Sleep-Wakefulness Variations in Arterial Stiffness: Assessment Using Ambulatory Recording of Arterial Pulse Transit Time

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Introduction and objectives. The incidence of cardiovascular events is related to the sleep–wakefulness cycle. In particular, the magnitude and speed of the changes in hemodynamic variables that occur during transitions between wakefulness and sleep and between sleep and wakefulness are regarded as factors that either predict or determine target organ damage and cardiovascular risk. Although increased arterial stiffness (AS) is associated with the development of cardiovascular abnormalities, it is not known whether there exist any changes in AS that are associated with circadian variations in the incidence of cardiovascular events. The aims of this study were to assess AS in healthy subjects over a 24-hour period, to characterize any differences that occur between sleep and wakefulness, and to investigate any changes in AS that occur during the transition from wakefulness to sleep or from sleep to wakefulness.

Methods. Twenty healthy volunteers with a dipper circadian blood pressure pattern underwent 24-hour ambulatory monitoring of blood pressure, heart rate and AS. In practice, AS was determined using the aorta-brachial pulse transit time and fractional pulsatility indices. Myocardial oxygen consumption was quantified using the double product (DP). An average was calculated for all variables for periods of sleep (23:00 to 06:00) and wakefulness (8:00 to 21:00) and for transitions from wakefulness to sleep (20:00 vs 02:00), and from sleep to wakefulness (06:00 vs. 10:00 hours).

Results. In complete contrast to DP, AS was greater during sleep than wakefulness ($P<.05$). Moreover, the changes in AS that occurred during transitions from wakefulness to sleep and from sleep to wakefulness were the opposite of those observed in DP ($P<.05$).

Conclusions. Arterial stiffness was greater during sleep than wakefulness, increased during the transition from wakefulness to sleep, and decreased during the transition from sleep to wakefulness.

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Variaciones sueño-vigilia de la rigidez arterial: estudio mediante registro ambulatorio del tiempo de tránsito de la onda de pulso

Introducción y objetivos. La incidencia de complicaciones cardiovasculares guarda relación con el ciclo sueño-vigilia. Particularmente, la magnitud y la velocidad de cambio de variables hemodinámicas durante los períodos de transición entre vigilia y sueño se consideran factores pronósticos y/o determinantes de daño de órgano diana y riesgo cardiovascular. Si bien los aumentos en la rigidez arterial (RA) se asocian a desarrollo de alteraciones cardiovasculares, se desconoce si existen variaciones en la RA con relación al patrón circadiano de incidencia de eventos cardiovasculares. El objetivo fue analizar la RA en sujetos sanos durante 24 h y caracterizar las potenciales diferencias entre sueño y vigilia y los cambios en la RA durante la transición de vigilia a sueño y de sueño a vigilia.

Métodos. En 20 voluntarios sanos con patrón *dipper*, se realizó durante 24 h monitorización ambulatoria de presión arterial, frecuencia cardiaca y RA. La RA se evaluó mediante el tiempo de tránsito de la onda de pulso aortobraquial e índices de pulsatilidad fraccional. Se cuantificó el consumo miocárdico de oxígeno mediante el doble producto (DP). Se promediaron las variables para el sueño (de las 23.00 a las 6.00), la vigilia (de las 8.00 a las 21.00) y las transiciones vigilia-sueño (a las 20.00 frente a las 2.00) y sueño-vigilia (a las 6.00 frente a las 10.00).

Resultados. Contrariamente al DP, la RA fue mayor durante el sueño que en la vigilia ($p < 0,05$). La RA varió en forma opuesta al DP durante las transiciones vigilia-sueño y sueño-vigilia ($p < 0,05$).

Conclusiones. La RA fue mayor durante el sueño que en la vigilia, aumentó durante la transición vigilia-sueño y disminuyó durante la transición sueño-vigilia.

Palabras clave: *Investigación básica. Ritmo circadiano. Rigidez arterial.*

ABBREVIATIONS

AS: arterial stiffness
DBP: diastolic blood pressure
DP: double product
HR: heart rate
MBP: mean blood pressure
PP: pulse pressure
PTTAB: aorta–brachial pulse transit time
SBP: systolic blood pressure

INTRODUCTION

The frequency of cardiovascular events is closely related to sleep-cycle patterns, with low frequency during sleep and maximum frequency during the mornings.[1] Although several factors (eg, increased blood pressure in the morning) have been proposed to explain the circadian pattern of frequency of events,[1] the determinants have not been entirely explained. In this respect, It is known that increased arterial stiffness (AS) plays an important role in the increase in age-related cardiovascular risk and hypertension,[2,3] but it is not known whether circadian variations in AS are related to the circadian pattern of the frequency of cardiovascular events.

The size and speed of changes in blood pressure and the heart rate (HR) during transition period between wakefulness-sleep and sleep-wakefulness are modified by different diseases and may be prognostic and/or determining factors in target organ damage and cardiovascular risk.[4,5] Furthermore, quantifying myocardial oxygen consumption has been recommended (via calculation of the "double product" [DP]), because it has been seen to increase during the morning, as a prognostic factor of myocardial ischaemia, regardless of systolic blood pressure (SBP), and the HR reached.[6] In this case, awareness of the variations in AS during the transitional period mentioned would allow important information about the cardiovascular system to be obtained, in periods of important hemodynamic changes.

