Blood Pressure Monitoring in Clinical Trials in the Absence of Ambulatory Blood Pressure Recording: Where Is the Stand?

To the Editor:

The American Heart Association position statement on blood pressure (BP) measurements\(^1\) will be useful for clinicians and academicians alike in arriving at a consensus. The BP recordings reported in clinical trials have an important bearing on the future clinical practice. Although ambulatory BP monitoring is recommended, it may not be possible in all settings because of many factors like patient discomfort, unavailability, or cost. In this situation, BP measurements in the office will still remain as a method to assess efficacy of antihypertensives.

In this context, many clinical trials report the BP lowering at the end of study, which is considered the efficacy endpoint. Can this one-time office reading at endpoint accurately describe the efficacy of an antihypertensive? It is obvious that BP recordings performed at one point do not offer conclusive evidence of antihypertensive efficacy of a drug. Many factors affect office-based BP measurements. However, the International Conference on Harmonization guideline or American Heart Association position statement does not give adequate importance to this criterion. The International Conference on Harmonization guideline for clinical evaluation of antihypertensives\(^2\) states, “in general, the effect of blood pressure at the end of the study is the primary endpoint, but the time course of the onset of the effect is also of interest; this can be defined by examining trough response each week or every 2 weeks in some studies.” This statement does not reflect the point that for meaningful evaluation of the efficacy of an antihypertensive drug, in the absence of ambulatory BP monitoring, the reduction from baseline averaged for all visits is important and should be the primary criterion for endpoint. Measurement of BP at just the last visit cannot be justified as a reliable primary endpoint. Clinical trials reporting efficacy of antihypertensive medications should report the average decline in BP at all visits.

Response:

The evaluation of blood pressure changes in clinical trials of antihypertensive treatment is an important issue, which the American Heart Association guidelines does not directly address. I agree with Dr Prabhakar that relying on a single set of measurements made at the last visit is an unreliable measure for a primary endpoint. A good example of this was the HOPE trial, in which there was a huge discrepancy between the effects of ramipril on blood pressure measured in the office or by 24-hour monitoring.\(^1\) Whereas one could argue that the change of office blood pressure is more relevant for clinical practice, there is evidence that it is less predictive of the drug’s effects on target organ damage and hence clinical outcomes. In a study of the effects of lisinopril on blood pressure and left ventricular mass,\(^2\) in which blood pressure was measured in the office, with 24-hour monitoring, and home monitoring, it was found that there was no correlation between the changes of office pressure and regression of left ventricular mass, whereas there were significant correlations between the changes of ambulatory and home pressure with left ventricular mass. Although the repeated use of 24-hour monitoring is impractical, home monitoring is both economical and practical, and because the number of readings can be made much higher than with office measurement, it is also statistically more reliable. It is surprising how infrequently home monitoring has been used in clinical trials of antihypertensive medications, but because it has been shown to predict clinical outcomes better than office blood pressure in treated patients, a good case could be made for its wider use. It should be recognized that the blood pressure changes observed with home and ambulatory monitoring are consistently smaller than those observed with clinic pressure.\(^3\) This would be an appropriate time to develop new guidelines for blood pressure measurement in clinical trials.

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