LOAD limits for ambulatory pulse pressure and double product in normotensive and hypertensive subjects

Normotansif ve hipertansif bireylerde ambulatuvar nabız basıncı ve ikili ürün LOAD limitleri

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ABSTRACT

Objective: The aim of this study was to to determine possible daytime (awake hours) and nighttime (sleeping hours) LOAD limits for ambulatory pulse pressure (PP) and double product (DP) in hypertensive (HT) subjects and secondly to assess whether there were significant differences in the LOAD values between hypertensive (HT) and normotensive (NT) subjects.

Methods: Seventy-eight untreated essential HT (46 female, 32 male; mean age 51.9±1.4 years) and 115 NT (89 female, 26 male; mean age 40.8±1.1 years) subjects participated in this study. Ambulatory blood pressure monitoring (ABPM) devices were applied to these subjects for 48 hours. Different possible ambulatory PP LOAD limits between 40 and 55 mmHg with 5 mmHg increments and ambulatory DP LOAD limits between 6000 and 12000 mmHg.beats/min with 1000 mmHg.beats/min increments were used. Then according to these limits, LOAD values of NT and HT subjects have been assessed for daytime, nighttime and 48 hours.

Results: There were significant differences between NT and HT subjects in all the values for both ambulatory PP and DP. Although mean (total, day and night mean) values of HT subjects were higher approximately by 20% than of NT subjects, LOAD values for ambulatory PP in HTs were 33%-415% higher than in NTs ($p<0.001$). Hypertensive subjects' mean (total, day and night mean) values of DP were by 23%-33% higher than NTs values, but LOAD values for ambulatory DP in hypertensives were approximately 43%-673% higher than in NT subjects ($p<0.001$).

Conclusions: We showed that although there were significant differences in the 48- hour, daytime and nighttime PP and DP means between NT and HT subjects, these differences became more prominent when possible LOAD limits were used for ambulatory PP and DP, One of these possible ambulatory PP and DP LOAD limits can be used in the clinical settings if a relationship with the end-organ damage will be showed by further studies. *(Anadolu Kardiyol Derg 2006; 6: 322-6)*

Key words: Ambulatory blood pressure monitoring, pulse pressure, double product, LOAD

ÖZET

Amaç: Bu çalışmanın amacı hipertansif ve normotansif bireyler arasında ambulatuvar nabız basıncı (PP) ve ikili ürün (DP, kalp hızı x sistolik kan basıncı) parametrelerinin tanımlanan bir zaman biriminde belli limitlerin üzerindeki ölçüm oranı olarak bilinen LOAD değerlerinin karşılaştırılmasıdır.

Yöntemler: Yetmiş sekiz yeni tanı konulmuş esansiyel hipertansiyon (HT) (46 kadın, 32 erkek; ortalama yaş: 51.9±1.4 yıl) ve 115 normotansif (NT) birey (48 kadın, 26 erkek; ortalama yaş: 40.8±1.1 yıl) çalışmaya alındı. Ambulatuvar kan basıncı monitörizasyonu (ABPM) 48 saat süreyle yapıldı. Kırk beş ile 55 mmHg arasında 5 mmHg aralıklı farklı muhtemel nabız basıncı LOAD limitleri ve 6000 ile 12000 mmHg.atım/dk. arasında 1000 mmHg.atım/dk. aralıklı ambulatuvar ikili ürün LOAD limitleri kullanıldı. Bu limitlere göre NT ve HT bireyler için LOAD değerleri gündüz, gece ve 48 saatlik zaman süreleri için ölçüldü.

Bulgular: Normotansif ve HT bireyler arasında hem ambulatuvar PP; hem de DP yönünden anlamlı bir fark bulundu. Hipertansif olanlarda ortalama PP (toplam, gündüz ve gece için) değerleri NT bireylere göre %20 yüksek olmasına karşın, HT olanlarda ambulatuvar LOAD değerleri NT bireylere göre %33-415 daha yüksekti ($p<0.001$). İkili ürün değerleri de HT olanlarda NT bireylere göre %23-33 daha yüksek olmasına karşın DP için LOAD değerleri karşılaştırıldığında HT olanlarda NT bireylere göre yükseklik %43-673 idi ($p<0.001$).

