BP we have achieved over the last four decades have kept pace with the advances in scientific knowledge. Judging from the results of worldwide surveys, the answer would have to be a resounding no.

WORLDWIDE REPORT CARD ON THE TREATMENT OF HYPERTENSION

The Problem in the United States

The National Heart, Lung, and Blood Institute launched the National...
nations for improving compliance with treatment regimens such as the angiotensin II subtype 1 receptor blockers [ARB]) combination drug therapy, and strategies for improving compliance with treatment regimens.

The Problem Worldwide  The 1999 World Health Organization (WHO)–International Society of Hypertension (ISH) Guidelines for the Management of Hypertension pointed out that the situation in other countries is similar or even worse than it is in the United States. A survey in the United Kingdom, for example, showed that only 6% of hypertensive subjects had their BP lowered to < 140/90 mm Hg. Surveys conducted by the WHO in Finland (North Karelia), Italy (Padua), Mongolia (Ulan Bator), and Cuba (Havana) revealed that rates of both awareness and treatment in these four communities, particularly in Mongolia, were considerably lower than those in the United States.  In addition, the Canadian Heart Health Survey of 23,129 participants chosen at random from all 10 provinces revealed that the prevalence of hypertension was 22%. Among the participants identified as hypertensive (n = 5628), 59% were aware of their high BP. Of that group, 58% were not receiving any treatment, 19% were treated with drugs, 16% were treated with drugs plus nonpharmacologic measures, and 7% were treated only with nonpharmacologic measures. Among the same group of aware hypertensive subjects, 16% were being treated and their BP was controlled (diastolic BP < 90 mm Hg), 24% were treated but their BP was not controlled, and 19% were neither treated nor had their BP controlled. Moreover, combined data from surveys conducted in France, Germany, Italy, and Spain show that only about 13% of hypertensive patients have their BP controlled to < 140/90 mm Hg (see Table 1).  

### Table 1. Prevalence, Awareness, Treatment, and Control of Hypertension in France, Germany, Italy, and Spain

<table>
<thead>
<tr>
<th>Country</th>
<th>Hypertensive Patients (%)</th>
<th>BP Controlled (%)</th>
</tr>
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<tbody>
<tr>
<td>France</td>
<td>56%</td>
<td>41%</td>
</tr>
<tr>
<td>Germany</td>
<td>56%</td>
<td>41%</td>
</tr>
<tr>
<td>Italy</td>
<td>56%</td>
<td>41%</td>
</tr>
<tr>
<td>Spain</td>
<td>56%</td>
<td>41%</td>
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BP, blood pressure.
SHORTCOMINGS OF OUR CURRENT METHODS OF TREATMENT

Even though the potential exists for lowering BP to < 140/90 mm Hg in the vast majority of hypertensive patients, the rate of adequately controlling high BP in < 30% of treated patients that has been reported in every national survey suggests that either patients are failing to comply with their prescribed medication regimens or physicians are not being aggressive enough in treating hypertensive patients.

Noncompliance With Therapy Noncompliance by patients has been attributed to a lack of understanding of the consequences of untreated hypertension, attitudes of indifference, side effects of the medication, inconvenient dosing regimens, or a combination of these factors. Thus, physicians must educate their patients about the substantial consequences of hypertension and emphasize the importance of taking their medication as prescribed. Patients who request a change in their antihypertensive medication are much more likely to do so because of side effects or inconvenience than for inadequate BP control. Compliance also can be improved if physicians prescribe drugs that are well tolerated and unlikely to interact with other medications. Moreover, agents that can be taken only once a day provide optimal convenience for the patient. ARB, for example, are a class of newer antihypertensive agents that appear to meet all these requirements. A recent managed care study showed the superiority of one of these agents over other classes of antihypertensive medication with regard to both compliance and persistence with therapy.

Insufficiently Aggressive Treatment In addition to the issue of patients’ compliance with therapy, the other possible explanation for our failure to achieve adequate control of BP in a much larger percentage of patients is that physicians are not being aggressive enough in treating their hypertensive patients. It is incumbent on physicians to choose the best available agents for treating their patients. Because the consequences of inadequately controlled BP are so potentially grave, if the BP is not brought under control with a given agent, physicians should be encouraged to not hesitate before switching to a different agent or trying combination therapy by adding other agents as necessary. The reasons why many physicians are reluctant to prescribe combination drug therapy remain to be addressed, but the findings from the Hypertension Optimal Treatment (HOT) trial may give them some reassurance that, contrary to the generally held view that lower BP levels are unacceptable to patients, a better quality of life is coupled to the lower BP values obtained in that study. Today, aggressive medical treatment also may be limited by the restricted drug formularies of our system of managed care, which restrict physicians’ choices and often exclude more costly medications.

