White Coat Hypertension Is Associated with a Greater All-cause Mortality

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Background: Prognostic significance of white coat hypertension (WCH) remains controversial and most of the studies have just focused on the progression to hypertension (HT) or whether or not it already causes target organ damage. Methods: We studied consecutive adults and eldelies with sustained normotension (NT), WCH, and HT applying to the Internal Medicine Polyclinic. A 10 day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, and a 24 hr ambulatory blood pressure monitoring (ABPM) was performed just for the cases with higher office and/or HBP measurements. Prevalences of smoking, overweight, obesity, impaired glucose tolerance, type II diabetes mellitus, hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia were calculated in each group and results were compared in between. Comparison of proportions was used as the statistical analysis method. Results: The study totally included 169 cases, 54 with sustained NT, 66 with WCH, and 49 with HT. The 115 patients with WCH and HT were both diagnosed via HBP and ABPM, and no difference was observed between the two methods for the diagnosis of WCH and masked or obvious HT. Except the smoking and overweight, almost all of the above disorders showed a stepwise and significant progression in frequencies from sustained NT toward WCH and HT. Conclusions: WCH should preferentially be accepted as a disorder associated with a greater all-cause mortality, rather than a predisposing factor of HT or atherosclerosis alone, and its management should be focused on the above comorbid disorders.

Key words —— sustained normotension, white coat hypertension, hypertension

INTRODUCTION

It is already known that hypertension (HT) increases risks of major cardiovascular events (myocardial infarction and stroke) and renal failure. Beside that HT is usually associated with obesity, impaired glucose tolerance (IGT) or type II diabetes mellitus (DM), and dyslipidemia like disorders. But diagnosis and management of HT is difficult due to the fact that blood pressure (BP) greatly varies depending on physical and mental stresses. For example, white coat hypertension (WCH) is a well-known clinical entity defined by persistently elevated BP in the doctor's office, whereas BP in other conditions is normal. Prognostic significance of WCH remains controversial and there are various reports about it.[1, 2] But most of the already per-formed studies of WCH have just focused on the progression to HT in time[3, 4] or whether or not it already causes target organ damage.[5] As a different topic, we tried to understand whether or not WCH is already associated with smoking, overweight, obesity, IGT or type II DM, and dyslipidemia like disorders as in HT.

MATERIALS AND METHODS

We took consecutive adults and elders with sustained normotension (NT), WCH, and HT applying to the Internal Medicine Polyclinic of the Dumlupinar University between January and July 2006. Their medical histories including smoking habit, DM, dyslipidemia, and already used medications were learnt and a routine check up procedure including fasting plasma glucose (FPG), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol

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(LDL-C), and urinalysis was performed. Current smokers and cases with a history of at least 5 year/pack were accepted as smokers. Patients on treatment for HT or with clinic or laboratory evidence of heart failure, coronary heart disease, valvular defects, insulin-dependent DM, or secondary causes of HT, dyslipidemia, or obesity were excluded. Office BP was checked after a 5 minute of rest in the seated position with the mercury sphygmomanometer on three visits and no smoking was permitted during the previous 2 hr. A 10 day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in the normotensives in the office due to the risk of masked HT, after a 10 minute education about proper BP measurement techniques.[6] The education included recommendation of upper arm while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12×26 cm for arm circumferences up to 33 cm in length and a large adult cuff with bladder sizes of 12×40 cm for arm circumferences up to 50 cm in length, and taking a rest at least for a period of 5 minute in the seated position before measurement. A 24 hr ambulatory blood pressure monitoring (ABPM) was obtained just in cases with higher office and/or HBP measurements, and it was performed with oscillo-metrical equipment (SpaceLabs 90207, Redmond, WA, U.S.A.) set to take a reading every 10 minute throughout the 24 hr. Normal daily activities were allowed, and subjects were told to keep the arm as relaxed during measurements. HT was defined as BP of > or = 135/85 mmHg on mean daytime (between 10 AM to 8 PM) ABPM.[6] WCH was defined as office BP of > or = 140/90 mmHg, but mean daytime ABPM of <135/85 mmHg, and sustained NT as average HBP of <135/85 mmHg and office BP of <140/90 mmHg, so the white coat effect was defined as the difference between the office and mean daytime ABPM.[6] Masked HT was defined as office BP of <140/90 mmHg, but mean daytime ABPM of > or = 135/85 mmHg.[6] Additionally, body mass index (BMI) of each case was calculated. Weight (in kilograms) is divided by square of height (in meters) to calculate BMI, and obesity is defined as a BMI of > or = 30 kg/m^2 and overweight as 25–29.9 kg/m^2.[7] Cases with an overnight FPG level >126 mg/dl on two occasions or already taking antidiabetic medications were defined as diabetics. An oral glucose tolerance test with 75 g glucose was performed in cases with a FPG level between 100 and 126 mg/dl, and diagnosis of cases

