AMBULATORY BLOOD PRESSURE CHARACTERISTICS-2: NORMOTENSIVES VERSUS HYPERTENSIVES

AMBULATUAR KAN BASINCI ÖZELLİKLERİ AÇISINDAN NORMOTANSİF VE HİPERTANSİFLERİN KARŞILAŞTIRILMASI

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ABSTRACT

Purpose: *Ambulatory blood pressure monitoring (ABPM) is known to be superior to a sphygmomanometer in defining the parameters of blood pressure in normotensive subjects and hypertensive patients. The aim of the present study was to compare the blood pressure characteristics in normotensive and hypertensive subjects by using ABPM devices.* ***Methods:*** *The recordings of 115 normotensive subjects and 78 untreated hypertensive patients, on whom ABPM was applied for 48 hours, were analyzed retrospectively. Rhythm analysis (peak, trough, MESOR, double amplitude, acrophase, bathyphase and slope values) were used to compare the ABPM measurements.* ***Results:*** *In both groups, SBP and DBP exhibited a clear circadian pattern with higher values during the activity period and lower values during rest. MESOR, peak and trough values of the 48-hour pattern in SBP and DBP were significantly higher in the hypertensive group than the normotensive group. The double amplitude of SBP rhythm was found to be higher in hypertensives, but DBP was not different significantly between the two groups.* ***Conclusion:*** *Understanding and analyzing ABPM data in hypertensive patients may help in defining limits for cardiovascular risk and also in developing efficient treatment strategies.*

Key Words: *Ambulatory Blood Pressure, Rhythm, Hypertensives.*

ÖZET

Bu çalışmada, hipertansif hastalar ve normotansif kişilerin ambulatuar monitörler (ABPM) ile elde edilen kan basıncı profilleri ritim karakteristikleri (MESOR, doruk ve çukur değerler ile bu değerlerin ortaya çıkma zamanı, ritmik genlik, ve kan basıncı ritmindeki sabah artışının ve akşam azalışının eğimleri) açısından karşılaştırılmıştır. Bu amaçla, Gazi Üniversitesi Tıp Fakültesi Kardiyoloji ve Farmakoloji Anabilim dallarında 48 saat süreyle ABPM kayıtları bulunan 115 normotansif ve 78 hipertansif kişinin sistolik (SBP) ve diastolik kan basıncı (DBP) profilleri kullanılmıştır. Her iki grupta da SBP ve DBP belirgin bir gün-içi ritmisite göstermiştir. Hipertansif grupta hem sistolik hem de diastolik profillerin MESOR ile doruk ve çukur değerleri normotansif gruba nazaran daha yüksek bulunmuştur. Hipertansiflerde SBP genliğinin normatansiflere nazaran daha yüksek olduğu saptanmiş, ancak DBP için iki grup arasında anlamlı bir fark bulunmamıştır. ABPM kayıtlarına dayanan bilgilerin klasik ölçümlere nazaran kardiyovasküler risk hakkında daha fazla bilgi sağlayacağı ve yeni tedavi stratejileri geliştirilmesine yardımcı olacağı düşünülmektedir.

Anahtar Kelimeler: *Ambulatuar Kan Basıncı, Ritim, Hipertansifler.*

INTRODUCTION

There is no absolute quantitative definition about the normal limit of blood pressure (BP), and the diagnosis of hypertension is mainly based on the results of epidemiological studies which defined the risk between increased BP level and morbid cardiovascular events. According to the JNC-VI (1), BP values of equal or less than 130 and 85 mmHg are the limits of normotension for systolic (SBP) and diastolic (DBP) pressures, respectively (1). However, these limits are not precisely descriptive enough due to the predictable rhythmic fluctuations in the BP

profile throughout the 24-hour day.

