Treated Hypertensives with Good Medication Compliance are Still in a State of Uncontrolled Blood Pressure in the Japanese Elderly

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Abstract

Objectives: Blood pressure (BP) is poorly controlled in many countries. Poor compliance was suggested as the main cause for poor BP control. The purpose of this study was to examine the association between compliance and the control of both casual blood pressure (BP) and 24-hr ambulatory BP in a Japanese elderly population.

Methods: The study was a cross-sectional survey. Casual BP and 24-hr ambulatory BP were measured at home. Hypertension was defined as casual systolic BP (SBP) ≥ 140 and/or diastolic BP (DBP) ≥ 90 mmHg, or as treated hypertension. A compliance rate of greater than 80% by the pill count method was defined as good compliance.

Results: Of the 178 treated hypertensives, 82.6% showed good compliance. Between the treated hypertensives with good compliance and those with poor compliance, no significant difference was found in either casual BP or ambulatory BP. Of the treated hypertensives with good compliance, the prevalence of achieved target ambulatory BP, i.e., daytime BP <135/85 mmHg, nighttime BP <120/75 mmHg, and 24-hr BP <125/80 mmHg, was, respectively, 35.4%, 43.5%, and 20.4%.

Conclusions: Casual BP and 24-hr ambulatory BP were poorly controlled in the community-living elderly although many of the treated hypertensives showed good compliance. It is unlikely that this inadequate control of hypertension is due to poor compliance on the part of the subjects.

Key words: blood pressure control, poor compliance, community-living elderly, ambulatory blood pressure monitoring, physician's attitude

Introduction

Hypertension is one of the most prevalent chronic conditions in the developed world, and it is the most important risk factor for cardiovascular disease (1–5). The reported prevalence of hypertension (defined as a casual blood pressure (BP) of 140/90 mmHg as the threshold) is higher than 20% in adult populations worldwide, suggesting that high BP is an important public health concern of global dimensions (6). The prevalence of hypertension increases with age, occurring in approximately 60% of Japanese aged 65 years or older (7).

The number of patients treated for hypertension has approximately doubled in the past 20 years worldwide (6). As a consequence, morbidity and mortality associated with high BP have decreased (8). Nevertheless, the obtained reduction in cardiovascular

morbidity and mortality has been lower than expected (9, 10). One of the reasons that treated hypertensive patients retain a higher risk for cardiovascular disease than normotensive individuals might be that the BP of treated patients is rarely lowered to adequate levels. Recent surveys in Spain showed BP control rates (clinic BP <140/90 mmHg) ranging from 13% to 26% (11), and BP was also poorly controlled in other countries (12–15). Noncompliance with medication regimens can place elderly persons at risk for declining health, increased healthcare expenses, and increased preventable hospital admission (16). Most previous research has focused on patients' low compliance with medication regimens as the main cause for this poor control of BP (4, 17). There is some evidence that compliance must be 80% or more in order to obtain significant BP reduction (18).

Casual BP does not provide sufficient BP information because of the limited number of BP measurements. It was reported that 24-hr ambulatory BP is an important indicator in predicting hypertension and is clinically helpful in managing hypertension (19–21). The reference values for ambulatory BP monitoring are defined as 135/85 mmHg for daytime and 120/75 mmHg for nighttime (21).

The purpose of this study was to examine the rate of compliance with antihypertensive medications and to determine whether

Received Apr. 18 2002/Accepted Jun. 17 2002

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antihypertensive drug compliance contributes to the control of casual BP or ambulatory BP in the Japanese elderly population living in the community.

