Original Article

A Study of the White-Coat Phenomenon in Patients with Primary Hypertension

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The objective of this study was to evaluate whether the discrepancy between clinic and home blood pressure (BP) in hypertensive subjects would disappear or diminish in magnitude if the BP measurement was taken under controlled conditions differing only with respect to location (clinic vs. home). Three hundred and sixty-seven patients aged 34–84 years with primary hypertension were enrolled. All of the patients or their spouses were taught to measure BP correctly with their own sphygmomanometer at home. The home BP value (HBP) was calculated as the average of 45 readings over 15 days. On days 6, 12, and 18 of the measurement period, rather than measuring their BP at home, patients and their spouses were asked to visit the hospital at the usual time of their BP measurement and to bring their own sphygmomanometer. The clinic BP value (CBP) was calculated as the average of the 9 readings taken on these visits by the patients or their spouses. The “white-coat phenomenon” (WCP) was considered to be present when the difference between the CBP and HBP was greater than 20/10 mmHg. The mean reading of home systolic/diastolic BP was 134.7/79.1 mmHg and the mean reading of clinic systolic/diastolic BP was 149.8/86.4 mmHg. In the total subject group, the prevalence rate of WCP was 31%–35% if the WCP was defined as ΔBP (CBP – HBP) ≥ 20 mmHg/10 mmHg. In conclusion, ruling out the influence of different factors, including time of day, the sphygmomanometer, the individual taking the BP measurement, the climate, and the patients’ health or mood, the WCP was still found to exist to a statistically significant degree. This study indicated that teaching patients to measure their own BP at home is an effective procedure to obtain a more accurate result of their BP level. It also helped to involve the patients more actively in controlling their hypertension. (*Hypertens Res* 2008; 31: 37–41)

Key Words: hypertensive, white-coat phenomenon, home blood pressure measurement

Introduction

The factors contributing to the disparities between home and clinic blood pressure (BP) readings have been explored by Ayman and Goldshine (1, 2), but the underlying reasons for the phenomenon have remained unclear. Mancia *et al.* (3)

used continuous intra-arterial recording of pressure in hospitalized patients and found that, as the physician approached the patients and placed the BP cuff on their arms, there was an immediate, dramatic, and clinically significant elevation in BP, which persisted throughout the entire procedure. The phenomenon is now known as the white-coat effect (WCE) or white-coat phenomenon (WCP). Most studies of WCE have

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Table 1. Characteristics of the 367 Hypertensive Patients

Item	Total (<i>n</i> =367)	Δ SBP $\geq$ 20 mmHg (<i>n</i> =116)	Δ SBP<20 mmHg (<i>n</i> =251)
Men/women	129/238	40/76	89/162
Women (%)	64.8	65.8	64.8
Age (years)	63.72 $\pm$ 9.48	63.00 $\pm$ 9.69	64.05 $\pm$ 9.34
Age of men (years)	64.78 $\pm$ 10.44	64.54 $\pm$ 11.04	64.89 $\pm$ 10.31
Age of women (years)	63.15 $\pm$ 8.81	62.21 $\pm$ 8.89	63.59 $\pm$ 8.76
Course of hypertension (years)	8, 3–50	8, 3–50	8, 3–44
Body mass index (kg/m ²)	25.17 $\pm$ 3.54	24.47 $\pm$ 3.59	25.49 $\pm$ 3.47
Blood lipids			
TC (mmol/L)	5.52 $\pm$ 1.20	5.68 $\pm$ 1.08	5.46 $\pm$ 1.24
TG (mmol/L)	1.82 $\pm$ 1.10	1.73 $\pm$ 0.85	1.86 $\pm$ 1.18
HDL-C (mmol/L)	1.39 $\pm$ 0.39	1.39 $\pm$ 0.33	1.40 $\pm$ 0.41
LDL-C (mmol/L)	3.18 $\pm$ 1.00	3.44 $\pm$ 0.98	3.07 $\pm$ 0.99
Apo-A (mmol/L)	1.38 $\pm$ 0.28	1.39 $\pm$ 0.27	1.38 $\pm$ 0.29
Apo-B (mmol/L)	1.04 $\pm$ 0.57	1.10 $\pm$ 0.53	1.01 $\pm$ 0.59
Blood glucose	5.78 $\pm$ 1.46	5.78 $\pm$ 1.76	5.78 $\pm$ 1.30
Echocardiogram			
IVS (mm)	11.00 $\pm$ 1.90	10.89 $\pm$ 1.57	11.06 $\pm$ 2.04
LVPW (mm)	10.54 $\pm$ 1.47	10.36 $\pm$ 1.20	10.63 $\pm$ 1.54
LA (mm)	33.12 $\pm$ 7.81	32.72 $\pm$ 8.51	33.31 $\pm$ 7.50
LV (mm)	43.36 $\pm$ 7.11	43.26 $\pm$ 10.00	43.41 $\pm$ 5.28
LVEF (%)	56.77 $\pm$ 5.14	57.52 $\pm$ 5.81	56.39 $\pm$ 4.80
Occupation (%)			
Teacher and scientist	41.96	36.90	46.20
Cadre	23.34	25.20	21.96
Worker	11.04	12.60	10.00
Others	23.66	25.20	21.90
Medicine taken (%)			
Diuretic	44.14	34.20	48.80
β -Blocker	42.51	39.30	44.00
CCB	54.22	44.40	58.80
ACEI	11.17	14.50	9.60
ARB	3.00	1.70	3.60

