Nocturnal Blood Pressure Monitored by Ambulatory Blood Pressure Measurement in Elderly Hypertensive Patients

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This study was designed to characterize the nocturnal fall of blood pressure (NFBP) of elderly hypertensive patients (EH), with or without cerebrovascular disease or diabetes mellitus, as measured by automated blood pressure (BP) monitoring. Systolic and diastolic BP and heart rate was measured every 15 minutes in 133 hospitalized patients with nearly similar schedules and diets. The patients were divided into five groups: I, normotensive elderly patients over age 65; II, EH without cardiovascular diseases, controlled without medication; III, EH with cerebral infarction, chronic stage; IV, EH with noninsulin-dependent diabetes mellitus; and V, hypertensives under age 65, without cardiovascular diseases. A significant NFBP was observed in the patients of groups I and V, a significant but smaller NFBP in the hypertensives of groups II and IV, and no NFBP in the patients of group III. Administration of the antihypertensive drugs, enalapril and nifedipine, tended to augment the NFBP. These preliminary observations showed that NFBP did occur in elderly hypertensives but the fall was smaller than that observed in younger hypertensives or elderly normotensives. Although the ambulatory BP measurements were useful in the overall clinical evaluation of elderly patients, NFBP in elderly patients was affected by hypertensive drugs and therefore NFBP should be interpreted with caution.

(Key words: nocturnal fall of blood pressure, elderly systolic hypertension, automated blood pressure monitoring, coefficients of variation)

Introduction

Noninvasive ambulatory 24-hours blood pressure (NFBP) monitoring has come to be regarded as more useful than casual measurements of blood pressure for evaluating the prognosis and severity of hypertension (1, 2). Arterial hypertension in the elderly is associated with an increase in cardiovascular morbidity and mortality which, however, may be reduced by the administration of antihypertensive therapy (3). However, the actual correlation between blood pressure measurements obtained while sitting in the clinic and the incidence of morbid events is relatively low (4). A possible explanation is the variability of daytime blood pressure which reflects the diet, time of day, activity or emotional state of the patient, and even the doctor-patient relationship ("white-coat hypertension") (5). Thus, the decision to initiate the treatment of hypertension in elderly patients based on office blood pressure readings is difficult as if is not infrequent that the treatment produces adverse effects. In particular, a severe nocturnal fall in blood pressure may precipitate a cerebrovascular attack (3). While NABP monitoring may be of value in this regard, there are few reports concerning such monitoring in the elderly hypertensive patients. The reliability of NABP itself depends on several factors including the measurement interval, and the active or sleeping state of the patient (6). The data obtained by NABP monitoring has been shown to differ from that obtained by invasive BP monitoring. This study was designed to determine the pattern of nocturnal blood pressure in elderly patients with hypertension and to determine the effect of various clinical conditions on the direction of nocturnal BP.

Patients and Method

A total of 133 hospitalized patients (66 male, 67 female) were evaluated. Of those studied, 74 were over 65 years old.
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Table 1. Patients Profile

<table>
<thead>
<tr>
<th>Disease</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (y.o)</td>
<td>65±</td>
<td>65±</td>
<td>65±</td>
<td>65±</td>
<td>&lt;65</td>
</tr>
<tr>
<td>(mean ± SD)</td>
<td>(71.5 ± 7.5)</td>
<td>(71.5 ± 2.1)</td>
<td>(71.5 ± 2.2)</td>
<td>(67.5 ± 1.6)</td>
<td>(52.9 ± 2.5)</td>
</tr>
<tr>
<td>Number</td>
<td>33</td>
<td>38</td>
<td>19</td>
<td>17</td>
<td>26</td>
</tr>
<tr>
<td>(men)</td>
<td>(15)</td>
<td>(20)</td>
<td>(10)</td>
<td>(9)</td>
<td>(12)</td>
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HTn: Hypertension, CVD: Cerebrovascular disease, DM: Diabetes mellitus