IMPLICATIONS OF THE HOT TRIAL

The HOT trial was conducted to assess the relationship between major cardiovascular events (nonfatal myocardial infarction, nonfatal stroke, and death from any cardiovascular cause) at three target levels of diastolic BP (≤ 90, ≤ 85, and ≤ 80 mm Hg) and to assess the potential benefit of adding low-dose aspirin to antihypertensive therapy. The mean follow-up period was 3.8 years. Results showed that aggressively reducing the diastolic BP to ≤ 85 mm Hg was beneficial, particularly in the subgroup of patients with diabetes. Additional reductions to as low as 70 mm Hg, however, neither conferred further benefit nor imposed additional risk. One important finding was that the target diastolic BP of ≤ 90 mm Hg was achieved in 92% of all these aggressively treated patients.

Because in the HOT study, treatment was especially beneficial in patients with diabetes, a debate is still ongoing regarding whether aggressively lowering BP can be beneficial in most hypertensive patients. Much of the debate seems to be about whether we should redefine the target diastolic BP as 80 to 85 mm Hg, even though the achievement of this level will in all probability require combination therapy in most patients. Unfortunately, this debate is unlikely to be resolved without further study, because the analyses in the HOT trial were unable to demonstrate large BP differences between the three target BP groups. In a way, the study is the victim of its own success; instead of the anticipated 5-mm Hg BP difference, the aggressive BP lowering caused only a 2-mm Hg difference between the groups.

ADDITIONAL CONSIDERATIONS IN THE TREATMENT OF HYPERTENSION

Clinical experience has shown that because hypertension is a manifestation of disordered homeostasis that involves a number of interacting physiologic mechanisms, optimal therapy should go far beyond simply lowering the BP. For example, one also needs to consider the hypertensive patient’s other diseases. The JNC VI provided a list of considerations for individualizing antihypertensive therapy, which recommends the agents that should be used in specific disease states. Moreover, it listed agents that may have favorable and unfavorable effects on various comorbid conditions. In addition, the JNC VI suggested that long-acting formulations with 24-h efficacy have an advantage over short-acting formulations, because once-daily dosing improves compliance, controls BP persistently and smoothly rather than intermittently,
and protects against abrupt increases in BP when patients arise after overnight sleep.\textsuperscript{5}

An ideal antihypertensive medication not only should be effective at lowering the BP, it also should be able to be combined beneficially with other antihypertensive agents. Further, it should not induce fluid retention, alter levels of blood urea nitrogen, insulin, or lipids, or introduce other metabolic perturbations. Finally, it also should have a favorable safety and tolerability profile, with a low rate of discontinuation because of side effects, and a low risk of adverse interactions with concomitantly administered drugs.\textsuperscript{5}

Valsartan, a potent, specific ARB that acts at the AT\textsubscript{1} receptor subtype, meets all of these criteria. It is effective at a dosage of 80 mg once daily, regardless of the age, gender, or race of the patient, and it has an excellent safety profile.\textsuperscript{22} Akin to the other ARB, the overall incidence of adverse effects with valsartan is similar to that of placebo. It has no known clinically significant pharmacokinetic interactions and thus can be combined beneficially with other antihypertensive agents. Additionally, unlike the angiotensin-converting enzyme inhibitors, valsartan and the other ARB are not associated with cough.\textsuperscript{22}

**SUMMARY: WHERE DO WE STAND?**

Surveys conducted in numerous countries have found that the percentages of patients being treated for hypertension are low and that those of whose BP are adequately controlled are even lower, despite the well-known association of high BP with cardiovascular disease and stroke and despite the many improvements in antihypertensive therapy that have been made over the last four decades. Currently, the treatment of individual patients is influenced largely by local medical standards, the policies of national and international committees, and, more recently, the policies of managed care organizations.\textsuperscript{17}

Where do these facts leave practicing physicians, who have such a direct effect on public health? Physicians and managed care providers alike need to become more open-minded in their approach to treating hypertension. Further clinical trials are needed to overcome the still prevalent inertia surrounding the issue of attaining adequate control of BP.

Finally, we need to begin focusing on preventing the development of hypertension in the first place as a means of reducing its future risks of morbidity and mortality.

**REFERENCES**


2. Veterans Administration Cooperative Study Group on Antihypertensive Agents: Effects of treatment on morbidity in hypertension. II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. *JAMA* 1970;213:1143–1152.


