Prevalence and predictors of white-coat response in patients with treated hypertension

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Abstract

Background: White-coat response, defined as higher office blood pressure readings than ambulatory readings, is common. Few studies have estimated its prevalence among subjects with treated hypertension, and almost none have defined its determinants. The objective of this study was to estimate the prevalence of white-coat response among subjects with treated hypertension and to determine whether the phenomenon could be predicted using clinical and psychometric data.

Methods: A total of 103 treated patients (55 men and 48 women) with uncontrolled hypertension who attended a hypertension outpatient clinic in Saskatoon between September 1993 and December 1995 were entered into the study. Patients had at least 2 clinic blood pressure readings of 140/90 mm Hg or higher, had no target organ damage or left ventricular hypertrophy, and had been prescribed 2 or more classes of antihypertensive drugs. Patients had blood pressure measured in the supine position in the clinic, were placed on 24-hour ambulatory blood pressure monitoring and then completed questionnaires before returning to the clinic. Patients were classified as exhibiting a white-coat response if their mean daytime ambulatory systolic/diastolic blood pressure was 139/89 mm Hg (both) or less, or if the systolic/diastolic pressure was at least 20/15 mm Hg (both) lower than the clinic reading.

Results: Eleven men (20%, 95% confidence interval [CI] 10%–33%) and 26 women (54%, 95% CI 39%–69%) showed white-coat response. Logistic regression modelling showed that determinants such as stress had significantly different effects among men and women. Separate models were therefore created for men and women. For women, perceived level of stress was the most important predictor of white-coat response (odds ratio [OR] per unit 7.0, 95% CI 1.3–36.0), followed by time since diagnosis. For men, depression was a weak predictor, with higher depression scores predicting sustained hypertension (OR per unit 1.2, 95% CI 1.01–1.5).

Interpretation: Sex is an important factor in white-coat response. Attempts to predict white-coat response from psychometric variables should take sex differences into account. Clinical variables were not effective as predictors of white-coat response.

In some people blood pressure measured in the office is substantially higher than their average ambulatory blood pressure.[1] This "white-coat response" may persist on subsequent visits, which suggests that it is a conditioned response that is habitual and specific to the clinical situation.[2,3] 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.[4]

Several investigators have attempted to identify clinical, psychological and demographic predictors of white-coat response, but findings have been conflicting or nonsignificant.[3,5–8] Female sex was a predictor of the response in one study.[7] Other variables examined to date have not been strong predictors.

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[9,10] 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 purpose of our study was twofold: to determine the prevalence of white-coat response (i.e., difference between clinic and ambulatory blood pressure, or a normal ambulatory blood pressure) in a population of subjects with treated hypertension whose clinic blood pressure remained uncontrolled despite therapy; and to determine whether selected psychological factors or clinical variables are predictors of white-coat response.

Methods

The University of Saskatchewan Advisory Committee on Ethics in Human Experimentation approved the study.

We considered consecutive patients with essential hypertension who attended the Hypertension Outpatient Clinic at the Royal University Hospital, Saskatoon, between September 1993 and December 1995 and whose clinic blood pressure remained uncontrolled despite being prescribed at least 2 different classes of antihypertensive medications. The same nurse recorded the clinic blood pressure with subjects in the supine position using Canadian Hypertension Society guidelines.[11] Study subjects had 2 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. The rate of compliance, estimated by pill counts, was 80% or more. Over 90% of eligible patients participated.

To detect a difference of 0.5 units in the score on the Perceived Stress Level questionnaire between subjects with a white-coat response and those with sustained hypertension, and assuming that the standard deviation of the data was 0.6 units (estimated from our previous study[12,13]), we needed to enter 31 subjects in either group. We assumed that about one-third of the subjects would meet the criteria for white-coat response. Therefore, we planned to study 100 patients.

Ambulatory blood pressure monitoring was done on a typical weekday with the SpaceLabs 90207 system (SpaceLabs Medical Products, Ltd., Mississauga, Ont.). Patients were encouraged to pursue their usual activities. Ambulatory monitors were attached at the completion of the clinic visit, calibrated and removed after 24 hours. Blood pressure was recorded every 20 minutes from 8 am to 10 pm and every 60 minutes from 10 pm to 8 am. Recordings were judged adequate if there were at least 25 usable blood pressure readings over a minimum of 8 hours, excluding sleeping hours. All recordings met these criteria.