Both in normotensive and hypertensive subjects, BP is characterized by a clear circadian pattern over 24 hours. In day-active subjects, both SBP and DBP tend to peak during the hours after awakening, remain high during the activity period (daytime) and fall to a trough value around midnight (2). This variability in BP throughout the day can serve for diagnostic purposes. Ambulatory blood pressure monitoring (ABPM) devices are used to measure BP repeatedly for 24-hour or longer periods. These are easily carried, automated devices, capable of obtaining and storing the results of repeated BP and heart rate without preventing people from performing their ordinary daily functions. These devices are increasingly used in clinical trials and are particularly important in the determination of white coat effect and dipping status (3).

In this study we compared the circadian rhythm characteristics of the BP of normotensive subjects and newly diagnosed hypertensive patients.

SUBJECTS AND METHODS

Subjects

This is part of a cohort study designed for the assessment of the prognostic values of ambulatory BP recordings for the development of cardiovascular events. The ABPM recordings of 115 normotensive subjects (26 men, 89 women, mean age±SEM was 40.8±1.1) and 78 newly diagnosed hypertensives (32 men, 46 women, mean age±SEM was 51.9±1.4) were analyzed retrospectively for BP characteristics. Any subject with a known history of cardiovascular events or any significant systemic disease was excluded from the study.

Measurement of blood pressure

Office BP measurements were obtained by sphygmomanometry in a sitting position at least twice on different days of the same week. ABPM devices (Model 90207, Spacelabs, Inc. Redmond, Washington) were attached to a waist belt and the subject wore an arm cuff of appropriate size on the non-dominant arm, which is inflated automatically at programmed intervals over 48 hours. The devices were programmed to measure SBP and DBP every 20 minutes from 06:00 to 24:00 and every 30 minutes from 00:00 to 06:00. Subjects were instructed not to restrict their usual routine daily activities except for staying motionless during measurements, if possible. Since movements of the equipment-applied arm can result in errors, all ambulatory blood pressure monitoring data were screened for error readings and subjects with successful readings of less than 80% were excluded from the study.

The subjects were requested to keep a diary for their bed and wake-up times. Each 24 hours was divided into activity and resting spans based on a subject's diary data. The reference time (zero) was taken as the awakening time based on diary records.

Originally, ABPM data were used to the assessment of normotensive and hypertensive groups. Subjects were accepted as hypertensive if his/her mean SBP/DBP values were higher than 140/90 mmHg in the activity period and 125/75 in the resting period and 135/85 within 48 hours. Conversely, subjects were considered as normotensive if his/her mean SBP/DBP values were less than 135/85 mmHg in the activity period, 120/70 in the resting period and less than 130/80 within 48 hours. Subjects whose BP values confined in between these limits during the corresponding periods were considered "borderline" and were excluded in the study.

Data analysis

The stored data in the solid-state memory of the devices were downloaded from the monitors into the Ambulatory Blood Pressure Report Management System software (Spacelabs, Inc. Redmond, Washington, version 1.0308) and the rhythmic patterns of blood pressure were analyzed by using partial Fourier analysis. The significance of best fit was estimated by zero-amplitude test (F-statistics) by using the ABPM-FIT program (University of Heidelberg, Germany, version 2.2) (4). The rhythm characteristics estimated from the fitted Fourier curves were Peak (maximum value), Trough (minimum value), MESOR (Midline Estimating Statistic of a Rhythmic Function) (rhythm-adjusted mean), Double amplitude (the difference between minimum and maximum levels), Acrophase (time of peak), Bathyphase (time of trough), and the slopes of the morning rise and evening dip. Slopes were calculated for periods of ± 3 hours at bed and wake-up time points. All

data were analyzed separately for each individual and the results were expressed as mean±SEM. Comparisons were performed by the Mann-Whitney U test and $p<0.05$ was considered statistically significant.

RESULTS

Chronobiologically, 48 hour continuous monitoring of BP profiles is recognized as being more reliable than 24-hour monitoring (5). To avoid "between-day" variances, the data of consecutive days are analyzed separately and then compared to each other. In this study, the 24-hour mean values of the SBP for the first and second days were compared to determine whether a difference was present between the days. No statistically significant difference in the mean values of SBP was found in these subjects.