Data are expressed as mean $\pm$ SD or mean, range. TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Apo-A(B), apolipoprotein-A(B); IVS, interventricular septum; LVPW, left ventricular posterior wall thickness; LV, left ventricle; LVEF, left ventricular ejection fraction; CCB, calcium-channel blocker; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker.

used ambulatory blood pressure monitoring (ABPM) in normotensive subjects. In the present study, however, we focused on aged hypertensive patients receiving antihypertension treatment, since an “abnormal” rise in clinic BP (CBP) in treated hypertensive patients can lead to a misdiagnosis of refractory or resistant hypertension (4). In such cases, clinicians might increase the dosage of antihypertensive drugs or implement further unnecessary medication, resulting in adverse side effects and added expense. Our aims were thus to evaluate the discrepancy between home BP (HBP) and CBP in hypertensive patients on antihypertensive treatment, and to clarify the magnitude of WCP in hypertensive subjects and its association with age, gender, occupation, and medication. We

planned to do this by repeatedly taking BP at the same hour, with the same sphygmomanometer, and by the same person, but at two different locations (the home and clinic).

Methods

Patients

A total of 367 patients from the outpatient hypertensive clinic were enrolled. All patients had been diagnosed with primary hypertension, had been receiving antihypertensive treatment for a long period of time (ranging from 3 to 50 years), and had a stabilized BP with no change in recent medication. Patients

Table 2. WCP Components in Both Genders

Age (years)	Men			Women		
	Subjects (n (%))	Δ SBP $\geq$ 20 mmHg (n (%))	Δ DBP $\geq$ 10 mmHg (n (%))	Subjects (n (%))	Δ SBP $\geq$ 20 mmHg (n (%))	Δ DBP $\geq$ 10 mmHg (n (%))
<40	2 (1.55)	0 (0.00)	1 (50.00)	2 (0.84)	1 (50.00)	1 (50.00)
40–49	12 (9.30)	5 (41.67)	5 (41.67)	16 (6.72)	6 (37.50)	7 (43.75)
50–59	17 (13.18)	6 (35.29)	6 (35.29)	56 (23.53)	20 (35.71)	24 (42.86)
60–69	56 (43.41)	19 (33.93)	20 (35.71)	106 (44.54)	36 (33.96)	35 (33.02)
70–79	34 (26.36)	5 (14.71)	8 (23.53)	48 (20.17)	12 (25.00)	15 (31.25)
$\geq$ 80	8 (6.20)	5 (62.50)	4 (50.00)	10 (4.20)	1 (10.00)	2 (20.00)
Total	129 (100)	40 (31.01)	44 (34.11)	238 (100)	76 (31.93)	84 (35.29)

WCP, white-coat phenomenon; SBP, systolic blood pressure; DBP, diastolic blood pressure.

had their own sphygmomanometers (a standard mercury sphygmomanometer, YuYue-GB 3053-93, 3053-1993, YuYue, SuZhou, China; an upper-arm cuff semiautomatic, OMRON-HEM-4011 C, HEM-446 C, Omron Healthcare Co., Ltd., Kyoto, Japan; or a fully automatic device, OMRON-HEM-746 C, Omron Healthcare Co., Ltd.) and were capable of measuring their BP regularly. All patients were taught to measure BP correctly with their own sphygmomanometer at home and were subjected to clinical evaluation, including CBP and pulse rate, echocardiogram examination, electrocardiogram, blood lipids, blood glucose and body mass index (BMI). Verbal informed consent was obtained from all patients and their spouses. Information on the characteristics of the patients was collected by a physician, and included their histories of hypertension and antihypertensive medications, and their occupations.

