PREVALENCE OF WHITE COAT EFFECT IN TREATED HYPERTENSIVE PATIENTS FROM CARAS SEVERIN COUNTY

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ABSTRACT

Objective: The objective of our study was to determine the prevalence of white-coat effect (i.e., difference between clinic and ambulatory blood pressure, or a normal ambulatory blood pressure) in a population of hypertensive patient with treated hypertension from Caras Severin county, a region in Romania, whose clinic blood pressure remained uncontrolled despite therapy and the incidence of cardiovascular events in this group for a period of follow-up 48±6 month. Material and methods: We included in our study 469 patients with treated essential hypertension, with one or more antihypertensive medications, who live in Caras Severin County, a region from Romania. They must have two or more clinic blood pressure readings of at least 140/90 mm Hg (either/or), 1 month apart but no greater than 200/120 mm Hg (either/or), were 18 years of age or more and had no target organ damage or left ventricular hypertrophy, as evidenced by echocardiography. Only 292 patients met the inclusion criteria. Results: 292 patients (100 men and 192 women; mean age, 55±12 years), all white, who met the inclusion criteria, were included in the study, from whom 88 patients (30.1%) had white coat effect. The median duration of follow-up was 48±6 months. The incidence of "white coat effect group" was great in women (p<0.001) and in smokers. The rate of cardiovascular events over an observation period of 48±6 month did not show any association with the white coat effect. Rezultate: Dintre cei 292 de pacienti inclusi efectul de halat alb a fost intalnit la 88 de pacienti (30,1%). Incidenta efectului de “halat alb” a fost mai mare la femei si la fumatori. Pe perioada urmaririi 27 de pacienti au prezentat evenimente cardiovasculare majore (11p cu accident vascular cerebral, 8p cu infart miocardic sau angina pectorala, 5p urgence hipertensive, 3p cu decompensarea fenomenelor de insuficienta cardiaica). Incidenta crescuta a evenimentelor cardiovasculare a fost asociata cu varsta avansata, sexul masculuin, fumatul, nivelul crescut al colesterolului seric si cu valorile crescute ale tensiunii arteriale la monitorizarea ambulatorie. Concluzii: In urma studiului consideram ca la pacientii hipertensivi care prezinta valori creschite ale tensiunii arteriale in ciuda tratamentului medicamentos administrat trebuie luata in considerare monitorizarea ambulatorie/24 h avand in vedere ca efectul de “halat alb” nu poate fi precis si cu acuratete. Nu a putut fi stabilita o asociere intre efectul de “halat alb” si incidenat evenimentelor cardiovasculare a pacientii urmariti. Cuvinte cheie: efectul de “halat alb”, judetul Caras Severin, monitorizarea ambulatorie a tensiunii arteriale 24 h, rata evenimetelor cardiovasculare

INTRODUCTION

The measurement of blood pressure (BP) in the physician’s office may trigger an alerting reaction and a rise in BP.1 In a study, Mancia et al have shown that the rise in intra-arterial BP during the visit is, on average, 27/14 mm Hg; it is maximal during the first 4 minutes of the visit, disappears within 10 minutes, and persists over several visits.2,3 The transient rise in BP from
before to during the visit is usually defined as “white-coat effect” or “white-coat phenomenon”, whereas the coexistence of persistently high office BP with normal ambulatory blood pressure measurement (ABPM), regardless of the extent of the white-coat effect, is often referred to as “white coat hypertension” (WCH).

WCH, which is also referred to as “office hypertension” or “isolated clinic hypertension” is generally defined as a persistently elevated office BP in the presence of a normal BP outside the office. From a practical standpoint, it is worth noting that the white-coat effect is a measure of BP change from before to during the visit, whereas white coat hypertension is an operative definition of clinically hypertensive subjects at a low potential risk because of apparently normal mean BP levels during daily life. A reliable estimate of the white-coat effect may be carried out through intra-arterial or noninvasive techniques, with beat-by-beat measurement of the BP rise from immediately before to during the visit. White coat hypertension is a common finding in hypertensive populations and in the population at large. The incidence has variably been recorded between 12% and 50%, depending on definitions. The importance of the condition lies in the relatively benign cardiovascular risk with which it is associated compared with established hypertension. The phenomenon of white coat effect or hypertension may reflect an abnormally vigorous sympathetic response to the environment of the measurement, especially the presence of the measuring nurse or physician. A document issued by the American Society of Hypertension had defined normalcy of ABP (i.e., average daytime BP <135 mm Hg systolic and <85 mm Hg diastolic). These values correspond to an office BP of 140/90 mm Hg. Depending on the upper limit set for mean daytime ambulatory blood pressure, the prevalence of white-coat response can range from 18% to 60% in populations with untreated hypertension. Most studies of white-coat response have been conducted in subjects with normal blood pressure and those with borderline hypertension who were not receiving drug treatment. Recently, however, Myers and Reeves have found that 70% to 73% of treated patients showed a white-coat response, and 31% to 32% exhibited a “marked white-coat effect”. Thus, white-coat response remains a consideration even among patients with treated hypertension.