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) lower than the clinic reading. All other subjects were considered to have sustained hypertension.

After beginning ambulatory monitoring, patients completed several questionnaires based on studies that explored the relation between white-coat response and factors such as stress, emotional reactivity, hostility and anger. The following psychometric tests were completed by the patients at their own pace: the Center for Epidemiologic Studies Depression (CES-D) Scale,[14] a 20-item self-report scale designed to measure symptoms of depression in the general population; the Cook–Medley Hostility Scale,[15] a 50-item true–false questionnaire that assesses the propensity to experience anger and hostility; the State–Trait Anxiety Inventory,[16] a 40-item questionnaire that measures anxiety at the time of assessment (state anxiety) and the general tendency to experience anxiety (trait anxiety); a 9-item Emotional Reactivity Scale,[17] designed to assess the tendency to become emotionally aroused; a 14-item Life Events Scale,[18] designed to measure actual life stressors; a 14-item Perceived Stress Scale;[18] a 13-item Life Concerns Scale used in the Saskatchewan Heart Health Study;[19] and the Perceived Stress Level questionnaire,[12,13] designed to measure perceived stress during clinical assessment. Scales with established reliability (Cronbach's α 0.80 or greater) include the CES-D Scale, the Cook–Medley Hostility Scale, the Emotional Reactivity Scale, the Perceived Stress Scale and the State–Trait Anxiety Inventory.[14–17,20] In our study the Cronbach's α values were as follows: CES-D scale 0.89, Cook–Medley Hostility Scale 0.84, State–Trait Anxiety Inventory 0.92, Emotional Reactivity Scale 0.90, Life Events Scale 0.51, Life Concerns Scale 0.75, Perceived Stress Scale 0.86 and Perceived Stress Level scale 0.63.

In a bivariate analysis, we used 2-tailed *t*-tests to test for significant differences between means for continuous variables and the χ^2 test to test for significant differences for categoric variables. A p value of less than 0.05 was considered significant for all analyses. We used logistic regression to determine whether specific psychological, clinical or demographic variables predict whether treated patients with uncontrolled hypertension had a white-coat response or sustained hypertension.

Results

A total of 103 patients (55 men and 48 women) were entered into the study, of whom 37 (36%) met the criteria for white-coat response. Eleven of the men (20%, 95% confidence interval [CI] 10%–33%) and 26 of the women (54%, 95% CI 39%–69%) had a white-coat response.

Table 1 shows the means of the clinical, demographic and psychologic determinants for the subjects with a white-coat response and those with sustained hypertension. Of the variables examined, only female sex ($p < 0.001$), time (in months) since the diagnosis of hypertension ($p < 0.05$) and clinic systolic blood pressure ($p < 0.05$) were significantly different between the 2 groups.

Table 2 shows the means of the clinical, demographic and psychometric variables according to sex and diagnosis. The effect of stress in relation to the diagnosis (white-coat response or sustained hypertension) was different between men and women. Women with a white-coat response had significantly higher stress scores on the Perceived Stress Level questionnaire than women with sustained hypertension ($p < 0.05$). Conversely, men exhibiting a white-coat response scored lower on the Perceived Stress Scale and the CES-D Scale than men with sustained hypertension ($p < 0.05$).

A difference in time since the diagnosis of hypertension between subjects with a white-coat response and those with sustained hypertension was evident only among women. The time since diagnosis was significantly longer for those in the former group than those in the latter group (273 v. 198 months) ($p < 0.05$). The mean clinic systolic blood

pressure for men was lower in the white-coat response group than in the sustained hypertension group ($p < 0.05$).

The psychometric scores, drug equivalents, sex and time since diagnosis of hypertension were entered into a logistic regression model to determine a prediction equation for white-coat response. Missing scores for some of the psychometric tests reduced the number of subjects to 90. We estimated separate logistic models for men and women since the effect of stress was found to be significantly different among the 2 sexes.

Perceived level of stress was a significant predictor of white-coat response in women: a woman with a higher score on the Perceived Stress Level questionnaire was more likely to exhibit this response (odds ratio [OR] per unit 7.0, 95% CI 1.3–36.0) (Table 3). Women with a long duration since the diagnosis of hypertension were more likely to exhibit a white-coat response than women with a short duration since diagnosis (OR per year 1.1, 95% CI 1.0–1.2). Using these 2 variables as a diagnostic test for white-coat response yielded a sensitivity of 77% and a specificity of 65%.