Sonuç: Normotansif bireyler ve HT olanlarda 48 saatlik, gündüz ve gece PP ve DP yönünden anlamlı farklılık olmasına karşın, PP ve DP için muhtemel LOAD limitleri kullanıldığında bu farklılık çok daha belirginleşmektedir. Ambulatuvar nabız basıncı ve DP LOAD limitlerinin klinik önemi ve uç organ hasarı ile ilişkili olup olamayacağı ileriki çalışmalarla ortaya konulmalıdır. *(Anadolu Kardiyol Derg 2006; 6: 322-6)*

Anahtar kelimeler: Ambulatuvar kan basıncı monitörizasyonu, nabız basıncı, ikili ürün, LOAD

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Introduction

It is known that pulse pressure (PP), the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP), is an independent predictor of increased artery stiffness and high cardiovascular risk (1, 4). Although several studies have shown that assessment of blood pressure (BP) by using ambulatory blood pressure monitoring (ABPM) was superior method than office measurements, there are only few studies addressed to investigate the relationship between ambulatory pulse pressure (PP) and its possible clinical meaning. Double Product (DP, mmHg.beats/min) is the multiply of two hemodynamic parameters, namely, systolic blood pressure and heart rate and it is a valuable index of myocardial oxygen consumption which parallels silent myocardial ischemia (5, 6). It has been also shown that LOAD (ratio of measurements over the described limits in a definite time) values, which were defined for systolic (SBP) and diastolic (DBP) blood pressures are important since they can describe end organ damage better than mean values (7, 8). But, there can be some limitations of these values, so alternative parameters to determine 24-h blood pressure profile have been studied (9, 10).

However, to our knowledge, LOAD values for ambulatory PP and DP have not been investigated yet.

Thus, in this study we aimed first to find out some possible daytime (awake hours) and nighttime (sleeping hours) LOAD limits for ambulatory PP and DP and secondly determine whether there were significant differences in the LOAD values between hypertensive (HT) and normotensive (NT) subjects.

Methods

Subjects

All subjects were examined by a physician after taking a full medical history. Laboratory tests (serum urea and creatinine; urinary analysis); electrocardiography and telecardiography were performed to exclude secondary causes of hypertension. The subjects with clinical or laboratory evidence of coronary artery disease and diabetes mellitus were excluded from the study. The hypertensive patients who have taken an antihypertensive agent in the last 2 weeks were also excluded. Two hundred and twenty-eight subjects participated in this study. We used the limits proposed by Staessen for the definitions of hypertension and normotension (11). A subject was accepted as HT if one of her/his average values were higher than 140/90 in daytime, 125/75 in nighttime and 135/85 mm Hg in 48-hour for the (SBP) and (DBP), respectively. The NT was defined if all of her/his average values were below 135/85 in daytime, 120/70 in nighttime and 130/80 mm Hg in 48 h. The subjects whose values were between these criteria were accepted as borderline and were excluded from the analyses (n=35).

Measurement of Blood Pressure

The ABPM devices (Model 90207 Spacelabs, In. Redmond, Washington, USA) were attached to a waist belt and the subjects wore an arm cuff of appropriate size at the non-dominant arm. Devices were programmed to measure SBP, DBP, PP and HR every 20 min. from 06:00 to 24:00 and every 30 min. from 00:00 to 06:00. Subjects were instructed not to restrict their daily life activity except for staying motionless during measurements, if possible.

Data Analysis

Daytime (awake hours) and nighttime (sleeping hours) were determined by using personal sleep-awake time and to validate accuracy of these times, actigraphs (Mini-mitter model AW64, Sunriver, Oregon, USA) were also applied to a subgroup of subjects (n=50).