of age and had a history of hypertension; 26 were under 65 years of age and had hypertension, while 33 were over age 65 and had no history of hypertension. The following clinical data were obtained from the patients history, physical examination and results of laboratory testing included the following: age, sex, and documentation of hypertension, cerebrovascular infarction, and diabetes mellitus (type 2, non-insulin-dependent diabetes mellitus) (Table 1). Appropriate evaluation failed to reveal a secondary cause for hypertension. The diagnosis of hypertension in this study was based on the following: systolic and diastolic blood pressure exceeding 160 and 95 mmHg as measured in the outpatient clinic. Excluded from study were those whose SBP or DBP on the day of study exceeded 160 mmHg (systolic) or more than 95 mmHg (diastolic). Measurements were recorded at least 7 days after admission.

The patients were divided into five groups: I, elderly (over 65 years of age) normotensive elderly patients (average SBP and DBP were less than 160 mmHg and 95 mmHg); II, elderly (over 65 years of age) hypertensives whose blood pressure was controlled without drug therapy, were in stage 1 or 2 on WHO criteria, and had no history of such circulatory disorders as cerebrovascular disease, myocardial infarction, diabetes mellitus; III, elderly hypertensive patients with a history of cerebral infarction (chronic stage); IV, elderly hypertensive patients with a history of non-insulin-dependent diabetes mellitus; V, hypertensive patients under age 65 who were controlled without drug therapy, were in stage 1 or 2 of WHO criteria, and had no history of disorders such as cerebrovascular disease, myocardial infarction, or diabetes mellitus. Patients with complications of their hypertension were selected as follows. Those with cerebrovascular infarction were evaluated at least 3 weeks after the stroke, when they were confirmed to be in the chronic stage and could function normally (eg, walk, talk, urinate, eat) and were emotionally stable. Patients with diabetes mellitus had type 2, non-insulin-dependent disease; their fasting blood sugar (FBS) was less than 180 mg/dl on the day of the study, and mean term which they have suffered was 5.8 ± 3.3 years. None received insulin, and none suffered from diabetic neuropathy (orthostatic hypotension). Seven diabetic patients were on oral hypoglycemic agents, while 10 patients were controlled without drug therapy. None of the diabetics was receiving drugs known to influence the autonomic nervous system.

In an attempt to standardize the experimental conditions, the pressure of infectious disease or insomnia on the day of testing led to the exclusion of that patient. All subjects ate almost similar diet (about 1,700 kcal/day), had their meals at similar times, were not administered antihypertensive agents and could engage in such activities as watching TV, reading books, and visiting relatives at specified times of the day. Antihypertensive drugs were administered to 48 patients (28 Ca2+ antagonists, 5 β-blocker, 9 angiotensin converting enzyme inhibitor, and 6 diuretics). Primarily, administration of antihypertensive drugs to any patients was stopped on administration, and the effect of drugs was washed out (at least 2 weeks). Blood pressure recording was begun in the early evening and was continued without interruption for a 24-hour period. Ambulatory BP measurements were recorded every 15 minutes by an indirect automated blood pressure monitoring device (ABPM630, Nippon Colin Co, Ltd., Komaki, Japan). The procedure was well tolerated and produced no pain or discomfort. Data on systolic and diastolic blood pressure (SBP, DBP), heart rate (HR), standard deviations (SD), and coefficients of variation (SCV) were analyzed during the following time periods: 6:00 PM to 9:00 PM; 9:00 PM to 0:00 AM (midnight); 0:00 AM to 3:00 AM; 3:00 AM to 6:00 AM; 6:00 AM to 9:00 AM using SAS statistical programs, (version 5, SAS Institute, Cary, WC, USA).

Statistical methods

Data are presented as mean ± standard deviation (SD). The unpaired t test was used to compare groups. The level of confidence chosen for statistical significance was p < 0.05.