with a 2 hr plasma glucose level > or = 200 mg/dl is DM and 140–199 mg/dl is IGT. Additionally patients with dyslipidemia were detected, and we used the National Cholesterol Education Program Expert Panel's recommendations for defining dyslipidemic subgroups.[7] Dyslipidemia is diagnosed when LDL-C is > or = 160 and/or TG > or = 200 and/or HDL-C <40 mg/dl. Prevalences of smoking, overweight, obesity, IGT, type II DM, hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia were calculated in each group and results were compared in between. Comparison of proportions was used as the statistical analysis method.

RESULTS

The study totally included 169 cases (91 females), 54 with sustained NT (21 females), 66 with WCH (43 females), and 49 with HT (27 females), and their mean ages were 57.3, 55.3, and 53.0 years, respectively. The characteristics of the groups were summarized in Tables 1, 2, and 3. The 115 patients with WCH and HT were both diagnosed via HBP and ABPM, and no difference was observed between the two methods for the diagnosis of WCH and masked or obvious HT. It was observed on ABPM that the white coat effect was initiated by leaving home to come to hospital. Six of the 49 hypertensive cases (12.2%) actually had masked HT and the mean age of them was 65.5 ± 6.1 years. As a surprising result of the study, the prevalences of smoking significantly decreased from the sustained NT toward HT and WCH groups, but actually 38.8% (21 in number) of the sustained HT, 65.1% (43 in number) of the WCH, and 55.1% (27 in number) of the HT cases were female and we totally studied 45 smokers, 39 of whom were male. Thus, the difference of gender distribution probably affected the prevalences of smoking between the groups. So, the highest the female ratio of the WCH group showed the lowest the smoking ratio and the lowest the female ratio of the sustained NT group showed the highest smoking ratio. Additionally, the prevalences of overweight were 31.4% in the sustained NT, 31.8% in the WCH, and 24.4% in the HT groups, and it was the only parameter, which did not show any significant difference between the groups. When we compared the sustained NT and WCH groups, obesity, IGT, hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia were significantly higher in the WCH group. Additionally, obe-

Table 1. Comparison of Cases with Sustained Normotension and White Coat Hypertension

Variables	Sustained NT[a]	WCH[b]	p-value
Total number and female ratio	54 (38.88%)	66 (65.15%)	
Mean age, standard deviation, and range (year)	57.34 ± 11.06 (36–80)	55.36 ± 8.61 (36–75)	
Prevalence of smoking	44.44% (24)	13.63% (9)	<0.001
Prevalence of overweight	31.48% (17)	31.81% (21)	>0.05
Prevalence of obesity	20.37% (11)	31.81% (21)	<0.05
Prevalence of IGT[c]	1.85% (1)	6.06% (4)	<0.05
Prevalence of DM[d]	14.81% (8)	18.18% (12)	>0.05
Prevalence of hyperbetalipoproteinemia	5.55% (3)	19.69% (13)	<0.001
Prevalence of hypertriglyceridemia	7.40% (4)	21.21% (14)	<0.001
Prevalence of dyslipidemia	12.96% (7)	33.33% (22)	<0.001

a) Normotension, b) White coat hypertension, c) Impaired glucose tolerance, d) Diabetes mellitus.

Table 2. Comparison of Cases with White Coat Hypertension and Hypertension

Variables	WCH[a]	HT[b]	p-value
Total number and female ratio	66 (65.15%)	49 (55.10%)	
Mean age, standard deviation, and range (year)	55.36 ± 8.61 (36–75)	53.05 ± 9.37 (38–76)	
Prevalence of smoking	13.63% (9)	24.48% (12)	<0.05
Prevalence of overweight	31.81% (21)	24.48% (12)	>0.05
Prevalence of obesity	31.81% (21)	55.10% (27)	<0.001
Prevalence of IGT[c]	6.06% (4)	8.16% (4)	>0.05
Prevalence of DM[d]	18.18% (12)	34.69% (17)	<0.01
Prevalence of hyperbetalipoproteinemia	19.69% (13)	12.24% (6)	>0.05
Prevalence of hypertriglyceridemia	21.21% (14)	18.36% (9)	>0.05
Prevalence of dyslipidemia	33.33% (22)	28.57% (14)	>0.05

a) White coat hypertension, b) Hypertension, c) Impaired glucose tolerance, d) Diabetes mellitus.