In both groups, SBP and DBP exhibited a clear circadian pattern with higher values during the activity period and lower values during rest. For the sake of clarity, only the circadian profile of the SBP is shown in Figure 1.

Ambulatory rhythm characteristics estimated from the fitted Fourier curves for SBP and DBP are presented in Table 1. Rhythm analysis of the data showed that MESOR, peak and trough values of the 48-hour pattern in SBP and DBP were significantly higher (more than 20%) in the hypertensive group than in the normotensive group. On the other hand, the double amplitude of SBP rhythm was found to be higher in hypertensives, but DBP was not different significantly between two groups (Table 1).

The acrophase and bathyphase of SBP and DBP were found to occur nearly in the same time period for the normotensive and hypertensive groups. There was a statistically significant time

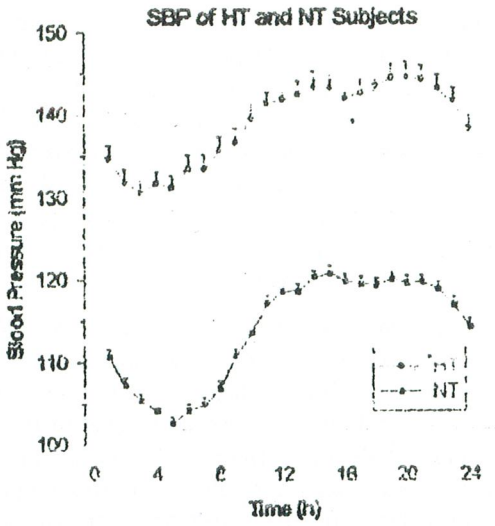

Fig. 1: 24-hour variations in systolic blood pressure (SBP) in normotensive and hypertensive subjects. Each point represents hourly means of the first day and the second day. Values are presented as mean ± SEM. "0" point on x-axis corresponds to the average wake-up time.

advance in the acrophase of SBP rhythm (around an hour). Even though the bathyphase of DBP rhythm in both groups displayed a considerable time delay, no statistically significant difference was found between the normotensive and hypertensive groups (Table 1).

Interestingly, the absolute slope of the morning rise for SBP and DBP were found to be significantly lower in the hypertensive group than in the normotensive group (Table 1). There was no difference in the slopes of the evening dip for SBP and DBP between these two groups of subjects.

DISCUSSION

This study confirmed the well-known 24-hour variation of SBP and DBP in healthy

Table-1: Rhythm analysis of 48-hour ABPM data in normotensive and hypertensive subjects. Results are presented as means of the first and the second days and are expressed as mean ±SEM.

	SBP		DBP	
	NT	HT	NT	HT
Peak (mmHg)	124.9 ± 0.8	152.5 ± 1.6*	80.4 ± 0.6	96.3 ± 1.1*
Trough (mmHg)	100.3 ± 0.7	124.1 ± 1.4*	58.0 ± 0.5	74.0 ± 1.0*
Acrophase (hr) 1	15:44 ± 0:21	14:46 ± 0:37*	15:05 ± 0:24	14:27 ± 0:32
Bathyphase (hr) 1	04:25 ± 0:17	06:45 ± 0:42	04:35 ± 0:24	07:20 ± 0:49
Double Amplitude (mmHg)	24.6 ± 0.7	28.5 ± 1.4*	22.4 ± 0.5	22.3 ± 1.1
Morning Slope (mmHg/hr)	3.8 ± 0.2	2.2 ± 0.4*	3.3 ± 0.2	1.8 ± 0.3*
Evening Slope (mmHg/hr)	-3.5 ± 0.2	-3.6 ± 0.3	-3.4 ± 0.1	-3.1 ± 0.2
MESOR (mmHg)	113.9 ± 0.7	138.8 ± 1.3*	70.2 ± 0.5	85.8 ± 0.9*

(SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, NT: Normotensive, HT: Hypertensive)
1 values are presented as the clock time,
*$p<0.05$ significantly different from the corresponding normotensive value

subjects and hypertensive patients with higher daytime values than night time (Fig. 1). The circadian rhythm of BP in the hypertensive group has the same circadian time pattern as the normotensives, but set at higher levels. MESOR, the rhythm adjusted 24-hour mean, peak and trough values of the hypertensive group were found to be more than 20% higher than normotensives (Table 1).

The importance of hypertension as the cause of cardiovascular morbidity and mortality is well recognized. Since there is no absolute quantitative limit for the normal level of blood pressure (BP), the definition of hypertension is mainly based on the results of epidemiological studies that defined the risk between increased BP levels and morbid cardiovascular events. According to current knowledge (JNC), BP values higher than 130/85 mmHg for systolic/diastolic pressures at office measurements are considered the danger limits for provisional end organ damage due to high BP levels.

Conventionally, the diagnosis of hypertension is mainly based on the repeated office measurements of BP on at least three successive occasions using classical sphygmomanometers. However, BP is a non-stable cardiovascular indicator that can display fluctuations due to emotional and clinical state, measurement technique, and time of the measurement, i.e. circadian rhythmicity. The concept of circadian BP variability has long been recognized, but only during the last two decades has ABPM technology allowed us a more complete understanding of the 24-hour BP pattern. Ambulatory monitoring of BP has some advantages when compared to conventional sphygmomanometric measurements performed by an arm cuff and a stethoscope. Data obtained by ABPM are highly reproducible (6, 7), capable of describing circadian variation in BP (6), devoid of observer bias and error (3, 8, 9), and are helpful in assessing the white-coat effect (10).

The circadian acrophase was estimated as the timing of the highest activity in the rhythm profile obtained by Fourier analysis and expressed as the time lag between midnight and the time when peak values occurred. Although several authors (11, 12) have reported that there is no change in the staging of BP rhythm in both normal and hypertensive subjects, we found in this study that acrophase in the hypertensive group displayed a time advance of around an hour than in the normotensives. This difference may be due to the relatively older age of our hypertensive group than those in the normotensive group. A phase advance in BP rhythm in relation with aging has also been reported (13).

BP values have been found to be at their lowest 2-4 hours before waking (14). The pressure starts to rise just before waking and increases sharply in the first hours of the activity span, and reaches a plateau 1-2 hours after waking (14). It is commonly considered that arousal and the beginning of daily physical activity significantly contribute to the morning rise in BP (2). The sharp increase of BP at the commencement of daily activity has been noted to be responsible for some cardiovascular events (15).

An interesting finding of this study is that the morning rise of SBP and DBP was significantly steeper in the normotensive group than in the hypertensive group. The reverse pattern was, in particular, expected for SBP rhythm since the double amplitude was found to be relatively greater in the hypertensive group. The only explanation could be the significant age difference between our study groups. There is no report yet on the age-dependent changes in the slopes of the morning rise and evening dip of the BP profile.

In conclusion, hypertension contributes to negative outcomes on the cardiovascular system. It might aggravate various clinical conditions such as retinopathy, nephropathy, coronary heart disease, atherosclerosis, stroke and central nervous system dysfunction. BP is often assessed by office determinations, and may be erroneous due to the rhythmic nature of BP. The possibility of monitoring arterial BP over the entire day offers advantages in the diagnosis and treatment of hypertension. Information on the circadian characteristics of BP both in normal and pathological conditions would help us in understanding the underlying mechanisms and preventing further cardiovascular events. It has also been demonstrated that ABPM can serve as a better indicator for assessing hypertensive end organ damage than sphygmomanometric office

measurements (16-20). Such studies will further help in defining the BP limits for cardiovascular risk.

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