Methods

Study population:

The study was a cross-sectional survey of a civilian, non-institutionalized population of Japan, and included an in-home interview. The study was conducted between November, 1998 and March, 2001 in Tsukuba, Ibaraki Prefecture (a city located about 50 km northeast of Tokyo, with a population of approximately 162,000) and in two towns near Tsukuba with populations of 9,500 and 24,700. The rates of aging in Tsukuba, and the two towns were approximately 12.4%, 16.3%, and 18.5%. We recruited participants for this study by visiting health education classes for senior clubs consisting of 30 to 50 members. Health classes were held near their homes in the community. Each town had 20 to 30 senior clubs, and a third to half of the members attended the health education classes, suggesting that subjects with health unawareness were also included. We excluded subjects who were bedridden or who suffered completely impaired cognition (22). No other inclusion or exclusion criteria were applied. Individuals with a history of stroke, coronary heart disease, diabetes mellitus, or other major complications remained eligible unless they met any of the exclusion criteria.

Casual BP measurements and 24-hr ambulatory BP monitoring:

An investigator visited each participant at home during the daytime to attach an ambulatory BP monitoring device and returned the next day to detach it. Casual BP was measured twice, each time with the subject in the sitting position after a rest of at least 5 minutes, by an investigator with a semi-automatic BP measuring device (HEM-722C, Omron Life Science Co. Ltd., Tokyo, Japan). The average of the four BP readings measured on two consecutive days was defined as the casual BP.

A 24-hr ambulatory BP profile was obtained with an automatic device, the A&D TM 2421 (A&D Co. Ltd., Tokyo, Japan) (23). The device was preset to measure BP every 30 minutes during the daytime period (6:00–22:00) and every 60 minutes during the nighttime period (22:00–6:00). The subjects were asked to carry out their normal activities during the monitoring period and to report their activities, especially time to get up, time to go to bed, and sleeping time in a diary. From the information in the diary, we defined daytime BP as that during the time participants were actually active, and defined nighttime BP as that during the time participants stayed in bed. The target ambulatory BP was 135/85 mmHg for the daytime BP, 120/75 mmHg for the nighttime BP (as established by the Sixth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI) (21)), and 125/80 mmHg for the 24-hr BP (as established by the 1999 WHO/ISH guidelines (24)).

Information about antihypertensive drugs:

Information about the antihypertensive medication regimen was obtained during the home visit interview. We asked participants to show me their prescribed drugs and to indicate how often they took the drugs. We also confirmed the information about their medications by examining the written drug information given to patients by the community pharmacy or hospital pharmacy. The

rate of compliance was calculated by the pill count method, which showed what percentage of the prescribed medication a participant took (25). An investigator counted the prescribed drugs not taken and furthermore asked patients how often they did not take their medications. Good compliance was defined as more than 80% adherence to the prescribed regimen of antihypertensive drugs (25).

Classification of participants:

Participants were classified as normotensives: NT (casual SBP<140 mmHg and DBP<90 mmHg, with the subject not undergoing any antihypertensive therapy), untreated hypertensives: UHT (casual SBP $\geq$ 140 mmHg and/or DBP $\geq$ 90 mmHg, with the subject not undergoing any antihypertensive therapy), treated hypertensives with good compliance: THTGC, and treated hypertensives with poor compliance: THTPC.

Statistical analysis:

Data were analyzed using the SPSS 8.0J statistics software. Values were expressed as the means $\pm$ SD. Student's t test was used to establish the statistical significance ($P<0.05$) of the differences. Categorical data were compared with chi-square analyses. Mean values of casual BP and 24-hr ambulatory BP from the four groups were compared by one-way ANOVA. When there were significant differences among the four groups, post hoc analysis was conducted with the Bonferroni test to identify underlying factors. Odds ratios for achieved target BP in the subjects with good compliance were estimated by logistic regression analysis; odds ratios and their 95% confidence intervals were calculated in the univariate model, and odds ratios adjusted for age, gender, family history of hypertension, current alcohol intake, current smoking, and body mass index (BMI) were also examined.

