**Clinical Significance of Ambulatory
Blood Pressure Monitoring
Evaluation of Severity of Hypertension, Efficacy of Treatment
and Effects on Nighttime Blood Pressure**

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SUMMARY

Blood pressure (BP) obtained by the physician in his office and ambulatory BP recorded every hour throughout 24 hours with a noninvasive automated BP monitoring device were compared in 10 normotensives and 162 hypertensives. Casual BPs significantly correlated with averages in ambulatory BPs (ABPs) throughout the whole day, day (7 am–10 pm) and night (0–5 am). However, it was noted that 6 of 10 normotensives and all of the moderate to severe hypertensives had ABPs of more than 150/90 mmHg at least once during the 24-hour period. The incidence of ABPs greater than 150/90 mmHg among all readings was higher in untreated and treated hypertensives with diastolic BPs in the office of more than 105 mmHg, and, when checked along with the clock time, higher not only in the morning but also in the evening. On the other hand, one-third or one-fifth of treated hypertensives with diastolic office BPs less than 90 mmHg or between 90 and 105 mmHg respectively had ABPs less than 150/90 mmHg throughout the whole day. When the effect of nicardipine (60 mg, t.i.d.) or slow-release nifedipine (27.3 ± 3.0 mg, b.i.d.) on minimum BP during the night was analyzed, long-acting nifedipine decreased BP throughout the night to levels not significantly different from normotensive controls, whereas short-acting nicardipine did not affect nighttime BPs. These results suggest that simple ABP monitoring throughout the day gives us useful information to evaluate the severity of hypertension and the efficacy of antihypertensive medication as well as to avoid overtreatment with long-acting hypotensive agents resulting in a great fall in BP during sleep.

Additional Indexing Words:

Essential hypertension Mild hypertension Ambulatory blood
pressure monitoring Nifedipine Nicardipine

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WITH the advent of a handy device for noninvasive automated blood pressure monitoring (ABPM), there is now an abundance of evidence that ABP is a better marker for the efficacy of antihypertensive medication and the potential risk of cardiovascular complications than BP determined in the physician's office.^{1),2)} Ambulatory or self-monitored BP at home is generally believed to be lower than BP recorded in physicians' offices.²⁾⁻⁴⁾ Waeber et al⁵⁾ recently reported that half of the patients with BP greater than 95 mmHg in physicians' offices, despite antihypertensive treatment, had ambulatory BPs of 90 mmHg or less, and that new antihypertensive therapy over a 3 month period decreased their mean daytime diastolic BP to an average of 79 mmHg, indicating that, if we treat hypertensives based on only traditional BP readings obtained in the office, the possibility of overtreatment may exist in some of the patients. In addition, there is increasing evidence that nighttime BP decreases in accordance with circadian rhythms even in hypertensives. Because of the development of antihypertensive drugs with a long half-life as well as progress in drug delivery systems, long-acting antihypertensive drugs have become available. These drugs may lower not only daytime BP but nighttime BP as well. Therefore, we monitored 24-hour BP with a noninvasive monitoring system in normotensives as well as hypertensives, with and without treatment, while they pursued normal activities at home or in the workplace. Our study was designed to compare office BP with ABP, investigate the efficacy of therapy and shed light on nighttime BP during treatment with long-acting antihypertensive drugs.

SUBJECTS AND METHODS

This study involved a total of 166 patients with essential hypertension with ($n=104$, mean age; 56.6 ± 1.8 (SE) years old) and without ($n=58$, mean age; 52.5 ± 1.9 years old) antihypertensive medication as well as 10 healthy normotensives aged 47.2 ± 5.1 years, who had never been noted to have hypertension. Each patient had a full clinical examination and laboratory screening tests to exclude secondary hypertension. For the classification of blood pressure levels, the criteria used were those recommended by the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure. However, referred first visit hypertensive patients who had diastolic BP of less than 90 mmHg in our clinic were included in this study. After casual office sitting BPs and heart rates (SBPOFFICE, DBPOFFICE, HROFFICE) were obtained in the clinic between 9 am and noon, automated ABPM was performed every hour during a 24-hour period using an ABPM-630 (Nihon Colin, Komaki, Japan), the accuracy of which was evaluated by