The objective of our study was to determine the prevalence of white-coat effect (i.e., difference between clinic and ambulatory blood pressure, or a normal ambulatory blood pressure) in a population of hypertensive patient in our area, with treated hypertension whose clinic blood pressure remained uncontrolled despite therapy and the incidence of cardiovascular events in this group for a period of follow-up 48 ± 6 months.

**MATERIAL AND METHODS**

We have conducted our study in Caras Severin County, a small region in Romania, after having been approved by the Ethics Committee of University of Medicine and Pharmacy “Victor Babes”, Timisoara. All patients gave written informed consent. All decisions concerning the study design, the collection, analysis, and interpretation of the data, and the intellectual content of the manuscript were made independently, without the involvement of the pharmaceutical industry sponsors.

We included in our study 469 patients with treated essential hypertension, with one or more antihypertensive treatment. They must have had two or more clinic blood pressure readings of at least 140/90 mm Hg (either/or), one month apart, but no greater than 200/120 mm Hg (either/or), were 18 years of age or more and had no target organ damage or left ventricular hypertrophy, as evidenced by echocardiography. Criteria for exclusion were: suspicion of secondary hypertension, recent acute myocardial infarction, recent stroke (occurring within the previous three months), recent hospitalization for chronic heart failure, recent revascularization or planned cardiovascular intervention during the succeeding three months, chronic obstructive pulmonary disease, any coexisting diseases that might seriously reduce life expectancy, pregnancy, and no cooperation to undergo repeated ambulatory blood-pressure monitoring. Only 292 patients meet the inclusion criteria. All patients had a complete clinical workup at the beginning of the study to rule out secondary hypertension and to assess the presence of end-organ damage.

Information about traditional cardiovascular risk factors, history of cardiovascular events, current medications, demographic and anthropometric data were collected. At that time, a sample of venous blood was drawn to assess baseline factors and routine 12-lead electrocardiogram was obtained.

BP was measured with a mercury sphygmomanometer in a quiet environment, with the patient in a sitting position after 5 minutes of rest, following the recommendations of the British Hypertension Society. Systolic BP (SBP) and diastolic BP (DBP) (Korotkoff phase I and phase V, respectively) represented in each visit the mean of three different readings measured at 5-minute intervals. ABPM was performed with the use of an oscillometric monitor.
on a regular working day, during the normal intake of the usual antihypertensive treatment. Following the standard protocol, readings at intervals of 30 minutes between 08:00 and 20:00 and at intervals of 60 minutes between 20:00 and 08:00. Daytime ambulatory blood pressure was defined as that between 08:00 and 20:00, and nighttime ambulatory blood pressure as that between midnight and 06:00. The average of SBP, DBP, and mean blood pressure were calculated for every one of the periods.

Before starting the study, reliability of BP values measured with the monitor were checked against simultaneous measurements with a mercury sphygmomanometer. Differences of < 5 mm Hg were allowed. Those patients with recordings showing an error rate in > 25% of the total readings were excluded from the study.

Subjects were identified as exhibiting white-coat response if their mean daytime ambulatory systolic/diastolic blood pressure was 139/89 mm Hg (both) or lower, or if the systolic/diastolic pressure was at least 20/15 mm Hg (both) lowers than the clinic reading. All other subjects were considered to have sustained hypertension.

**Statistical analysis**

For each variable, values are expressed as mean±SD. Differences between groups were sought by using t test and X² for discontinuous variables. Event rates for new cardiovascular events, fatal plus nonfatal, during the time of follow-up are presented as the number of events per 100 patient-years, based on the ratio of the observed number of events to the total number of patient-years of exposure. A p value of less than 0.05 was considered significant for all analyses.

**RESULTS**

292 patients (100 men and 192 women; mean age, 55 ± 12 years), all white, who met the inclusion criteria, were included in the study, from whom 88 patients (30.1%) had white coat response.