Results

A total of 276 elderly (female: 184 (66.7%)) participated in the 24-hr ambulatory BP monitoring program and gave their written informed consent. Of the participants, 12 were excluded because of incomplete 24-hr ambulatory BP recordings or because they fit any of the exclusion criteria. Finally, 264 were eligible for analysis. The participants who were ineligible for analysis were similar to those who were eligible in gender, prevalence of history of cerebral infarction, and rate of compliance. Demographic characteristics of the study subjects are shown in Table 1. There were no significant differences between the subjects with antihypertensive drugs and without antihypertensive drugs except body mass index. Of the 178 treated hypertensives, 147 (82.6%) showed good compliance in taking their antihypertensive medication; 152 (85.4%) were being treated with calcium channel blockers, and 71 (39.9%) were prescribed two or more antihypertensive drugs in combination. Of the 178 treated hypertensives, 80 (44.9%) had systolic hypertension (casual SBP $\geq$ 140 mmHg and casual DBP<90 mmHg).

There were no significant differences in age, gender, or education level among NT, UHT, THTPC, and THTGC (data not shown). Fig. 1 showed the comparison of casual BP and ambulatory BP among NT, UHT, THTPC, and THTGC. Both casual BP and 24-hr ambulatory BP were significantly higher in the untreated or treated hypertensives than in the normotensives. There was no significant difference in the 24-hr ambulatory BP between treated

Table 1 Characteristics of subjects with anti-HT drugs and without anti-HT drugs

	With anti-HT drugs	Without anti-HT drugs
N	178 (67.4%)	86 (32.6%)
Age, years	75.4±7.0	75.2±7.3
Gender		
Male	60 (33.7%)	26 (30.2%)
Female	118 (66.5%)	60 (69.8%)
Alcohol intake (current)	52 (29.2%)	19 (22.1%)
Smoking (current)	21 (11.8%)	9 (10.5%)
BMI, kg/m ²	24.2±3.6	23.1±3.7*
Frequency of administration on anti-HT drugs/day	1.6±0.7	—
Good compliance on anti-HT drug	147 (82.6%)	—
Subjects with prescribed 2 or more anti-HT drugs	71(39.9%)	—
Classes of anti-HT drugs		
Calcium channel blocker	152 (85.4%)	—
ACE-inhibitor	41 (23.0%)	—
α-adrenergic blocker	14 (7.9%)	—
β-adrenergic blocker	11(6.2%)	—
Diuretic	24 (13.5%)	—
Casual SBP ≥ 140 mmHg and casual DBP < 90 mmHg	80 (44.9%)	—

Values are means±SD; Number (%); BMI, body mass index; anti-HT, antihypertensive.

Good compliance, rate of compliance ≥ 80%; ACE-inhibitor, angiotensin-converting enzyme inhibitor.

* P<0.05.

Fig. 1 Comparison of casual BP and ambulatory BP among NT, UHT, THTPC, and THTGC (n=264).

BP, blood pressure; SBP, systolic BP; DBP, diastolic BP.

NT, normotensives; UHT, untreated hypertensives; THTPC, treated hypertensives with poor compliance; THTGC, treated hypertensives with good compliance.

* P<0.001 vs casual BP or ambulatory BP in UHT, THTPC, and THTGC; † P<0.05 vs UHT by ANOVA.

hypertensives with good compliance and those with poor compliance, although casual BP of treated hypertensives with good compliance was slightly lower than those with poor compliance.

The prevalence of achieved target ambulatory BP in treated hypertensives with good compliance, defined as a daytime BP of <135/85 mmHg, a nighttime BP of <120/75 mmHg, and a 24-hr BP of <125/80 mmHg, were 35.4%, 43.5%, and 20.4%, respectively (Table 2). There was no significant difference in the achievement of BP control between treated hypertensives with good compliance and those with poor compliance. We further examined the prevalence of achieved target BP by stratifying the

treated hypertensives according to gender. There was no significant difference between males and females (Table 2).