comparing oscillometric readings with Korotkoff's readings at the same site. The subjects were asked to perform their normal daily activities, including those performed during a regular working day. Oscillometric readings of systolic and diastolic BP and pulse rate were obtained at 1-hour intervals throughout the 24-hour period. Tracings were analyzed only if at least 20 time points were available. Actually, the data from 4 hypertensives were discarded. The following analyses of systolic (SBP), diastolic (DBP) and mean BP (MBP) and heart rate (HR) were performed using a microcomputer: average of all readings obtained during the 24-hour monitoring period (SBPWHOLE, DBPWHOLE, MBPWHOLE, HRWHOLE), average of the readings obtained during the daytime from 7 am to 10 pm (SBPDAY, DBPDAY, MBPDAY, HRDAY), average of all measurements during sleep from 0 am to 5 am (SBPNIGHT, DBPNIGHT, MBPNIGHT, HRNIGHT) and minimum BP during sleep. The same parameters in the patients treated with nicardipine (20 mg 3 times a day, $n=11$, mean age; 55.0 ± 2.7 years old) or slow-release nifedipine (10–20 mg twice a day, $n=22$, mean age; 57.8 ± 2.6 years old) were analyzed as well.

All data are expressed as the mean $\pm$ SE. Standard statistical analyses, paired or unpaired Student's *t*-test, correlation coefficients, and Fisher's probability test, were used to analyze the data.

RESULTS

Oscillometric measurements significantly correlated with Korotkoff's readings obtained from the same arm at the same site (for SBP, $r=0.961$, $p<0.01$; for DBP, $r=0.874$, $p<0.01$, $n=32$ each). The absolute difference from Korotkoff's value was -0.63 ± 1.8 mmHg in SBP and -0.47 ± 5.0 mmHg in DBP.

Figure 1 shows the circadian pattern of BP in normotensives and untreated hypertensives. The circadian BP pattern in both groups showed the highest values during the day and lowest values at night. The highest values were usually found in the morning or in the afternoon and the lowest values were generally found between 2–3 am. A comparison between office BPs in hypertensives and average BPs obtained during ABPM is presented in Table I and Fig. 2. SBPOFFICE and DBPOFFICE were significantly correlated with ambulatory SBP or DBP throughout the whole day, day and night. In addition, HROFFICE was also significantly correlated with ambulatory HR during all time periods.

To determine the effect of antihypertensive medication, patients were separated into 6 groups according to office DBP, i.e., less than 90, 90–105,

Fig. 1. Circadian changes in systolic (SBP) and diastolic (DBP) blood pressure obtained by ambulatory blood pressure monitoring in normotensives (open circles) and untreated hypertensives (closed circles).

Table I. Correlation between BP Obtained in the Office and Ambulatory BP Recorded Every Hour by an Automated Device

	SBPOFFICE	DBPOFFICE	HROFFICE
SBPWHOLE	0.527**	0.304**	0.052
SBPDAY	0.577**	0.352**	0.048
SBPNIGHT	0.412**	0.231**	0.069
DBPWHOLE	0.444**	0.403**	0.110
DBPDAY	0.498**	0.437**	0.112
DBPNIGHT	0.353**	0.294**	0.115
HRWHOLE	0.080	0.227**	0.558**
HRDAY	0.086	0.209**	0.529**
HRNIGHT	0.122	0.190*	0.450**

** $p < 0.01$, * $p < 0.05$.

more than 105 mmHg, and antihypertensive drugs, present or absent. Results including normotensives are shown in Fig. 3. The difference between SBPOFFICE and SBPWHOLE or SBPDAY was about 20 or 10 mmHg in hypertensives with SBPOFFICE less than 105 mmHg, and about 30 and 20 mmHg in moderate or severe hypertensives. The difference between DBP obtained in the office and DBPWHOLE or DBPDAY was the same as in patients with DBPOFFICE less than 90 mmHg or higher by 10 or 20 mmHg in hypertensives with DBPOFFICE between 90 and 105 mmHg, or

Fig. 2. Correlation between SBP obtained in the office (SBPOFFICE) and mean SBP recorded by ambulatory blood pressure monitoring from 7 am to 10 pm (SBPDAY).