Results

The 24-hour BP measurements obtained at 15-minute intervals in 65 hypertensive subjects are shown in Fig. 1. At night, the ambulatory SBP was significantly lower in the patients under age 65 (group V) than in those over age 65 (group II). The SBP fell significantly in both groups, being significantly lower between 0:00 AM to 6:00 AM. However, the nocturnal blood pressure...
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Fig. 1. Diurnal variation in systolic and diastolic blood pressure (SBP, DBP), heart rate (HR), and coefficients of systolic blood pressure measurement values (SCV) in two groups of hypertensive patients aged above and below 65 years. • significant fall (p<0.05) as compared with the mean values obtained between 6:00 AM and 9:00 AM in the patients under age 65. • significant fall (p<0.05) as compared with the mean value obtained between 6:00 AM and 9:00 AM in patients over age 65.

Fig. 2. Nocturnal variation in systolic and diastolic blood pressure (SBP, DBP), heart rate (HR), and coefficients of systolic blood pressure measurement values (SCV) in four groups of elderly patients. ○ normotensive patients (group I), □ hypertensive patients without circulatory disorders (group II), ■ hypertensive patients with cerebrovascular disease (group III), ● hypertensive patients with diabetes mellitus (group IV). ○ significant fall (p<0.05) as compared with the mean values obtained between 6:00 AM and 9:00 AM in normotensives, ● significant fall (p<0.05) as compared with the mean values obtained between 6:00 AM and 9:00 AM in hypertensives (group II), ○ significant fall (p<0.05) as compared with the mean values obtained between 6:00 AM and 9:00 AM in group III patients, ● significant fall as compared with mean values obtained between 6:00 AM and 9:00 AM in group IV patients.
but significantly in both groups. In patients with HT, HR fell at night between 21:00 PM and 6:00 AM. The SCV did not change significantly in either group.

Elderly hypertensive patients with or without cerebrovascular disease (CVD) were then compared (group II vs. III). Nocturnal blood pressure pattern was different between patients groups II and III. The SBP tended to fall in patients without CVD. The SBP in patients with CVD was slightly higher at night than in the morning. The DBP in patients with CVD did not fall at night. The HR was not significantly lower at night in patients with CVD. BP and HR of elderly hypertensive patients with diabetes (group IV) showed a slightly different pattern. The SBP in the diabetic patients was higher between 6:00 PM and 0:00 AM than at night, and there was a significant nocturnal fall in blood pressure (mean differences 136.0 ± 3.0 mmHg vs. 148.2 ± 4.0 mmHg, 12.2 mmHg). There were no significant differences in the DBP and HR of the diabetic patients vs. the normal subjects. The SCV of the diabetic patients was not significantly different from that of group I patients.

The effects of antihypertensive therapy with enapril and nifedipine were also studied. Figure 3 shows the BP and HR before and after treatment with the angiotensin converting enzyme inhibitor, enapril 5 mg/day (once a day, 30 minutes after breakfast) for 2 weeks to hypertensive patients aged over 65 without any complication (group II) in whom antihypertensive drug administration was necessary to control their blood pressure. The administration of enapril led to a significant nocturnal decrease in SBP and DBP. The HR remained unchanged while the SCV was increased. Administration of the Ca²⁺ antagonist, nifedipine given orally to 6 patients at a dose of 40 mg/day, augmented the nocturnal fall in BP almost as much as enapril (data not shown).

**Discussion**

To standardize the environment as much as possible, we selected only those inpatients whose condition was stable since the nocturnal fall in blood pressure has been shown to be affected by a variety of factors such as daily activities, (eating, urination or evacuation, sleeping and posture) (6, 7). While we measured the NABP every 15 minutes, most of the previous investigations determined it every 30 or 60 minutes, perhaps reflecting the capacity of the pump used to inflate the cuff. To evaluate the SD or the CV of NABP, the interval between measurements ideally should be as short as possible. However, measurement obtained at very close intervals can interfere with sleep or change in the sleep pattern (8). A 15-minute interval has been reported not to significantly alter the sleep pattern (9). While we did not confirm an absence of change in sleep pattern by obtaining an EEG in all patients, they slept well during the study as determined both subjectively and objectively. Previous reports have shown a nighttime fall in blood pressure in normal young people, but not in inpatients suffering from certain diseases (10–12).