For men, depression and clinic systolic blood pressure were entered as weak predictors of white-coat response (Table 3). Men who scored higher on the CES-D Scale were more likely to have sustained hypertension than to exhibit a white-coat response (OR per unit 1.2, 95% CI 1.0–1.5). Men whose clinic systolic blood pressure was higher were also slightly more likely to have sustained hypertension than to manifest a white-coat response (OR per mm Hg 1.1, 95% CI 1.0–1.2). Using these 2 variables as a diagnostic test for white-coat response yielded a sensitivity of 55% and a specificity of 92%.

Interpretation

A total of 36% of our subjects whose clinic blood pressure remained high despite antihypertensive drug treatment were found to exhibit a white-coat response. Other investigators have reported prevalence rates of white-coat response of 21% to 73%.[9,10,21,22] This wide range likely reflects differences in the criteria used to define white-coat response.

Several studies have suggested that white-coat hypertension is benign and that antihypertensive therapy is not required,[23–25] whereas other studies have suggested that it may not be innocent.[26–32] However, given that some normotensive subjects have ambulatory readings in the range of those seen in our white-coat group,[33] the risk of complications due to hypertension in our subjects with a white-coat response should not be great.

The sex difference in white-coat response is striking. Myers and Reeves[10] found a significant difference in the prevalence of the response between women and men. This difference persisted even after the definition of white-coat response was changed to a difference between clinic and ambulatory blood pressure readings of at least 40/20 mm Hg. However, other studies have not demonstrated any difference in prevalence among men and women.[9,21] In our sample, women were more than twice as likely as men to exhibit a white-coat response.

The reason for the sex difference is unclear. It may be related to a difference in perception of the purpose of the visit. MacDonald and colleagues[34] found a significant difference between diastolic blood pressure readings obtained in a situation perceived to be evaluative versus a nonevaluative situation. In any event, sex differences in white-coat response should be considered in future

Table 1: Means of clinical variables and psychometric test scores by diagnosis of white-coat response or sustained hypertension in 103 subjects with uncontrolled hypertension

Variable	Group: White-coat response *n = 37*	Group: Sustained hypertension *n = 66*
Sex, no. of subjects†		
Male	11 (20%, 95% CI 10–33)	44
Female	26 (54%, 95% CI 39–69)	22
	Mean (and 95% CI)	
Age, yr	60 (56.6–63.4)	59 (56.0–61.8)
Body mass index	28 (26.1–30.0)	30 (28.6–31.1)
Time since diagnosis of hypertension, mo‡	271 (216.8–324.9)	202 (170.3–233.6)
Drug equivalents*	2.5 (2.3–2.7)	2.6 (2.4–2.7)
Clinic systolic blood pressure (SBP), mm Hg‡	148 (141.5–154.5)	157 (152.9–160.6)
Clinic diastolic blood pressure (DBP), mm Hg	91 (88.4–93.7)	93 (90.5–94.7)
Clinic heart rate, beats/min	72 (68.3–75.7)	73 (70.7–76.3)
Psychometric test scores		
State–Trait Anxiety Inventory (STAI) – state	33 (29.7–37.0)	36 (33.1–38.5)
STAI – trait	36 (32.6–40.0)	37 (34.4–39.5)
Perceived Stress Scale	19 (16.4–21.5)	20 (18.2–22.1)
Emotional Reactivity Scale	28 (25.3–30.5)	26 (23.5–27.5)
Cook–Medley Hostility Scale (CMHS)	16 (13.7–18.4)	18 (16.1–19.9)
Center for Epidemiologic Studies (CES-D) Scale	8 (5.3–11.6)	11 (9.2–13.6)
Life Concerns Scale	17 (15.1–18.9)	19 (16.8–20.8)
Life Events Scale	1.4 (0.9–1.9)	1.5 (1.1–1.8)
Perceived Stress Level (PSL) questionnaire	2.3 (2.1–2.5)	2.2 (2.0–2.4)

Note: CI = confidence interval.
*Number of different classes of antihypertensive drugs being taken.
†$p < 0.001$.
‡$p < 0.05$.

studies involving patients in whom hypertension is diagnosed on the basis of high clinic readings.[10] Use of qualitative methods would be appropriate to explore sex differences from the patients' perspective.