Fig. 3. Casual blood pressures obtained in the office (OFFICE) and by ambulatory blood pressure obtained during the whole day (WHOLE), the day (7 am-10 pm; DAY) and the night (0-5 am; NIGHT) in normotensives and hypertensives with or without medication. Heart rate is shown by a circle. Each value indicates the mean $\pm$ SE. ** or *: $p < 0.01$ or $p < 0.05$ vs the untreated or treated group with DBPOFFICE < 90 mmHg, ++ or +: $p < 0.01$ or $p < 0.05$ vs the untreated or treated group with DBPOFFICE between 90 and 105 mmHg, respectively.

more than 105 mmHg, respectively. Among these groups, of interest is the observation that 60% of normotensives and all of the moderate to severe hypertensives with DBPOFFICE more than 105 mmHg, whether or not treated, did show ABP of more than 150/90 mmHg at least once during 24-hour ABPM as shown in Table II. On the other hand, 34 (21.6%) of the treated hypertensive patients with office DBP less than 90 or between 90-105 mmHg respectively had ABPs less than 150/90 mmHg throughout

Table II. Number of Patients with Ambulatory BPs<150/90 mmHg and Time Points of Ambulatory BPs over 150/90 mmHg throughout the Day

DBPOFFICE	NORMOTENSIVES	HYPERTENSIVES					
		UNTREATED			TREATED		
		DBP<90	90≤DBP<105	DBP≥105	DBP<90	90≤DBP<105	DBP≥105
n	10	15	28	15	53	37	16
AGE	47.2±5.1	55.8±3.8	51.8±2.8	49.3±2.7	59.3±1.9	54.4±2.0	53.8±3.4
Number of patients who had ambulatory BPs less than 150/90 mmHg throughout the day							
	4 (40%)	3 (20%)	8 (28.6%)	0 (0%)+	18 (34%)	8 (21.6%)	0 (0%)+**
Time point of BPs more than 150/90 mmHg throughout the day							
	19/219 (8.7%)	91/246 (26.3%)	210/619* (33.9%)	168/324*** (51.9%)	282/1221 (23.1%)	327/833** (39.4%)	249/364**** (68.4%)

Each value indicates the mean ± SE. ** or * p<0.01 or p<0.05 vs the untreated or treated group with DBPOFFICE<90 mmHg, ++ or + p<0.01 or p<0.05 vs the untreated or treated group with DBPOFFICE between 90 and 105 mmHg, respectively.

Fig. 4. Percent of time points exceeding 150 mmHg in systolic blood pressure and/or 90 mmHg in diastolic blood pressure in normotensives and hypertensives divided on the basis of the presence or absence of the hypotensive agents, and level of diastolic blood pressure obtained in the office (DBP-OFFICE).

the 24-hour period. The incidence of ambulatory BPs greater than 150/90 mmHg among all readings was significantly higher in the hypertensive groups and highest in the treated group with moderate to severe hypertension. The incidence of ABP greater than 150/90 mmHg along with the clock time is shown in Fig. 4. Even in the normotensives, about half had higher BP in the evening and hypertensives had two peaks in the morning and in the evening.

Minimum BP during the night, on the other hand, is shown in Table III. To see the effect of long-acting antihypertensive medication on nighttime BP, data from hypertensives treated with nicardipine (20 mg 3 times a day) or slow-release nifedipine (10–20 mg twice a day) are shown in Fig. 5 as MBP. It is evident that nighttime BP in patients treated with nicardipine was not different from BP in hypertensives without drugs, but significantly higher compared with BP in normotensives between 2 and 7 am, while administration of long-acting nifedipine twice a day (mean dosage 27.3 ± 3.0 mg/day) decreased MBP throughout the night to levels which were not signi-

Table III. Minimum Blood Pressure and Heart Rate during the Night Obtained by ABPM

	SBP	DBP	Range	HR	Range
Normotensives	93.3±4.3	59.6±2.9	69/44-113/67	60.5±3.0	47-73
Hypertensives untreated					
DBPOFFICE<90	107.5±5.0	65.5±3.2	89/48-142/84	62.7±1.9	54-73
90≤DBPOFFICE<105	113.4±5.2**	67.9±2.0	85/48-137/83	62.3±1.5	45-80
DBPOFFICE≥105	121.9±6.2**	72.8±3.9*	89/54-147/83	63.7±2.8	47-82
Hypertensives treated					
DBPOFFICE<90	111.1±2.7**	66.1±1.7	76/45-152/82	57.1±1.2	44-69
90≤DBPOFFICE<105	120.0±2.9***	71.6±2.2***	78/46-150/96	62.2±1.9	39-83
DBPOFFICE≥105	122.8±5.6***	73.0±3.8*	80/54-153/93	63.1±3.1	47-93

Each value represents the mean ± SE.