In this study, a fall in nocturnal blood pressure was observed in elderly hypertensive who lacked significant vascular complications as well as in those with diabetes mellitus. However the fall was less than in people without hypertension over age 65 or in hypertensive patients under age 65 without remarkable vascular complications. No fall in nocturnal blood pressure was observed in elderly hypertensives with cerebrovascular disease.

Possible explanation for this observation include an impairment of blood flow regulation (ex, vasovagal reflex) due to atherosclerosis, or the impairment of cerebral blood flow by cerebral infarction (13). Additional study is required to explain the lack of a nocturnal blood pressure fall in the elderly hypertensives with cerebro-
vascular disease. NABP monitoring has been shown to have some problems as compared with intra-arterial BP recording. For instance, the extent of the nocturnal fall in blood pressure has been small, perhaps maybe due to an interference with sleep (14). However, in our study, the nocturnal fall was 24.6 mmHg in normotensive elderly patients; the HR also fell significantly at night and there was no apparent interference with sleep. Another previously reported problems was an incorrect DBP obtained by NABP monitoring, therefore, it is important to carefully define DBP. SBP has been reported to be an important marker for the regulation of cerebral blood flow (15). We believe that NABP is particularly important in the control of BP in the elderly patient, for a variety of factors may affect the conventional blood pressure readings in elderly patients, and the value of nocturnal blood pressure in the elderly may be especially different from that of daytime BP. In the present study, the CV was unchanged not only in the elderly normotensive patients (group I) but also in the elderly hypertensive patients without cardiovascular complications (group II). These findings are consistent with those of Meyer et al who performed intra-arterial recordings with analysis of beat to beat data (16). The CV in the elderly hypertensive patients with cerebral infarction (group III) or with diabetes mellitus (group IV) was not significantly different from that in group II. The evaluation of SCV was difficult because it was affected by many factors. We think that more study is necessary to evaluate the change of CV in the elderly hypertensive patients. Antihypertensive treatment of elderly patients with atherosclerosis could lower the arterial pressure excessively to hypotensive levels; this could increase the risk of an acute myocardial infarction or aggravate the severity of dementia due to multiple cerebral infarction (13, 17, 18). We prefer to maintain the BP of the older hypertensive at a level slightly higher than that of the young hypertensives. Thus in many case the BP can be controlled without drug therapy. Nevertheless, some patients require the administration of agents such as a Ca^{2+} antagonist or ACE inhibitor for adequate control. For this reason we evaluated the effect of antihypertensive drugs enarapril and nifedipine on nocturnal BP. Our study of enarapril and nifedipine indicates that nocturnal BP is lowered by such a drug therapeutic approach, even though vascular disease such as hypertension and cerebral infarction would tend to elevate it as reported previously (13, 17, 18). The SCV of the nocturnal BP of the hypertensives over age 65 (group II) did not differ significantly from that of normotensives in that age group (group I). One reason may be that the elderly patients studied had as much activity of daily life as the young patients. BP variability has been reported to be increased in patients with severe diabetes mellitus (19). The diabetic patients studied had mild disease; none required insulin and none suffered from severe autonomic nerve failure or autonomic complications. The conditions may thus not have increased SCV in the patients. Enarapril tended to increase the CV for unknown reasons. The β-blocker, atenolol has been reported to have no effect on the CV of BP in young hypertensive patients (20).

Here, we investigated the change in the CV of BP of elderly patients induced by two anti-hypertensive agents. The results support the idea that NABP monitoring is important in evaluating the anti-hypertensive effects of such agents throughout the day. These observations indicate that nocturnal ambulatory blood pressure measurements, while useful in the overall clinical evaluation of elderly patients, may be affected by such factors as anti-hypertensive therapy; thus the NFBP should be interpreted with caution. The monitoring the nocturnal blood pressure of elderly patients appears to be a promising technique for evaluating their prognosis and helpful in determining the treatment protocol.

Acknowledgments: The authors wish to thank Professor M. Horne and Dr. S. Pelvis for their critical reading of the manuscript.

References


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