TREATMENT OF HYPERTENSION IN 1981

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SUMMARY Antihypertensive drugs reduce cardiovascular morbidity and mortality. This was demonstrated by controlled clinical trials. While most complications are dramatically reduced it is not certain whether the incidence of myocardial infarction is decreased by treatment or whether the severity of the infarct is reduced. The prognosis in patients with borderline and mild hypertension varies widely depending on the number of other risk factors present. Patients with mild hypertension and low risk profiles may not obtain enough benefit from treatment to justify the side effects, inconvenience, and expense of such therapy. Such patients should be individually evaluated as to the need and desirability of treatment.

Patients who are not treated with drugs should be seen for an annual follow-up to detect progression. Low sodium diets are effective but they are not practical because it is difficult to adhere to the required degree of sodium restriction. Weight-reducing diets also reduce blood pressure but compliance again is difficult, although it is worth advocating for the few patients who will maintain the diet more or less indefinitely.

Between 1973 and 1977 in the United States there has been an 8% decline in deaths due to heart disease, a 17% decrease in deaths due to stroke, and an increase in average life expectancy from 71.3 to 72.8 years. Could this be the result of more widespread treatment? (Hypertension 3 (suppl II): II-230-II-232, 1981)

KEY WORDS • drug therapy • high blood pressure • controlled trials • prevention of complications • risk factors

THAT antihypertensive drug treatment can reverse the pathological changes associated with malignant hypertension has been known for at least 30 years. This reversal, however, was thought to be limited to severe hypertension, and it was not until 10 years ago, when as a result of the Veterans Administration trial, the treatment of moderate hypertension became generally accepted.

The cardiovascular complications of hypertension can be divided into two main groups as follows: 1) those specifically or primarily related to hypertension, such as hemorrhagic stroke, congestive heart failure, renal failure, and so on; and 2) those due to atherosclerosis principally of the coronary and cerebral arteries. As is well known, hypertension aggravates atherosclerosis and therefore atherosclerotic events are more common in hypertensive than in normotensive individuals. In fact, hypertension is the leading risk factor in coronary heart disease.

Patients with severe hypertension usually die of hypertensive complications because they do not live long enough to develop the more slowly progressive atherosclerotic events. On the other hand, patients with mild hypertension usually die from myocardial infarction or, if they are quite old, from atherothrombotic stroke or an entirely unrelated disorder such as cancer.

Therefore, severe hypertensives tend to develop "hypertensive" complications while patients with mild hypertension usually develop atherosclerotic complications. This is important in considering the results of treatment because we would like to know, particularly in mild hypertension, how effective treatment is in preventing atherosclerotic complications.

The first multiclinic controlled trial on the effectiveness of treatment in hypertension was the Veterans Administration Cooperative Study. The first Veterans Administration Study was organized in 1957. Its major goal was to evaluate the relative effectiveness of the drugs then available in reducing blood pressure. These drugs included chlorothiazide, reserpine, and hydralazine. After demonstrating that a combination of these three drugs was highly effective we decided to use this combination regimen in the morbidity-mortality trial that began in 1964 and continued until 1969.

The morbidity-mortality trial included 512 patients with diastolic blood pressures varying over a wide range from 90-129 mm Hg. Patients were assigned double-blind to either active drugs or placebo. The moderately severe group with initial diastolic blood pressures between 115 and 129 mm Hg were followed for an average of only 18 months. The study was stopped earlier than planned because of the marked...
difference in morbidity-mortality between the placebo and treatment groups. In fact, the ratio of major complications between the placebo group and treatment group was 27 to 1, or 2600% less in the treated patients.

The patients with initial diastolic blood pressures between 90 and 114 mm Hg were followed longer than the more severe patients. The average follow-up was 3.3 years, and in some it was longer than 5 years. By the life table method of analysis, there was an approximate 200% reduction in complications with treatment. While this was a striking reduction it soon became evident that the therapeutic benefit was greater the higher the level of blood pressure. The major benefit occurred in the patients in the moderate range (105–114 mm Hg) of diastolic blood pressure where complications were 300% lower in the treated group as compared to the control patients. In the mild group, with initial diastolic blood pressures between 90 and 104 mm Hg, the major morbidity-mortality was only 30% lower in the treated patients and this was not statistically significant. Perhaps with a larger sample size the differences between treated and nontreated would have become significant. In any case, the differences due to treatment of mild hypertension are not as striking as in patients with moderate or moderately severe hypertension. The Veterans Administration Study concluded that whereas the benefit of treating moderate to severe hypertension had been conclusively demonstrated, further studies designed on a larger scale were needed to determine the effectiveness of treatment in patients with mild hypertension.

