Editors' Corner: White-coat hypertension: misnomers, misconceptions and misunderstandings. What should we do next?

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Few issues in current research on high blood pressure have stimulated greater interest than the so-called white-coat hypertension. The reason is sound: it is hoped that identification of individuals in whom blood pressure is raised only temporarily by an emotional reaction to the clinical environment in which blood pressure is measured will allow one to avoid treating those subjects in whom daily life blood pressure (and blood pressure-related cardiovascular risk) is normal, preserving them from the adverse effects and quality of life and cost problems related to long-term drug administration, and improving the overall cost:benefit ratio of antihypertensive therapy.

The interest in white-coat hypertension, however, has not been matched by collection of consistent data on several important problems generated by or related to this matter. Admittedly, several of these problems are difficult to approach and solve, but the popular conceptions with which white-coat hypertension has been interpreted as a clinical entity have ignored most of them, and researchers have not really attempted to perceive whether the term is appropriate, the concept sound and all implications correctly understood. The present Editorial addresses these problems and emphasizes that data in this field have sometimes been interpreted simplistically, important evidence is still lacking and further studies are needed.

White-coat hypertension: is the concept sound and the term appropriate?

Blood pressure measurements by a doctor and to a lesser extent by a nurse often lead the patient to experience an alerting reaction associated with an increase in blood pressure [1–3]: this phenomenon has appropriately been defined as a white-coat effect. The term white-coat hypertension, however, has been coined under the assumption that the difference between the higher pressure values measured in the clinic and the lower values monitored automatically during daytime reflects the white-coat effect [4–7]. There is no question that, although clinic blood pressure is often affected by the alerting reaction to the doctor's or nurse's measurements of blood pressure, ambulatory blood pressure data are not polluted by any substantial alerting component in response to automatic or semi-automatic cuff inflations [8]. There are, however, several arguments against interpreting the clinic–daytime ambulatory blood pressure difference as an accurate measure of the white-coat effect. For example, when assessed directly by measurements taken before, during and after the visit of a doctor or a nurse in charge of measuring blood pressure, the white-coat effect appears to be characterized both by a blood pressure increase and by a tachycardia [1–3], whereas the clinic–daytime ambulatory blood pressure difference is not accompanied by any similar difference in heart rate [9]. Furthermore, the real (i.e. directly assessed) white-coat effect has been shown to be independent of the patient's age and clinic blood pressure values [1,10]; in contrast, the clinic–daytime ambulatory blood pressure difference increases progressively with ageing and clinic blood pressure values [9,11]. Finally, in hypertensive patients there appears to be no significant correlation between the white-coat effect assessed directly by continuous blood pressure measurements before, during and after a doctor's visit and the clinic–daytime ambulatory blood pressure difference (Parati and Mancia, unpublished data). The conclusion can thus be drawn that the term white-coat hypertension, based as it is on an interpretation of the cause of the difference between clinic and daytime ambulatory blood pressure, is a misnomer because this difference does not measure the white-coat effect and may be caused by several other mechanisms; it also underlies a misconception, because the interpretation that white-coat hypertension is purely emotional in nature is, at best, unproven. A recent World Health Organization report suggests the use of the most descriptive term isolated clinic (or office) hypertension, which is more appropriate to our present state of ignorance [12]. The same caution should also apply to the interpretation of the difference between clinic and home blood pressure [13].

An additional question, of conceptual and terminological relevance, concerns the relationship between white-coat or isolated clinic hypertension and the time-honoured term borderline hypertension to denote those subjects whose clinic blood pressures are sometimes above and sometimes below the arbitrary divider of 140/90 mmHg. It is not likely that the two definitions describe widely different groups of subjects and it cannot be ruled out that the term white-coat or isolated clinic hypertension represents essentially a more sophisticated definition, if not a rejuvenation, of the old term borderline hypertension.

What is the prevalence of isolated clinic hypertension?

There are other misunderstandings concerning the prevalence and the risk of white-coat or, more properly, isolated clinic hypertension. Insofar as prevalence is concerned, some studies have reported that isolated clinic hypertension accounts for as much as 60% of the overall hypertensive population [14] and have thus argued this to be the most common type of hypertension encountered in clinical practice. We now know, however, that these high values originate from an obvious misunderstanding, namely the erroneous assumption that the upper limit of normality of daytime ambulatory blood pressure is the same as that of clinic blood pressure, 140 mmHg systolic and 90 mmHg diastolic [15]. In fact, the Pamela study [9], other smaller population studies [16,17] and a meta-analysis of available data on ambulatory blood pressure monitoring [18] have all shown the upper limit of daytime ambulatory blood pressure normality to be less than 130/85 mmHg for systolic and diastolic blood pressure values, respectively. This implies that the term isolated clinic hypertension must be reserved for individuals in whom daytime ambulatory blood pressure values lower than 130/85 mmHg are documented. According to the Pamela data [9], these individuals are probably less than 10–15% of the hypertensive population, that is a clear minority among hypertensive subjects. Given the high prevalence of hypertension, however, this still means that there is a large number of individuals and hence a large potential impact of this phenomenon on the cost:benefit ratio of antihypertensive treatment, should isolated clinic hypertension not require treatment (see below).

