

Management of the Difficult Hypertensive Patient

A. JARRELL RAPER, M.D.

Associate Professor of Medicine, and Director, Outpatient Cardiology Services, Medical College of Virginia, Health Sciences Division of Virginia Commonwealth University, Richmond, Virginia

Hypertension, while usually easily handled, can in certain patients present difficult problems in management.

Previous Neurological Disease

A history of stroke sometimes creates doubt as to the advisability of lowering the blood pressure as this might reduce flow to the brain, causing the patient to have another stroke. It is recognized that *severe* hypertensives clearly do better if they are treated,^{1,2} but the *mild-to-moderate* hypertensive patient with a history of stroke is a more difficult problem, and uncertainty about proper management has been so great that a large multicenter clinical trial—randomized, double-blind, and placebo-controlled—of 452 patients was done by the Stroke-Hypertensive Study group, and its results reported in 1974.³ All 452 patients had a history of a previous stroke and all had mild-to-moderate diastolic hypertension. This study showed that long-term outpatient treatment of the blood pressure neither caused nor prevented a second stroke. Other benefits such as a reduction in the number of episodes of congestive heart failure were evident in the treated group. It would seem, then, that patients with a history of stroke should be treated for their diastolic hypertension, unless there are other contraindications.

Isolated Systolic Hypertension

Another difficult problem is that of “isolated systolic hypertension,” that is, blood pressure of 180/74 mm Hg, a condition common among older people.

Data from the Framingham study have shown that the age-corrected morbidity ratio is correlated with systolic or diastolic hypertension or both,⁴ as it is for stroke, congestive heart failure, and renal disease. Increased systolic blood pressure is therefore clearly a risk factor for cardiovascular damage, and one might assume that it ought to be lowered. Of the large, carefully conducted blood pressure treatment trials that show patient benefit (decreased death or morbidity), all required that patients have *diastolic* hypertension to get into the study and did *not* include those with such pressures as 180/74 mm Hg; these might have a stiff aorta and great vessels, requiring a high systolic pressure to pump a given stroke volume into the vascular system. In addition, treatment of the patient's 180 mm Hg systolic pressure will also lower the diastolic pressure, which may be undesirable. Symptomless coronary heart disease does exist, and blood flow through the coronary arteries is, of course, heavily dependent upon *diastolic* pressure, even more so in the presence of diseased arteries.

When encountering a patient with a wide pulse pressure or with a severe systolic hypertension and normal diastolic pressure, one should look for aortic insufficiency. Severe anemia, arteriovenous fistula, or thyrotoxicosis can also produce systolic hypertension.

Once these conditions are ruled out, the

Correspondence and reprint requests to Dr. A. Jarrell Raper, Box 105, Medical College of Virginia, Richmond, VA 23298.

decision to treat or not to treat must be faced. Unfortunately, there are no data to indicate that such patients can be helped by treating their isolated systolic hypertension. In the face of this uncertainty, treatment is recommended only when the patient has clear evidence of definite cardiovascular damage that appears to be due to the hypertension per se; definite left ventricular hypertrophy might be present, for example, with no other explanation.

The systolic blood pressure usually rises with age in the American population⁵ which puts some millions of primarily elderly people at risk for untreated hypertension or at risk for treatment-induced complications. This is an important clinical problem that has not yet had the systematic and careful study which it deserves.

Mild Diastolic Hypertension

Whether or not to treat mild diastolic high blood pressure (96 mm Hg) may also cause uncertainty, but the Veterans Administration Cooperative Study Group, interpreted by Doctor Freis, has helped to clarify this question.⁶ If the diastolic blood pressure is high enough (over 104 mm Hg), one should go ahead and treat on the basis of the blood pressure alone. At lower levels, the presence of "risk factors" for hypertensive damage should be sought. These include the usual risk factors for atherosclerosis, such as hypercholesterolemia, diabetes, family history, obesity, among others, and age (youth), and race (black). If several risk factors for hypertensive damage are present, or if cardiovascular damage itself is already evident, one should treat the patient with borderline hypertension.

Lack of Response to Therapy

Occasionally, a patient may not respond to the prescribed medication. One reason for this might be incorrect cuff size. In dealing with an obese patient, this can be an important factor, causing as much as 10 mm Hg diastolic error, or more. Current recommendations of the American Heart Association are for a cuff (bladder) width "25% greater than the diameter of the arm"; thus, the standard cuff bladder, 12 × 22 cm, is suitable for a 10 cm (4-inch) diameter arm.