The stored data in the solid-state memory of the ABPM devices were downloaded from the monitors into the "Ambulatory Blood Pressure Report Management" software (version 1.0308, Spacelabs, In. Redmond, Washington, USA). All ABPM data were screened for erroneous readings and subjects with successful readings less than 80% were excluded.

Data from 78 essential HT (46 female, 32 male; mean age - 51.9±1.4 years) and 115 NT (89 female, 26 male; mean age 40.8±1.1 years) subjects were analyzed separately for each individual. Mean values of SBP, DBP, HR, PP and DP for 48 hours, daytime, and nighttime were calculated. Different possible ambulatory PP LOAD limits between 40 and 55 mmHg with 5 mmHg increments and ambulatory DP LOAD limits between 6000 and 12000 mmHg.beats/min with 1000 mmHg.beats/min increments, were used and then assessed for daytime and nighttime separately. We preferred these possible limits, because they were close to either daytime or nighttime means' of the NT or HT subjects ambulatory measurements. LOAD values and means of daytime, nighttime and 48 h were calculated as the mean of two days.

Values were expressed as mean ± SEM. The differences between groups were assessed by using Mann Whitney U Test and a ``p`` value <0.05 was considered statistically significant.

Results

The main characteristics of the population studied are given in Table 1. Twenty five percent of NT subjects and 17 percent of HT subjects were smokers. Hypertension history in first degree relatives was 38% in NT subjects and 34% in HT ones. Significant correlation was established between actigraphy and diary time points in a subgroup of subjects ($r=0.81$, $p<0.001$ for go-to-bed; $r=0.78$, $p<0.001$ for wake-up). Thus, data in the personal diaries were used for go-to-bed and wake up times to define the personal daytime and nighttime.

It was found that there was a statistical difference between all the values of NT and HT subjects for ambulatory PP and DP ($p<0.001$; Table 2). However, these differences were noted more clearly when the limits for LOAD values were used for ambulatory PP and DP ($P<0.001$; Figure 1, 2). Mean (total, day and night) values for ambulatory PP in hypertensive subjects were approximately 20% higher than in normotensives, but LOAD values for ambulatory PP in hypertensives were approximately 33%-415% higher than in normotensives ($p<0.001$). Mean (total, day and night mean) values for ambulatory DP in 48-hour measurement in hypertensive subjects were 23%-33% higher than in normotensive ones, but hypertensive LOAD values for ambulatory DP were approximately 43%-673% higher than in normotensives ($p<0.001$).

Discussion

Several studies have shown that ambulatory blood pressure monitoring is a better method in the assessment of hypertension than office measurements (12-15). Ambulatory blood pressure monitoring also offers a more valid assessment of an individual's true blood pressure level (12, 13).

White et al. (8) have suggested that systolic and diastolic BP LOAD's were better correlated with cardiac target organ involvement than 24-hour average BP measurements. Also, LOAD values were proposed to characterize the primary or secondary hypertension (16). Previous studies have usually used 24-hour ABPM for BP changes (3, 7, 23). But there can be some limitations of these values, so alternative parameters to determine 24-hour BP profile have been studied (9, 10). Since PP (17-20) and DP (6) have been shown as important parameters in the assessment of the target organ damage in cardiovascular diseases, we aimed first to find out some possible daytime (awake hours) and nighttime (sleeping hours) LOAD limits for ambulatory PP and DP and secondly determine whether there was a significant difference in the LOAD values between hypertensive (HT) and normotensive (NT) subjects. We preferred 48-hour ABPM to increase the accuracy of data analysis, as it was suggested by Tamura and Mochizaki (24, 25).