** p<0.01 vs normotensive controls, * p<0.05 vs normotensive controls.

+ p<0.05 vs treated hypertensives with DBPOFFICE less than 90 mmHg.

Fig. 5. Circadian variations in mean blood pressure (MBP) obtained by ambulatory blood pressure monitoring in normotensives (n=10), untreated hypertensives (n=58) and hypertensives treated with either nicardipine 20 mg 3 times a day or slow-release nifedipine with a mean dosage of 27.3±3.0 mg/day (b.i.d.). The arrow indicates the time of drug administration.

ificantly different from those in normotensives.

DISCUSSION

Our study in the outpatient hypertension clinic revealed a circadian variation in BP which was higher in the daytime and lower during sleep. However, hypertensives, whether or not they were treated with hypotensive

agents, had two peaks, in the morning and in the evening. Surprisingly, normotensives, who had no history of hypertension, had BPs of more than 150/90 mmHg at least once during a 24-h period in 6 of 10 cases and a higher incidence of BP above 150/90 mmHg in the evening. This might be attributed to ABPM during the workday, because, at such times in the evening, many people are busy finishing their work at the workplace. Until now, the effect of antihypertensive drugs on BP circadian rhythm has been investigated mainly in inpatients. In such cases, daily activities in the hospital were different from those in the usual workplace.

Secondly, a significant positive correlation of BP at the office with ABPM parameters is reasonable since these arm measurements are essentially the same parameters under different circumstances. Furthermore, ABPM is very reliable in predicting the severity of hypertension, i.e., patients with moderate to severe essential hypertension with DBPOFFICE more than 90 mmHg had ABPM patterns with BP over 150/90 mmHg at least once during the 24-h period. Moreover, the difference between BP in the office and ABPM was greater in moderate or severe hypertension than in mild hypertension, 20 mmHg in SBP and 10 mmHg in DBP, similar to the findings of others.⁶⁾⁻⁹⁾

One more clinically significant role of ABPM may exist in the evaluation of the efficacy of antihypertensive medication. When DBP obtained at the office was lower than 90 mmHg and between 90 and 105 mmHg, about one-third and one-fifth, respectively, of the treated patients had BPs less than 150 mmHg systolic and/or 90 mmHg diastolic throughout the day. On the other hand, when DBP in the office exceeded 105 mmHg, none of the patients had BPs less than 150 mmHg systolic and/or 90 mmHg diastolic during the 24-h period. On the contrary, it should be noted that, even when DBPOFFICE was between 90–105 mmHg in untreated hypertensives, 28.6% had lower ABP throughout the day. Based on these observations, DBPOFFICE is not a reliable parameter for estimating overall BP control in the workplace. This was also evident from the findings that a correlation between BP at the office and ABPM is rather lower than expected. One of the reasons may be that some patients had much higher BPs in the office than at home or in the workplace, i.e., so-called white coat hypertension.^{10),11)} Our study included first-visit patients. This might be another reason, because alerting responses to a clinic visit wane on repeated measurements and BP declines with repeated clinic visits.^{6),12),13)} ABPM is, therefore, extremely effective in excluding such cases and avoiding overtreatment.

The other point to be made in our present study is that we were able to monitor nighttime BP during sleep with and without antihypertensive

medication. Of course, BP may fluctuate from beat to beat. Only 6 points during 0–5 am cannot reflect the real minimum BP at night. However, Pomidossi G et al¹⁴⁾ reported that sampling BP every 60 min could estimate the real BP level obtained by intra-arterial recordings, but not BP variability. ABPM based on one or four readings per h on 2 successive days was reported to be indistinguishable.¹⁵⁾ Thus, this time interval may be enough to evaluate the extent to which BP decreased during treatment. Some patients treated with slow-release nifedipine twice a day showed a decrease in BP during the night, while nicardipine administered 3 times a day did not produce such a change. Plasma half-life was reported to be 81 min for the latter¹⁶⁾ and 5–6 h for the former.¹⁷⁾ A greater fall not only in the daytime but also in the nighttime may be harmful to hypertensives with impaired cerebral autoregulation, especially the elderly. Although to what extent the nighttime BP should be decreased by hypotensive agents or whether overtreatment per se involves real risk of cerebral or cardiovascular accidents is not clear at present, ABPM gives us useful information in evaluating severity of hypertension and efficacy of hypotensive agents as well as in avoiding overtreatment resulting in a great fall during not only the daytime but also the nighttime.

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