Daily Schedule of BP Measurement over the 18-Day Measurement Period

Day 1–5: BP measured at home; Day 6: BP measured at the clinic; Day 7–11: BP measured at home; Day 12: BP measured at the clinic; Day 13–17: BP measured at home; Day 18: BP measured at the clinic.

All the measurements were taken at the same hour of the day by the same person with the same sphygmomanometer.

HBP Measurement

For HBP measurement, patients or their spouses were instructed to measure the patient's BP once daily using triplicate readings for 15 days. The readings were taken at home using their own sphygmomanometer after an at least 30-min rest with the patient in a comfortable sitting position. The pulse rate was measured for 30 s after the BP was taken. The average of 45 readings was defined as the HBP.

CBP Measurement

All patients were scheduled three visits for the measurement

of BP in the outpatient clinic at the same hour when they measured their BP at home (even in the evening or early morning). The patients or their spouses measured their BP with their own device under similar conditions as at home, using triplicate readings collected after an at least 30-min rest. The average of these 9 office readings was defined as the CBP.

Definition of WCP

We arbitrarily defined WCP as a difference between clinic systolic BP (SBP) and home SBP of ≥ 20 mmHg (Δ SBP ≥ 20 mmHg) or a difference between clinic diastolic BP (DBP) and home DBP of ≥ 10 mmHg (Δ DBP ≥ 10 mmHg).

Statistical Analysis

The normally distributed data were presented as the means $\pm$ SD. The non-normally distributed data were presented as the median and range, and the categorical data were presented as rates. For statistical comparisons, χ^2 test, *t*-test and nonparametric test were used if appropriate. Relationships between two groups were assessed by Pearson correlation. Values of $p < 0.05$ were considered to indicate statistical significance. All analyses were conducted using the SPSS package (version 11.5).

This protocol was approved by the Research and Development Office of Dalian Medical University.

Results

A total of 367 primary hypertensive patients from the outpatient clinic at the Second Affiliated Hospital of Dalian Medical University were enrolled. Table 1 shows the clinical characteristics of the enrolled patients. The average age was 63.72 ± 9.48 years (range: 34–84 years), or 64.78 ± 10.44 years for the 129 males and 63.15 ± 8.81 years for the 238 females. The duration of diagnosed hypertension showed a non-normal distribution, with the median being 8 years (range: 3–50 years), and almost half of the subjects (46.32%) had had hypertension for more than 10 years. The mean BMI

Table 3. The SBP and Pulse Rate in Hypertensive Subjects (Mean±SD)

Item	Clinic SBP (mmHg)	Home SBP (mmHg)	Clinic pulse (bpm)	Home pulse (bpm)
Total subjects (<i>n</i> =367)	149.8±16.4*	134.7±13.9	69.6±9.3*	68.7±8.3
ΔSBP≥20 mmHg (<i>n</i> =116)	154.7±18.0*	135.2±14.3	70.4±8.1*	68.4±6.8
ΔSBP<20 mmHg (<i>n</i> =251)	147.8±15.3* [†]	134.5±13.8	69.4±9.8*	68.9±8.9

**p*<0.001 vs. home measurement. [†]*p*<0.01 vs. ΔSBP≥20 mmHg group in clinic. SBP, systolic blood pressure.

Table 4. The DBP and Pulse Rate in Hypertensive Subjects (Mean±SD)

Item	Clinic DBP (mmHg)	Home DBP (mmHg)	Clinic pulse (bpm)	Home pulse (bpm)
Total subjects (<i>n</i> =367)	86.4±10.5*	79.1±10.2	79.6±9.3*	68.7±8.3
ΔDBP≥10 mmHg (<i>n</i> =128)	87.8±11.1*	78.7±10.2	70.5±8.7*	68.7±8.1
ΔDBP<10 mmHg (<i>n</i> =239)	85.8±10.3*	79.2±10.3	69.2±9.6*	68.7±8.5

**p*<0.001 vs. home measurement. There was no significant difference between group ΔDBP≥10 mmHg and group ΔDBP<10 mmHg, *p*>0.05. DBP, diastolic blood pressure.

was 25.2±3.5 kg/m², with the value being 25.0–29.9 kg/m² in 58.58% of patients, and ≥30 kg/m² in 8.72% of patients. Seventy-four point sixty-six percent of the patients were taking two drugs, and 25.34% were taking a single drug. A calcium channel blocker (CCB) was used in most cases (54.22% of the patients receiving combination therapy and 41.94% of those receiving monotherapy were taking a CCB).