Ambulatory pulse pressure has recently been reported as an important prognostic factor in cardiovascular disease [17-20]. It is a pulsatile component of blood pressure. Major determinants of PP are ventricular ejection interacting with the viscoelastic properties of the large arteries and wave reflection (20). Ambulatory pulse pressure increases from central to peripheral arteries as a consequence of a substantial increase in SBP and a slight lowering of DBP. The mechanisms influencing PP are related to the status of conduit arteries, that is, the viscoelastic properties of the arterial wall and timing of the reflected waves (20, 21). Increased stiffness and earlier wave reflections within the thoracic aorta increase the PP due to an increase in SBP and a decrease in DBP (20). It was shown that the widest PPs were due to both an increase in SBP and a decrease in DBP [22]. In our

Table 1. Demographic properties of the population studied

Parameters	Normotensives (n=115)	Hypertensives (n=78)
Age, years	40.7 ± 1.1	52.0 ± 1.4
Gender, M/F	25 / 90	32 / 46
Height, cm	162.0 ± 0.8	163.0 ± 1.0
Weight ,kg	68.8 ± 1.3	73.4 ± 1.3
Smokers, %	25.2	18.0
Hypertension history in first degree relatives, %	38.3	34.6

Data are expressed as mean ± SEM
F- female, M- male

Table 2. Mean values of 48-hour, daytime, and nighttime values of ambulatory blood pressure monitoring

Parameters	Normotensives (n=115)	Hypertensives (n=78)
SBP Office, mmHg	121 5 ± 1 2	148 8 ± 1 4*
48-hour, mm Hg	113 6 ± 0 7	138 8 ± 1 3*
Daytime, mm Hg	118 4 ± 0 7	142 3 ± 1 5*
Nighttime, mm Hg	104 5 ± 0 7	131 6 ± 1 4*
DBP Office, mmHg	79 2 ± 0 8	95 6 ± 1 0*
48- hour, mm Hg	70 0 ± 0 5	85 9 ± 0 9*
Daytime, mm Hg	74.4 ± 0.5	89.3 ± 1.0*
Nighttime, mm Hg	61.7 ± 0.5	79.4 ± 1.0*
PP 48- hour, mm Hg	43.6 ± 0.5	52.8 ± 1.0*
Daytime, mm Hg	44.0 ± 0.5	53.1 ± 1.0*
Nighttime, mm Hg	42.9 ± 0.5	52.2 ± 1.0*
DP 48-hour, mm Hg.beats/min	8458.7 ± 91.5	10655.5 ± 182.5*
Daytime, mm Hg.beats/min	9378.6 ± 98.7	11504.3 ± 197.6*
Nighttime, mm Hg.beats/min	6728.1 ± 86.6	8968.0 ± 159.9*

Data are expressed as mean ± SEM;
*- differences are significant, p< 0.001
DBP- diastolic blood pressure, DP- double product,; PP- pulse pressure,
SBP- systolic blood pressure

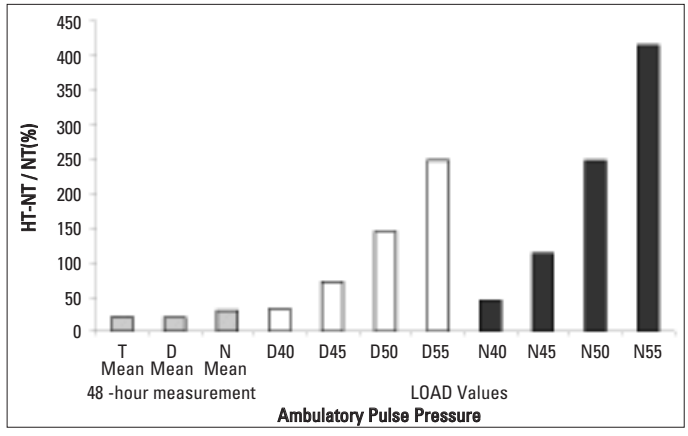

Figure 1. Means of 48- hour measurement and representative LOAD values are shown as the ratio of the difference between hypertensive (HT) and normotensive (NT) subjects to the NT

D- daytime, i.e. D45: ratio of LOAD limit for 45 mmHg for daytime period, N- nighttime, T- total