Table 3. Comparison of Cases with Sustained Normotension and Hypertension

Variables	Sustained NT[a]	HT[b]	p-value
Total number and female ratio	54 (38.88%)	49 (55.10%)	
Mean age, standard deviation, and range (year)	57.34 ± 11.06 (36–80)	53.05 ± 9.37 (38–76)	
Prevalence of smoking	44.44% (24)	24.48% (12)	<0.01
Prevalence of overweight	31.48% (17)	24.48% (12)	>0.05
Prevalence of obesity	20.37%	55.10%	<0.001
Prevalence of IGT[c]	1.85%	8.16%	<0.01
Prevalence of DM[d]	14.81%	34.69%	<0.001
Prevalence of hyperbetalipoproteinemia	5.55% (3)	12.24% (6)	<0.05
Prevalence of hypertriglyceridemia	7.40% (4)	18.36% (9)	<0.01
Prevalence of dyslipidemia	12.96% (7)	28.57% (14)	<0.01

a) Normotension, b) Hypertension, c) Impaired glucose tolerance, d) Diabetes mellitus.

sity and DM were significantly higher in the HT than the WCH groups. Similarly, the prevalences of obesity, IGT, type II DM, hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia were significantly higher in the HT than the sustained NT groups. As another interesting result of the study, the hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia showed some increases in the WCH than the HT groups, but the differences were statistically insignificant.

DISCUSSION

WCH is a condition characterized by elevated BP in medical settings combined with normal

ABPM or self-measured HBP. As already detected in a previous study by us,[8] the both methods were equally effective for the diagnosis of WCH and HT, here. Similarly, recent HT guidelines propose self-measurement of HBP as an important means to evaluate response to antihypertensive therapy, to improve compliance with therapy, and most importantly, as an alternative to ABPM to confirm or refute the WCH.[9] Appropriateness of HBP to guide antihypertensive treatment was only tested in one large-scale randomized trial: the Treatment of Hypertension Based on Home or Office Blood Pressure (THOP) trial, and it was shown that antihypertensive treatments based on home instead of office BP led to a less intensive drug treatment, but also to less effective BP control with no difference in general well being and left ventricular mass.[10] In another study, both ABPM and HBP appeared to be appropriate methods for detection of masked HT,[11] as another handicap of the office BP measurements. In the previous study,[8] we observed very high prevalences of WCH in society, 33% in the second, 46% in the third, 50% in the fourth, 48% in the fifth, 36% in the sixth, 19% in the seventh, and 8% in the eighth decades of life, and prevalence of HT initially started to be higher than 40% in the sixth and it reached up to 75% in the eighth decades of life. On the other hand, the prevalence of HT was detected as only 3% in the third, 8% in the fourth, and 21% in the fifth decades of life in the same study. The high prevalences of WCH in society were also shown in some other reports.[12, 13] So as a hypothesis, we had come to the result that all hypertensives, 75% in the eighth decade, may arise from the previously WCH cases, but this process takes a very long period of time, reaching up to the normal life span of human being. On the other hand, in a recent review article it was postulated that patients with WCH are characterised by the following features: absence of organ damage induced by HT, absence of risk of future cardiovascular disease related to HT, and absence of lowering of BP from antihypertensive treatment.[14]

As an important point of this study, we evaluated the WCH not as a cause of HT or atherosclerosis, but as a coexisting, thus an alarming sign of something going bad for health. When we compared the the sustained NT, WCH, and HT groups, the WCH cases were found in between according to the frequencies of almost all of the following disorders, obesity, IGT, type II DM, hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia, and nearly all of the disorders showed a gradual and statistically significant progression in frequencies from sustained NT toward WCH and HT cases. But, although the Adult Treatment Panel III reported that although some people classified as overweight actually have a large muscle mass, most of them have excess body fat, and overweight and obesity do not only predispose to coronary heart disease (CHD), stroke, and numerous other conditions, they also have a high burden of other CHD risk factors including dyslipidemia, type II DM and HT,[7] we did not detect any significant difference between the three groups according to overweight, here.

As the conclusions, due to the the high prevalence of WCH even in early decades and the high prevalence of HT in elders, HT may be thought a sequela of WCH. But this process takes a very long period of time, reaching up to the normal life span of human being. Thus, WCH should preferentially be accepted as a disorder associated with a greater all-cause mortality, rather than a predisposing factor of HT or atherosclerosis alone, and its management should be focused on the above comorbid disorders.

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