Other reasons why the patient may not be responding to treatment could involve technical factors. For instance, if the patient is engaged in conversation while the pressure is being taken,

the diastolic blood pressure rises slightly. A cold room also raises the blood pressure, systolic and diastolic, as does recent cigarette smoking or an office "climate" that is rushed and hurried. A number of referrals have turned out to be patients who are able to recall that the office atmosphere in which their blood pressure was previously taken was hectic, or that they *themselves* were very rushed and hurried.

Another reason for non-response is that the patient may not be taking his or her medication. An estimated 25% to 50% of patients (depending upon definitions used) will be "non-compliant." Sometimes these individuals return regularly to see their doctor, even though they are not taking their medication; they may even count out the appropriate number of pills and throw them in the trash, so that the number remaining in the bottle appears to be correct to the physician. The best weapon against this is a good doctor-patient relationship in which the patient is assured of the physician's interest. For example, it helps to ask the patient if he or she is taking the prescribed medication regularly. If the answer is yes and the patient seems to be certain about it, the physician should inquire if the medication was taken on schedule that day and the night before. If the patient appears at all uncertain, the physician can then describe the difficulty created by not following treatment, and how this can inadvertently cause over-treatment. Patient education as to the nature of the disease and how complications are avoided has been carefully studied as a means to help compliance, but it has not been as successful as had been hoped.

Simplicity of treatment is very important. Most antihypertensive medications need only be taken twice a day at most. Drug combinations may help if the right combination can be found to fit the patient's needs.

A patient may be complying with prescribed medication and yet still not respond to treatment. The most common cause for this is subtle fluid retention. The body can retain anywhere from 5 to 11 pounds (depending on body size) of extra fluid without producing obvious edema that can be detected on physical examination; thus, a severe hypertensive should be weighed on every office visit. The extra fluid can be eliminated by salt restriction or by more powerful diuretics; this will often restore the responsiveness of the patient to the same program of

antihypertensive medication. Frank congestive heart failure also interferes with the response to medications, as does deteriorating renal function, when blood pressure medicines can become ineffective.

Malignant (Accelerated) Phase of Hypertension

Non-response to treatment may be caused by the fact that the patient is entering the malignant phase of hypertension; high diastolic pressures (130 mm Hg) will be present. This is, of course, a body-wide problem; the basic lesion, fibrinoid necrosis, occurs in arterioles all over the body. The condition can be diagnosed in the office by the following clinical manifestations:

1. Acute hypertensive retinitis or retinopathy: flame-shaped hemorrhages, and fluffy exudates, perhaps with papilledema.
2. Hypertensive encephalopathy: diffuse cerebral dysfunction, perhaps with somnolence, coma, and/or convulsions.
3. Malignant nephrosclerosis: microscopic or gross hematuria and proteinuria

These manifestations are totally curable by lowering the blood pressure to normal, unless the renal lesion has progressed far enough to produce gross decrease in renal function, at which point renal damage may be arrested or slowed, but not cured.

Once malignant hypertension has been halted, the prognosis is still poor. However, as long as the blood pressure is kept down, this syndrome will not return. Patients with newly-discovered malignant hypertension should be hospitalized for immediate control of the blood pressure.

Secondary Hypertension

Trouble may occur with pressure control when the patient has an unrecognized cause of high blood pressure. Pheochromocytoma is a classic example and these patients have notoriously erratic blood pressure that is very difficult to control. Coarctation of the aorta can cause real trouble as very satisfactory blood pressure levels may be produced *below* the coarctation and yet be uncontrollable above the coarctation. Perhaps the patient is on birth-control hormones which in some cases can cause pro-

nounced hypertension. The possible use of artificial female hormones should be ascertained in women of childbearing age or even post-childbearing years.

Severe Hypertension

Severe hypertension can be difficult to manage. Hemodynamic studies have shown that these patients have normal cardiac output, normal heart rate, normal stroke volume, and normal cerebral blood flow unless they are in heart failure or severe renal failure. Subtle alterations in blood flow to several other parts of the body occur and renal blood flow is usually reduced. The small arterioles, because of their size, offer extremely high resistance to blood flow throughout the body. Treatment should begin with a diuretic, not because there will be an adequate response to the diuretic alone but because it decreases the amount of other medications that are required, and is therefore a reasonable foundation for therapy.