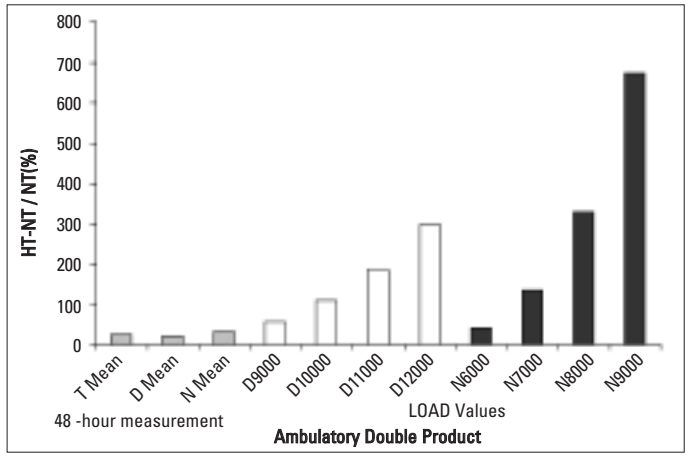

Figure 2. Means of 48-hour measurement and representative LOAD values are shown as the ratio of the difference between hypertensive (HT) and normotensive (NT) subjects to the NT

D- daytime, i.e. D9000: ratio of LOAD limit for 9000 mmHg.beats/min for daytime period, N- nighttime, T- total

study 48 h, daytime and nighttime mean PP values were significantly higher in HT group (Table 2).

Verdecchia et al. have reported that ambulatory PP is a potent independent predictor of total cardiovascular risk in untreated essential hypertension (2). Mancia et al. have also emphasized PP can be related to the target organ damage (3). To investigate the prognostic value of ambulatory PP, Verdecchia et al. studied 2010 initially untreated and uncomplicated subjects with essential hypertension from the PIUMA database (2). They concluded ambulatory PP appeared to provide a more precise estimate of cardiovascular risk. They also emphasized that an average 24-hour PP of >53 mmHg could identify a high cardiovascular risk. However, to our knowledge, none of previous studies has addressed the LOAD values for ambulatory PP assessment. In our study, we examined possible LOAD values for ambulatory PP. In addition to previous studies, we showed that although there were approximately 20% differences between 48 h, daytime and nighttime means of the ambulatory PP of NT and HT subjects, when LOAD values were used, these differences became more prominent with the higher LOAD limit.

Major cardiac events including acute myocardial infarction, unstable angina pectoris and sudden death follow a circadian pattern, and occur during the first hour before and the 3 h after awakening (26). In this time period, heart rate and SBP are reported to increase (3, 5, 20). White (5) has reported that verapamil exerted beneficial effects for the treatment of increases in ambulatory DP. Double product, the multiply of heart rate and SBP, strongly correlates with myocardial oxygen consumption. Myocardial oxygen consumption reflects the load on the heart. Several epidemiologic studies have shown that rising heart rate was closely related with increased cardiovascular mortality (26, 27). Deedwania et al have reported that many of myocardial ischemic events were preceded by a nearly 20% increase in the DP approximately 5 min before onset of ST-segment depression (28). Azevedo et al. suggested that ambulatory DP was a more accurate parameter compared to the mean daily BP values in the assessment of the target organ damage (6). Although it is difficult to measure DP directly, it is easy to assess it by analyzing data, which are provided by ABPM as in this study. None of previous studies were investigated the ambulatory DP LOAD values. We found that there were significant differences between all the values of NT and HT subjects for ambulatory DP and these differences were seen clearly when the LOAD limits were used for ambulatory DP assessment.

Conclusion

We showed that, for all the different possible LOAD limits for ambulatory PP and DP there were significant differences between hypertensive and normotensive subjects. When these limits were used for ambulatory PP and DP, the discrimination between NT and HT groups have become more prominent. Thus, it is possible to use one of these limits as LOAD limit for ambulatory PP and DP. In another study, the relationship between these possible ambulatory PP and/or DP LOAD values and target organ damage must be investigated to find out, which one is the most valuable in clinical practice. Further studies are needed to determine the clinical importance of the ambulatory PP and DP LOAD limits.

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