The answer to the question related to mild hypertension came ten years later when the results of two important trials were published. One was the Australian trial which included patients with initial diastolic blood pressure between 95 and 109 mm Hg. Over a 4-year period of follow-up, the treated patients had a 29% reduction in cardiovascular complications (p < 0.01) as compared to the control group. The second study was the Hypertension Detection and Follow-Up Program, which was in essence a comparison of fully treated (step care) with variably treated (referred care) patients. Among approximately 8000 patients with diastolic blood pressures in the range of 90–104 mm Hg followed for 5 years, there were 26% fewer deaths due to cardiovascular causes in the step care as opposed to the referred care patients.

Did the benefit of treatment demonstrated in patients with mild hypertension include prevention of atherosclerotic complications? Most important, does treatment reduce the incidence of myocardial infarction? The Veterans and Australian trials had too few patients to answer this question definitively. Nevertheless, the results were essentially the same in both studies. In both studies there was a reduction in fatal infarction but not in nonfatal infarcts. In fact, the treated patients in both studies actually had somewhat more nonfatal infarcts than the control groups. These results suggest that treatment does not reduce the incidence of infarcts but it does seem to lower the mortality associated with this complication. In this connection, Bock* has reported that if a patient was under antihypertensive treatment and the blood pressure was well controlled at the time of a myocardial infarct, survival following an infarct was 3 times higher than in the patients who were not treated.

Treatment with antihypertensive agents produces hemodynamic changes which should be beneficial to the patient who develops a myocardial infarction. For example, the reduction in afterload will lower the oxygen demands of the left ventricle thereby reducing the size of the infarcted zone. Also, congestive heart failure often complicates severe infarction and treatment will minimize that development. Finally, inhibition of the sympathetic innervation of the heart may reduce the incidence of serious arrhythmias. Despite the recent evidence of some benefit of treatment in myocardial infarction, it must be remembered that antihypertensive drugs are not as effective in preventing heart attacks as they are in preventing other complications such as stroke.

The favorable results obtained from the Australian trial and the Hypertension Detection and Follow-Up Program raise new questions as to who should be treated. All patients with diastolic blood pressures of 100 mm Hg or more as an average of three visits should be treated. But should everyone with a diastolic of 90 mm Hg or higher be treated? Some experts believe that they should. However, I agree with those who believe that the treatment of borderline (diastolic 90–94 mm Hg) and mild (in the range of 95–99 mm Hg) hypertension should be individualized.

Massive numbers of hypertensive patients are in the 90–99 mm Hg range. In the United States alone, they make up approximately 30 million or more individuals. The treatment and follow-up of so many patients would place a heavy load on our medical resources. However, a large percentage of these patients have low risk profiles and, therefore, would benefit little if at all from drug treatment. Proper selection will eliminate these patients from treatment.

To facilitate selection for treatment of patients in the 90–99 mm Hg diastolic range, I have constructed a score sheet in which the various risk factors for both atherosclerosis and hypertension are listed (table 1). The table lists the various prognostic indices and supplies a score to each. At the end of the examination the risk factors present are added up and summed. If the score is 3 or greater and the diastolic blood pressure average over 3 office visits is 95–99 mm Hg inclusive, the patient will be treated. Patients with an average diastolic of 90–94 mm Hg require a severity score of 4 or more to be treated.

How should we manage the patients with low-risk profiles who we decide not to treat? They must be followed and checked on periodically simply because blood pressure tends to rise with age and many mild cases will graduate in time to a more severe grade where treatment will be required. A yearly check-up should be enough for this purpose.

Patients in this category who are too mild for drug treatment also should be encouraged to institute dietary changes aimed at controlling their blood
pressure. Low sodium diets are of unproven effectiveness unless the sodium restriction is very severe, that is, below 20 mEq per day. Unfortunately, this cannot be achieved without effort and sacrifice so great that most patients will not adhere to such a diet. However, there is evidence that a more modest reduction in dietary sodium will lower blood pressure but not as markedly as the stricter diets.11

An effective dietary approach, particularly in obese patients, are the weight-reducing diets. Numerous trials have indicated their usefulness, one of the most recent being the studies by Riesen and associates12 in which the sodium content of the diet was controlled. An average loss of 20 pounds was associated with normalization of blood pressure in nearly all patients with mild hypertension. The problem with weight-reducing diets; however, as with the low sodium diets, is long-term compliance, but it is well worth encouraging.

Some recent vital statistics from the United States suggest a possibly important trend. As a result of the Veterans Administration Cooperative Study, Secretary Elliot Richardson and Dr. Theodore Cooper initiated the National High Blood Pressure Education Program whose main purpose was to educate the public that the complications of hypertension are reversible. This program reached full operation beginning in 1973. The interesting point is that in the period between 1973 and 1977 some unusual changes occurred in the vital statistics. In the 4-year period, deaths due to heart diseases declined 8%, deaths due to strokes fell a striking 17%, and even average life expectancy gained 1.5 years from 71.3 to 72.8 years.

Although it cannot be proven that the changes in the vital statistics are due to more effective treatment of hypertension, they are consistent with what one would expect if the results of the various controlled trials were applied generally. There is at least reason to hope that cardiovascular death rates will decline further as the treatment of hypertension becomes more widespread and efficient.

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