The median duration of follow-up was 48 ± 6 months. Characteristics of the patients according to category of white coat response or sustained hypertension are summarized in Table 1.

Eighty-eight patients (30.1%) with treated hypertension from our subjects had “white coat effect”. The incidence of patients “with effect group” was greater in women (p<0.001) and in smokers (p<0.001) patients. During the follow-up, 27 patients had a cardiovascular event (11 with stroke, eight with coronary heart disease, myocardial infarction, or angina pectoris; three with progressive heart failure; five with hypertensive emergency). (Table 2)

The higher incidence of cardiovascular events was associated with older age, male sex, current smoking, high cholesterol level and higher value on ambulatory blood pressure measurement. The incidence of cardiovascular events in the group of patients with „white coat effect” was lower than in those with sustained hypertension (p<0.001).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>White coat effect (n=88)</th>
<th>Sustained hypertension (n=204)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>53±10 yr</td>
<td>56±9yr</td>
<td>NS</td>
</tr>
<tr>
<td>Female sex</td>
<td>62/88 (70.5%)</td>
<td>100/204 (49.01%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index</td>
<td>30 ± 5</td>
<td>29 ± 4</td>
<td>p=0.14</td>
</tr>
<tr>
<td>Current smoking</td>
<td>68%</td>
<td>40%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total serum cholesterol concentration (mg/dl)</td>
<td>240 ± 12</td>
<td>239 ± 8</td>
<td>p=0.24</td>
</tr>
<tr>
<td>Office BP (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>150 ± 8</td>
<td>151 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic</td>
<td>92 ± 4</td>
<td>93 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>ABPM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 H systolic</td>
<td>126 ± 7</td>
<td>147 ± 8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24 H diastolic</td>
<td>82 ± 8</td>
<td>93 ± 7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Daytime systolic</td>
<td>128 ± 7</td>
<td>152 ± 8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Daytime diastolic</td>
<td>84 ± 3</td>
<td>95 ± 5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nighttime systolic</td>
<td>118 ± 10</td>
<td>139 ± 6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nighttime diastolic</td>
<td>72 ± 7</td>
<td>84 ± 6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are means ± SD; the body-mass index is the weight in kilogram divided by square of height in meters.
The "white coat effect" and "white coat hypertension" differ in their definitions, pathophysiological mechanisms, and clinical significance. "White coat effect" is defined as a BP change from before to during the visit. "White coat hypertension" is an attempt to define a low-risk stratum of clinically hypertensive subjects with normal BP levels out of the medical setting, regardless of their rise in BP from before to during the visit. A white coat effect was found in total of 36% of our subjects, whose clinic blood pressure remained high, despite antihypertensives. Other investigators have reported prevalence rates of white-coat response of 21% to 73%. The variable definitions of "white coat effect" may be the explanation of this wide range of value.

Several studies have suggested that white-coat hypertension is benign and that antihypertensive therapy is not required, whereas other studies have suggested that it may not be innocent. In our study, the "white coat effect" was found to be associated with low incidences of cardiovascular events in our study population. In a study, Myers and Reeves found a significant difference in the prevalence of the response between women and men. However, other studies have not demonstrated any difference in prevalence among men and women. In our study, women were associated more than man with "white coat effect".

Several investigators have been used psychological testing, mental stress testing, exercise testing, or examination of levels of anger, anxiety or depression to test for blood pressure variances between patients with a white-coat response and those with sustained hypertension. We did not use such a test in our study. The rate of cardiovascular events over an observation period of 48±6 months did not show any association with the white coat effect.

### DISCUSSION

The "white coat effect" and "white coat hypertension" differ in their definitions, pathophysiological mechanisms, and clinical significance. "White coat effect" is defined as a BP change from before to during the visit. "White coat hypertension" is an attempt to define a low-risk stratum of clinically hypertensive subjects with normal BP levels out of the medical setting, regardless of their rise in BP from before to during the visit. A white coat effect was found in total of 36% of our subjects, whose clinic blood pressure remained high, despite antihypertensives. Other investigators have reported prevalence rates of white-coat response of 21% to 73%. The variable definitions of "white coat effect" may be the explanation of this wide range of value.

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### CONCLUSION

We consider that patients whose blood pressure remains high despite adequate antihypertensive therapy should be considered for 24-hour ambulatory blood pressure monitoring because a white-coat effect cannot be predicted reliably. The prevalence of white-coat effect is greater in female sex and in smokers. The rate of cardiovascular events over an observation period of 48±6 months did not show any association with the white coat effect.

### REFERENCES