Odds ratios for achieved target BP in the hypertensives with good compliance did not differ significantly from those with poor compliance: the odds ratio (95% CI) for achieved target casual BP was 1.08 (95% CI: 0.47–2.47); that for daytime ambulatory BP was 0.95 (95% CI: 0.42–2.14); that for nighttime ambulatory BP was 1.54 (95% CI: 0.68–3.52); and that for 24-hr ambulatory BP was 1.07 (0.40–2.84). After adjustment for age, gender, family history of hypertension, current alcohol intake, current smoking, and BMI (kg/m²), the odds ratios were similar across all groups

Table 2 The prevalence of achieved target blood pressure in treated hypertensives

	Casual BP<140/90 mmHg	Day ABP<135/85 mmHg	Night ABP<120/75 mmHg	24-hr ABP<125/80 mmHg
Poor compliance	10 (32.3%)	11 (36.7%)	10 (33.3%)	6 (19.4%)
Good compliance	50 (34.0%)	52 (35.4%)	64 (43.5%)	30 (20.4%)
Male	16 (26.7%)	17 (28.8%)	19 (32.2%)	11 (18.3%)
Female	44 (37.3%)	46 (39.0%)	55 (46.6%)	25 (21.2%)

BP: blood pressure, ABP: ambulatory blood pressure.

Table 3 Odds ratios for achieved target BP in treated hypertensives (n=178)

	Casual BP<140/90 mmHg		Day ABP<135/85 mmHg		Night ABP<120/75 mmHg		24-hr ABP<125/80 mmHg	
	OR (95%CI)	OR (95%CI)*	OR (95%CI)	OR (95%CI)*	OR (95%CI)	OR (95%CI)*	OR (95%CI)	OR (95%CI)*
Poor compliance	1	1	1	1	1	1	1	1
Good compliance	1.08 (0.47–2.47)	1.13 (0.49–2.64)	0.95 (0.42–2.14)	0.90 (0.39–2.07)	1.54 (0.68–3.52)	1.44 (0.61–3.44)	1.07 (0.40–2.84)	1.04 (0.38–2.80)
Goodness of fit-test		0.53		0.88		0.52		0.91

OR, odds ratio; 95%CI, 95% confidential interval.

ABP, ambulatory blood pressure.

* odds ratios were adjusted with age, gender, body mass index ≥ 25 , history of family hypertension, current alcohol intake, and current smoking.

Poor compliance, compliance rate <80%; good compliance, compliance rate $\geq 80\%$.

Table 4 Prevalence of achieved target BP according to the number and the class of anti-HT drugs in treated hypertensives with good compliance

	Casual BP<140/90 mmHg	Day ABP<135/85 mmHg	Night ABP<120/75 mmHg	24-hr ABP<125/80 mmHg
Number of anti-HT drug				
With one anti-HT drug (n=88)	28 (31.8%)	31 (35.2%)	43 (48.9%)	21 (23.9%)
With more than 2 anti-HT drugs (n=59)	22 (37.3%)	21 (35.6%)	21 (35.6%)	9 (15.3%)
Classes of anti-HT drug				
Calcium channel blocker only (n=69)	24 (34.8%)	23 (33.3%)	36 (52.2%)	16 (23.2%)
Calcium channel blocker plus other drugs (n=56)	21 (37.5%)	20 (35.7%)	20 (35.7%)	8 (14.3%)

Chi-square test.

anti-HT, antihypertensive; BP, blood pressure; ABP, ambulatory blood pressure.

(Table 3).

The prevalence of achieved target casual BP, day ambulatory BP, and night ambulatory BP in the subjects with good compliance who were prescribed two or more antihypertensive drugs was, respectively, 37.3%, 35.6%, and 35.6%; moreover, only 9 (15.3%) satisfied the 24-hr ambulatory BP requirement. The prevalence of achievement for target casual and ambulatory BP control was not significantly different between the subjects with good compliance prescribed a calcium channel blocker only and those prescribed a calcium channel blocker plus one or more other antihypertensive drugs (Table 4).

Discussion

Despite the rising number of treated hypertensives in recent years, hypertension has not been adequately controlled. The risk of mortality depends on achieved BP rather than on initial BP (9, 10), with a goal of achieving and maintaining a casual SBP below 140 mmHg and a casual DBP below 90 mmHg. It was reported that 37% of hypertensives achieve the target BP in Europe (12), 24% in the United States (13), 27% in New Zealand (14), and 33.7% in Japan (this study).