Hydrochlorothiazide is usually used, 50 mg twice a day, unless fluid retention is a problem, in which case furosemide is used; a low-salt diet can help, as can weight loss if the patient is grossly obese. It is extremely difficult to get a grossly obese patient to lose weight, but when successful, the weight loss will lower the blood pressure to a surprising degree.

Of course, other medications are going to be needed in addition to the thiazide. Methyldopa or propranolol could be added. Methyldopa is marketed as Aldomet. The highest dose that does any good in a large patient is a total of about 3.5 gm a day divided into two doses. Beyond that, little, if any, blood pressure change occurs and there is the possibility of an increase in toxicity.

Propranolol is marketed as Inderal and is a beta-receptor blocker. It affects not just the cardiovascular system but also blocks beta-receptors in the lungs and receptors in the endocrine system, so that there is the possibility of worsening of the asthmatic patient, or leaving the labile diabetic patient defenseless against hypoglycemia. It has recently been found that larger doses of propranolol are useful, and European and Australian physicians are using up to 1 gm per day if the patient needs it and can tolerate it well.⁷ We have not given quite this much at the Medical College of Virginia, but we are gradually moving to higher doses. Exactly

why propranolol has a good effect on the blood pressure in these high-dosage ranges (beyond what seems to do any good for angina pectoris) is something of a mystery. Propranolol is better tolerated in some ways than guanethidine, and causes less orthostatic hypotension.

Guanethidine is a useful and powerful antihypertensive but causes orthostatic hypotension, as well as intestinal and sexual problems. The dose is extremely variable, and must be individually adjusted, but nearly all hypertensive patients respond favorably to this drug. The problem is that it can produce intolerable side effects. Guanethidine and phenoxybenzamine given together have been shown to be useful in a few patients who do not respond to guanethidine and a diuretic alone.

A new beta-blocker has been recently marketed—metoprolol (Lopressor). It is promoted as being less toxic to the pulmonary and endocrine systems. There is evidence that it is especially useful in patients with obstructive lung disease, although it is not completely devoid of action on pulmonary beta receptors.

If a patient is unresponsive to thiazide plus propranolol or guanethidine, a vasodilator may be added. Hydralazine is an excellent vasodilator and would be even more powerful if we could give enough. Long-term treatment must be limited to about 200 mg a day for an average-size patient because of a lupus-like syndrome that occurs at higher doses with disturbing frequency. I do not know of a single convincing case of lupus-like syndrome at MCV caused by less than 200 mg of hydralazine, and I have been looking specifically for it for the last twelve years.

Prazosin (Minipres) has been recently marketed as a vasodilator. There is some evidence that it has an additional alpha-blockade effect, but the exact balance between these two actions is not well known. It is useful up to 20 mg a day.

If all these drugs have been tried and the hypertension is still uncontrolled, hospitalization is indicated. At this time the physician can determine if any further action is required, such as an arteriogram, to eliminate the possibility of renal artery stenosis if the patient seems to be otherwise a reasonable surgical candidate for its correction. Hospitalization also presents an opportunity to look for other causes of hypertension that might be corrected. Under these conditions, it is always possible to control the blood pressure somehow, using parenteral medications. Later, the patient can be taken off parenteral medication and put on oral agents. The patient will usually be more responsive to the drugs, at least for a while, after hospitalization.

REFERENCES

1. CARTER AB: Hypotensive therapy in stroke survivors. *Lancet*1:485-489, 1970.
2. MARSHALL J: A trial of long-term hypotensive therapy in cerebrovascular disease. *Lancet*1:10-12, 1964.
3. Hypertension-Stroke Cooperative Study Group: Effect of antihypertensive treatment on stroke recurrence. *JAMA* 229:409-418, 1974.
4. KANNEL WB, GORDON T, SCHWARTZ MJ: Systolic versus diastolic blood pressure and risk of coronary artery disease. *Am J Cardiol*, 27:335-346, 1971.
5. *Blood pressure levels of persons 6-74 years*. Vital and Health Statistics Series 11, No. 203, US Department of Health, Education and Welfare.
6. Veterans Administration Cooperative Study Group on Antihypertensive Agents: Effects of treatment on morbidity in hypertension. *JAMA* 202:1028-1034, 1967; 213:1143-1152, 1970.
7. KINCAID-SMITH P: Management of severe hypertension, in JH LARAGH (ed): *Hypertension Manual*. New York, Dun-Donnelay, 1975, p 794.