What is the cardiovascular risk of isolated clinic hypertension?

There is a lot of poor understanding of this crucial issue, too. Available data could hardly conflict more than they do. Thus, although some studies have reported white-coat hypertension to be characterized by increased left ventricular mass, altered left ventricular function, renal dysfunction or microalbuminuria [19–23], no evidence of structural or functional organ damage has been associated with this condition in other studies [24–28]. Furthermore, one study reported that white-coat hypertensives share the more frequent occurrence of dyslipidaemia and insulin resistance that has been described in established hypertension [13], whereas another study reported these subjects to be hardly distinguishable from the normotensive population on metabolic counts [29]. Finally, although in one follow-up study white-coat hypertensives showed a cardiovascular morbidity similar to that of normotensive subjects and lower than that of patients with an ambulatory blood pressure elevation [30], in another follow-up study they showed a strikingly high rate of a rapid increase in ambulatory blood pressure to abnormal values [31]. These discrepancies may be explained in terms of the different blood pressures (ambulatory or home) with which clinic blood pressure has been compared, the higher or lower values of ambulatory blood pressure below which a diagnosis of isolated clinic hypertension is made, the differences in demographic characteristics of the subjects and the small size of the samples considered, rendering prospective comparisons between normotensives and white-coat hypertensives unreliable. Therefore, no sound conclusion can yet be drawn concerning whether isolated clinic hypertension is associated with an increased cardiovascular risk or represents an innocent condition. This means that no clinical guidelines on isolated clinic hypertension can be regarded as scientifically appropriate and thus any decision about its treatment remains a matter of the physician's judgement in each individual case. This judgement, however, cannot disregard the large body of evidence showing that even casual blood pressure values have some prognostic importance. Thus, even in the presence of a normal or low 24 h average blood pressure, the possibility of an increased risk (possibly due to a high number of blood pressure peaks or an increased blood pressure variability [32,33]) cannot be excluded.

What needs to be done?

The prognostic importance of isolated clinic hypertension has largely been approached by cross-sectional studies, sometimes even without an appropriate control group [29, 35,36]. Furthermore, the few follow-up studies which have addressed this problem have either focused on subjects that can hardly fit an appropriate definition of this condition (e.g. an elevation of clinic blood pressure that faded at subsequent visits [37,38]) or used retrospective analysis of data collected in an uncontrolled fashion over a period of a few years [30]. The ideal experiment to address this problem would be a prospective study comparing the cardiovascular morbidity and mortality of untreated subjects in whom clinic blood pressure is above 140/90 mmHg and daytime ambulatory blood pressure is below 130/85 mmHg with those of subjects in whom clinic and ambulatory blood pressures are both normal. It should be emphasized, however, that this trial will have to be of an exceedingly large size and long duration in order to record the number of events necessary to give it sufficient statistical power. An acceptable substitute might be a study examining whether a discrete type of organ damage of proven clinical significance (e.g. left ventricular hypertrophy [39]) develops at similar or different rates and attains similar or different magnitudes in the two groups. The time necessary for organ damage to appear or to progress may also be a long one, however.

While longing for an ideal study, which in reality might be unfeasible or hardly feasible, efforts should be devoted to characterizing the clinic–daytime ambulatory blood pressure difference under various conditions, determining precisely its persistence or attenuation over time in the absence or presence of antihypertensive treatment and

understanding the factors involved in its production. It is, of course, possible that a white-coat effect is involved, its precise quantification being prevented by the inability of clinic blood pressure measurements to coincide with the brief and variably timed peak blood pressure response to the doctor or the nurse. It is inconceivable, however, that other determinants of the difference, namely modulation of daily life blood pressure by behavioural and non-behavioural influences [40], do not participate. Their participation is indeed supported by the recent evidence that the office–daytime ambulatory blood pressure difference correlates inversely with daytime ambulatory blood pressure [41].

Finally, avoiding the erroneous identification of the white-coat effect with the clinic–daytime ambulatory blood pressure difference will allow one to focus on the real white-coat effect. It would be important to know the prevalence and magnitude of the pressor response to the doctor's or nurse's measurement of blood pressure under different hypertensive conditions. It would also be crucial to obtain more detailed information concerning whether the white-coat phenomenon occurs only at the first few visits or persists over time and reflects a generalized hyper-reactivity to emotional stimuli, leading to the repeated occurrence of brief blood pressure increases [42]. This might have some clinical significance because brief blood pressure increases in animals have been shown to precede established hypertension [43] and lead to organ damage. The recent availability of techniques for non-invasive beat-to-beat monitoring of blood pressure [44] may now make collection of this information possible in hypertensive patients. Even though these problems may not all be solved easily in the near future, clearing our minds of some of the ideologies that are beleaguering our thought might at least help us to be aware of these problems and to acknowledge the limitations of our present understanding.

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