Several investigators have 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.[6–8,35] In our study, a lower depression score was predictive of white-coat response for men. For women, a higher perceived level of stress was predictive of such a response. Clinically, however, these differences are not enough to substitute (as diagnostic tools) for ambulatory blood pressure monitoring.

In an earlier study we found that a high perceived level of stress, as measured by the Perceived Stress Level questionnaire, was predictive of having uncontrolled versus controlled hypertension.[12] In the current study we used a second scale measuring perceived stress, the Perceived Stress Scale,[18] to validate our findings. Unexpectedly, the stratified analysis results for the 2 measures were conflicting. Men with sustained hypertension had a significantly higher perceived stress score, as measured by the Perceived Stress Scale, than men with a white-coat response, whereas women with a white-coat response had a significantly higher level of perceived stress, as measured by the Perceived Stress Level questionnaire, than women with sustained hypertension. Thus, there may be a differential response among women and men to the various scales used to measure perceived stress. It appears that women exhibit a different stress response than men to clinic visits that affects their blood pressure measurements. Perception of stress is an area that requires further study. From a practical perspective, all patients whose blood pressure remains high despite adequate antihypertensive therapy should be considered for 24-hour ambulatory blood pressure monitoring because a white-coat response cannot be predicted reliably.

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Competing interests: None declared.

Table 3: Logistic regression model of selected variables for women (*n* = 42) and for men (*n* = 48)

Sex; variable	Odds ratio (and 95% CI)
Female	
Time since diagnosis of hypertension	1.1 (1.0–1.2)
PSL questionnaire	7.0 (1.3–36.0)
Male	
CES-D Scale	1.2 (1.01–1.5)
Clinic SBP	1.1 (1.02–1.2)

Table 2: Means of clinical variables and psychometric test scores by sex and diagnosis

	Sex; mean (and 95% CI)			
	Male		Female	
Variable	White-coat response *n = 11*	Sustained hypertension *n = 44*	White-coat response *n = 26*	Sustained hypertension *n = 22*
Clinical and demographic variables				
Age, yr	56 (52.0–59.6)	59 (55.0–62.2)	62 (57.2–66.3)	60 (54.1–65.0)
Body mass index	28 (25.1–31.0)	30 (29.1–31.0)	28 (25.4–30.2)	29 (26.1–31.5)
Time since diagnosis of hypertension, mo	266 (132.1–400.6)	204 (162.0–246.3)	273 (213.6–332)	198 (148.2–246.8)*
Clinic SBP, mm Hg	141 (131.4–151.5)	155 (150.6–160.1)*	151 (142.5–159.2)	159 (152.4–166.4)
Clinic DBP, mm Hg	91 (87–95)	93 (90.5–95.8)	91 (87.5–94.7)	91 (87.7–95.2)
Clinic heart rate, beats/min	68 (63.1–73.3)	74 (70.5–77.4)	74 (68.8–78.4)	72 (67.2–77.7)
Drug equivalents	2.5 (2.2–2.9)	2.6 (2.4–2.8)	2.5 (2.2–2.7)	2.6 (2.3–2.9)
Psychometric test scores				
STAI – state	32 (24.8–38.7)	36 (32.8–39.9)	34 (29.5–38.7)	35 (30.4–39.0)
STAI – trait	34 (28.2–40.4)	38 (34.5–41.6)	37 (32.4–41.9)	35 (31.7–38.2)
Perceived Stress Scale	16 (12.5–19.3)	21 (18.6–23.2)*	20 (16.9–23.6)	19 (15.8–22.3)
Emotional Reactivity Scale	26 (21.7–30.1)	26 (23.3–28.0)	29 (25.4–32.1)	25 (21.3–29.1)
CMHS	16 (11.9–19.3)	19 (17.1–21.2)	16 (13.1–19.4)	16 (11.4–19.6)
CES-D Scale	5 (1.9–8.6)	12 (9.4–15.2)*	10 (5.6–14.1)	10 (6.4–12.7)
Life Concerns Scale	18 (13.4–21.9)	20 (17.5–22.5)	17 (14.5–18.9)	16 (12.8–19.5)
PSL questionnaire	2.1 (1.9–2.3)	2.3 (2.1–2.6)	2.4 (2.1–2.6)	2.0 (1.7–2.2)*
Life Events Scale	1.1 (0.0–2.2)	1.2 (0.8–1.6)	1.5 (0.9–2.1)	2.0 (1.1–2.8)

*$p < 0.05$.

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