In many studies of BP control, BP has been analyzed in treated hypertensives without considering the rate of compliance, even though poor compliance with antihypertensive treatments reportedly contributes to inadequate BP control in more than two-

thirds of patients with hypertension (21). We conducted this study to determine, by measuring 24-hr ambulatory BP, whether inadequate BP control is really due to poor compliance in taking prescribed antihypertensive medications. In this study, 82.6% of treated hypertensives showed good compliance. Even though the subjects who adhered to their prescribed antihypertensive drug regimens more than 80%, casual BP and ambulatory BP, especially systolic BP, were still inadequately controlled. Logistic regression analysis of the relation between BP control and drug compliance revealed that the odds ratio for achieved target BP in treated hypertensives with good compliance did not differ from those with poor compliance. The present findings suggested that poor compliance with antihypertensive drugs did not necessarily contribute to inadequate BP control as Nuesch et al. (26) reported that non-compliance is not necessarily the main factor in explaining treatment resistance by measuring ABP and using a medical event monitoring system.

In the present study population, about 60% of treated hypertensives were prescribed only one antihypertensive drug. The prevalence of achieved target BP was small even in the subjects prescribed more than two antihypertensive drugs. In addition to these, 152 (85.4%) of all treated hypertensives were prescribed calcium channel blockers; among those subjects, 69 (55.2%) were treated with only one calcium channel blocker. Since Muratani reported that greater than 70% of elderly hypertensives in Japan are prescribed calcium channel blockers (27), calcium channel

blockers are the most common antihypertensive drugs, followed by angiotensin-converting enzyme inhibitors, β -adrenergic blockers, and diuretics in Japan (27). The present study failed to establish an association between poor BP control and the number or class of hypertensive drugs prescribed, since we found no significant differences in the rates of achievement for target casual BP or target ambulatory BP between the subjects prescribed only a calcium channel blocker and those prescribed a calcium channel blocker together with other antihypertensive medications. Many of elderly hypertensives appeared to be under-treated.

Recent surveys conducted in several European countries (11, 12, 28), and in the United States (29, 30) suggest that the conservative approach of physicians contributes to poor BP control. Despite inadequate BP control, most patients are currently treated in a monotherapy regimen (12, 28), and physicians do not intend to lower these patients' BP by using additional antihypertensive drugs. Spanish doctors introduced therapeutic modifications in only 13% of the patients, even if BP control was inadequate (11). The same conservative attitude was observed in other parts of Europe (11, 12) and in the United States (29). A similar phenomenon was observed in Japan. Japanese guidelines for the treatment of hypertension set the therapeutic goal of casual BP in the elderly at a higher level than that set by JNC-VI (21) or that set by WHO/ISH (24) BP; the target clinic SBP is set for individuals in their 60s, 70s, or 80s at 140, 150–160, or 160–170 mmHg, respectively (31). It was suggested that many Japanese physicians appear to

assume that the elderly tend to already have target-organ damage, and they are afraid of unfavorable events that occur more often when BP falls to a certain level (32, 33). This cautious attitude and resultant conservative treatment may partly contribute to inadequate BP control. A third to half of the members of senior clubs attended the health education classes, suggesting that subjects with health unawareness were also included. However, the present study may have a limit to the universality of the results because it was a small study performed in only limited subjects.

In conclusion, casual BP and 24-hr ambulatory BP are not adequately controlled in the community-living elderly despite a good compliance with their medication regimens. In addition, the rate of well-controlled BP is not related to the number or the class of antihypertensive drugs prescribed. Adherence with drug regimens is important, however, it is unlikely that poor compliance in the community-living elderly may be the main cause for inadequate control of BP. Physician's conservative attitude may partly contribute to inadequate BP control. Further randomized studies are needed to confirm these findings.

Acknowledgements

This study was supported by a grant from the Heparin Research Foundation. The authors are grateful to the public nurses in Ishige and Chiyokawa for their excellent support.

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