Pseudoresistant Hypertension Attributed to White-Coat Effect

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An increase in blood pressure (BP) when taken in the office setting was recognized as early as 1940, when Ayman and Goldshine reported that BP readings measured in the clinic were higher than BP recorded in the home. The authors attributed the increase in clinic BP to “the excitement and tension associated with the visit to the clinic or doctor’s office.” In 1966, Sokolow et al using a noninvasive portable BP recording device showed that readings taken during usual daily activities (ambulatory BP) were lower than casual office BP. Floras et al subsequently confirmed these findings with continuous intra-arterial BP recordings by observing higher BP in the clinic compared with the awake ambulatory BP.

Advances in ambulatory BP monitoring led to several studies by Pickering and his colleagues in which home BP and ambulatory BP were noted to be similar and BP lower during sleep and higher in the office setting. Based on these observations, they proposed the term “white-coat hypertension” (WCH) to describe the phenomenon of higher office BP and lower awake ambulatory BP. Pickering et al then proceeded to report on a series of 292 patients with untreated, borderline hypertension, finding that 21% exhibited WCH defined as a high office diastolic BP of 90 to 104 mm Hg and a “normal” awake ambulatory BP <134/90 mm Hg. This cut point for ambulatory BP was selected on the basis of being below the 90th percentile of the normotensive distribution for both systolic and diastolic BPs. Subsequent reports on clinical cardiovascular outcomes in relation to BP status led to refinements in the definition of WCH, which evolved into an office systolic BP ≥140/90 mm Hg in the presence of an awake ambulatory BP <135/85 mm Hg. Virtually all of the studies on WCH were concerned with making a diagnosis of hypertension in untreated patients.

At this time, this author wondered about the fate of the 20% to 25% of patients with WCH who may have ended up taking antihypertensive drug therapy because of misdiagnosis. This interest led to an investigation of the white-coat response in treated hypertension. In 71 patients prescribed antihypertensive drug therapy by their family physician who were then referred to a hypertension specialist, the mean office BP of 166/95 mm Hg was substantially higher than the mean awake ambulatory BP of 139/86 mm Hg. Because most of these patients had exhibited a decrease in BP from office to awake ambulatory BP, it did not seem appropriate to use the arbitrary cut points of Pickering and colleagues to single out the minority who satisfied the criteria for WCH used to diagnose untreated patients. As a result, a new term, “white-coat effect” (WCE), was proposed to designate treated hypertensive patients who showed a decrease in awake ambulatory BP compared with office or clinic BP of ≥20 mm Hg systolic and/or 10 mm Hg diastolic. This difference was selected because its presence would likely influence the intensity of antihypertensive drug therapy being prescribed. This definition of WCE has come to be recognized as a measure of office-induced hypertension in treated hypertensive patients.

Fast forward to 2012 and the concepts of WCH and WCE appear to merge in the article by Franklin et al in this issue of Hypertension. In a meta-analysis of 1593 adults residing in the community who had isolated systolic hypertension based on clinic readings, the authors performed 24-hour ambulatory BP monitoring and followed their subjects for a median of 10.6 years for the development of cardiovascular events. Untreated isolated systolic hypertension subjects with WCH defined as an office systolic BP ≥140 mm Hg and awake ambulatory BP <135 mm Hg had the same risk of experiencing a cardiovascular event as did untreated normotensive subjects. Similarly, individuals receiving treatment for hypertension had the same cardiovascular risk if both clinic and ambulatory BPs were normal or if clinic BP was high and ambulatory BP was normal (WCH). A third important finding in this study was that treated WCH subjects had almost twice the cardiovascular risk as did untreated WCH subjects. Other than emphasizing the importance of using 24-hour ambulatory BP monitoring to make an accurate assessment of an individual’s BP status, the authors also concluded that the term “WCH” should not be used to describe treated patients even if their BP readings satisfied the criteria for diagnosing WCH in untreated subjects. In doing so, they wished to avoid the confusion that might arise if some WCH patients are considered to be at increased risk of experiencing a cardiovascular event, whereas others with this diagnosis are not. Instead, they proposed the term “treated normalized hypertension” to describe what they had initially called “treated WCH.”

One might question the need for creating a neologism to describe treated WCH when these patients were really exhibiting a form of resistant hypertension. In an American Heart
Association monograph on resistant hypertension, Calhoun et al 11 listed WCE as a cause of pseudoresistance to hypertension. Therefore, it might be more appropriate to label the treated WCH population in the study of Franklin et al 10 as having “pseudoresistant hypertension,” which could be qualified further to “pseudoresistant hypertension because of WCE.” Use of either term conveys the meaning that the patients are really not hypertensive on treatment despite having high office BP readings. This nomenclature avoids any confusion between untreated WCH patients who have no increased cardiovascular risk and treated hypertensives who have a higher risk despite meeting the conventional criteria for WCH.

Thus, high office BP and normal awake ambulatory BP can be considered in several ways (Table). WCE indicates office BP ≥20 mm Hg systolic and/or 10 mm Hg diastolic higher than the awake ambulatory or home BP, regardless of being on or off treatment and throughout the entire BP range, with no arbitrary cut points for normal BP versus hypertension. WCH applies to untreated individuals who satisfy the conventional definition of office BP ≥140/90 mm Hg and awake ambulatory BP <135/85 mm Hg. Treated patients who meet these criteria can be deemed to have pseudoresistant hypertension (because of WCE). It should be noted that both WCH and pseudoresistant hypertension are really subsets of WCE with the cut points defining normal versus high BP superimposed. Finally, one can always use terms such as “white-coat response” or “white-coat phenomenon” to denote patients with higher office BP and lower ambulatory BP who do not fit any of these definitions.
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