Table 2 shows the age and gender of all subjects. There was no significant difference in the percentage of patients exhibiting WCP by gender.

The prevalences of WCP are shown in Tables 3 and 4. CBP was significantly higher than HBP (149.8±16.4/86.4±10.5 vs. 134.7±13.9/79.1±10.2 mmHg; *p*<0.001). There was no significant difference in HBP between the group with ΔSBP≥20 mmHg and that with ΔSBP<20 mmHg, but the CBP was significantly different between these groups (154.7±18.0 vs. 147.8±15.3 mmHg; *p*<0.01). There was no significant difference in DBP between the group with ΔDBP≥10 mmHg and the group with ΔDBP<10 mmHg (*p*>0.05). Among the total patients group, patients with “systolic WCP” accounted for 31.61%, those with “diastolic WCP” accounted for 34.88%, and those with both systolic and diastolic WCP accounted for 21.80%.

Discussion

Measurement of HBP has various advantages over conventional clinical measurement, such as a higher reproducibility, better representation of the usual BP profile of the patient, greater correlation with target organ damage, and greater ability to predict morbidity (5).

Possible Impact Factors of WCP

It has been reported that WCP appears to be the result of generalized anxiety and generalized hyperreactivity of the autonomic nervous system (6, 7), and that it is highly stimulus-specific (8). A study by Murata *et al.* (7) indicated that WCP may reflect a decrease in endothelial function and the presence of initial-stage atherosclerosis. However, Helvacı *et al.* (9) found a high prevalence of WCP even in the early decades. Gerin *et al.* (10) also suggested that improved methods of measuring BP in the clinical setting are unlikely to resolve the confounding influence of WCP. A report by Den Hond *et al.* (11) lent support to the idea that conditioning is the mechanism responsible for the development of the WCP. A unique design of our study was that it kept the CBP measurement at the same hour as the HBP measurement (whether early morning, daytime or evening) and used measurement with the same sphygmomanometer (brought to the clinic by the patients) and by the same person (the patients or their spouses) as at home; thus the only difference was the location (home vs. clinic). The observed BP elevation at the clinic did not disappear or decrease in magnitude over the nearly 1-month period of the study. Thus the results suggested that the elevation was not caused by an interaction between the patient and the “white coat,” or physician. Instead, it was likely caused by the change of environment from home to clinic. This meant that repeated visits to the same physician and the same clinic did not result in a reduction in WCP as a consequence of familiarization. These observations strongly implied that psychological rather than physiological variables are responsible for the differences in pressure readings.

Possible Outcome of WCP

Nearly one-third of our patients had HBP measurements of 130–140/70–80 mmHg and CBP measurements of 150–160/80–90 mmHg. Before the concept of the WCP was explained to them, these patients thought their sphygmomanometers were not accurate or that their BP could not be controlled. The most frequent and worst outcome of hypertension in China is stroke. The evidence that HBP is effective at predicting stroke is derived from a population-based prospective study in Japan (the Ohasama study (12)). The authors demonstrated that HBP provided more useful prognostic information on stroke than CBP and increased the predictive power of stroke guidelines. In the same study, HBP measurements also more accurately and reliably reflected target organ damage and prognosis of cardiovascular disease than conventional BP measurements (13). Erdogan *et al.* (14) found that coronary flow reserve was not different between a group exhibiting WCP and a control group. And Tseng *et al.* (15) found that Taiwanese exhibiting WCP showed a low frequency of target organ damage. The prognosis of patients with WCP is similar to that of true normotensives (16, 17). If our conceptualization is reasonable, then 31% of the 160 million hypertensive subjects in China (18) might currently be overtreated.

The appropriateness of HBP measurement to guide antihypertensive treatment has been tested in a single large-scale randomized trial known as the THOP (Treatment of Hypertension Based on Home or Office Blood Pressure) trial (19). The THOP trial showed that antihypertensive treatment based on home instead of office BP measurements led to less intensive drug treatment with no differences in left ventricular mass or general well-being. Our results indicate that WCP remains after controlling for the time of day, the sphygmomanometer, the person conducting the measurement, the climate, and the patients' health and mood. We suggest that teaching subjects to measure their own BP at home would help patients be more actively involved in controlling their hypertension.

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