AH depends on blood pressure, the HR, and smooth arterial muscle tone.[2,7,9] It is known that the increases in SBP could determine increases in AS when the artery distends and causes it pulsate in an area with a higher pressure/diameter^2 ratio, but this is subject to establishing whether the magnitude of the circadian changes in SBP of normotensive individuals determines changes in AS. In this respect, given that healthy arteries, in normotensive conditions, work in an almost lineal zone of pressure/arterial^2 diameter, circadian variations in the SBP might not determine significant changes (pressure-dependent) in AS. Furthermore, increases in HR could lead to an increase in the viscous response of the arterial wall (response determining the velocity) that determines greater dynamic resistance to deformation[7] and, consequently, greater AS, but it is not clear whether circadian cycles in the HR modify the AS. Finally, it is not known whether circadian cycles in smooth arterial muscle tone, related, for example, to the variations in plasma values of vasoactive substances, or in the activity of the sympathetic system may determine changes in AS.

In this context, the purpose of the work was to analyse the AS of healthy subjects during a 24-hour period and characterise potential differences in the AS between the period of sleep and waking and the changes in AS during the waking-sleeping and sleeping-waking transitions. In addition, the changes in blood pressure, HR and DP were characterised to analyse the relationship between the changes in these variables and in AS.

METHODS

Population Studied

A total of 20 healthy subjects (10 men), normotensive and with a dipper-type pressure pattern (Table 1).[10,11] The inclusion criteria were absence of family history of diabetes, smoking and dyslipidemia, and family history of early-onset cardiovascular disease. No individuals were receiving pharmacological or vitamin or nutritional supplements, and none reported the symptoms of sleep disorders. The study was conducted in accordance with international human research guidelines.

Outpatient Registers

During a day of normal activity, each individual's blood pressure was monitored on an outpatient basis, using the Diasys-Integra II (Novacor, Paris, France) device.[3,10,12] Following international recommendations,[11] their blood pressure readings, HR, and aorta-brachial pulse transit time (PTTAB) were taken every 15 min between 8.00 and 23.00, and every 30 min between 23.00 and 8.00. The body position sensor of the equipment enabled us to exclude from the night time period the readings not taken in a decubitus position. Each subject completed a diary of activities of the times when they went to bed, slept, woke up, got up, eat, and any other event capable of affecting the readings was entered.

TABLE 1. **Characteristics of the Population Studied (Average [Standard Deviation])**

Age, y	37 (13)
Height, cm	172 (10)
Weight, kg	70.42 (12.4)
BMI	23.66 (2.23)

BMI indicates body mass index.

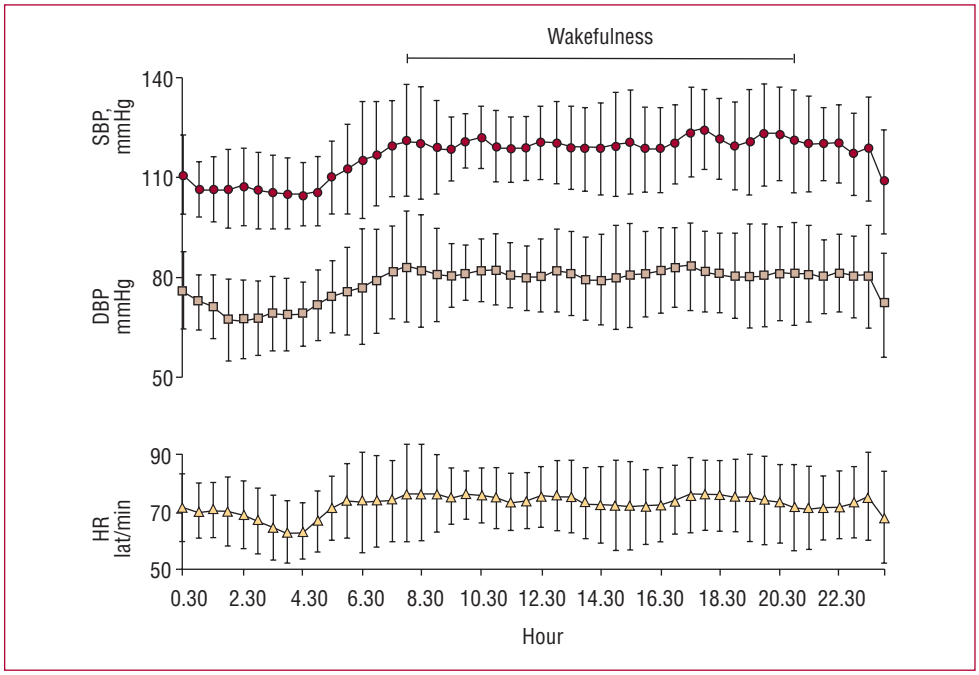

Figure. 1. Systolic blood pressure values (SBP) and diastolic (DBP), and heart rate (HR) obtained during the 24 hours of recording of the population studied, expressed as an average (standard deviation).

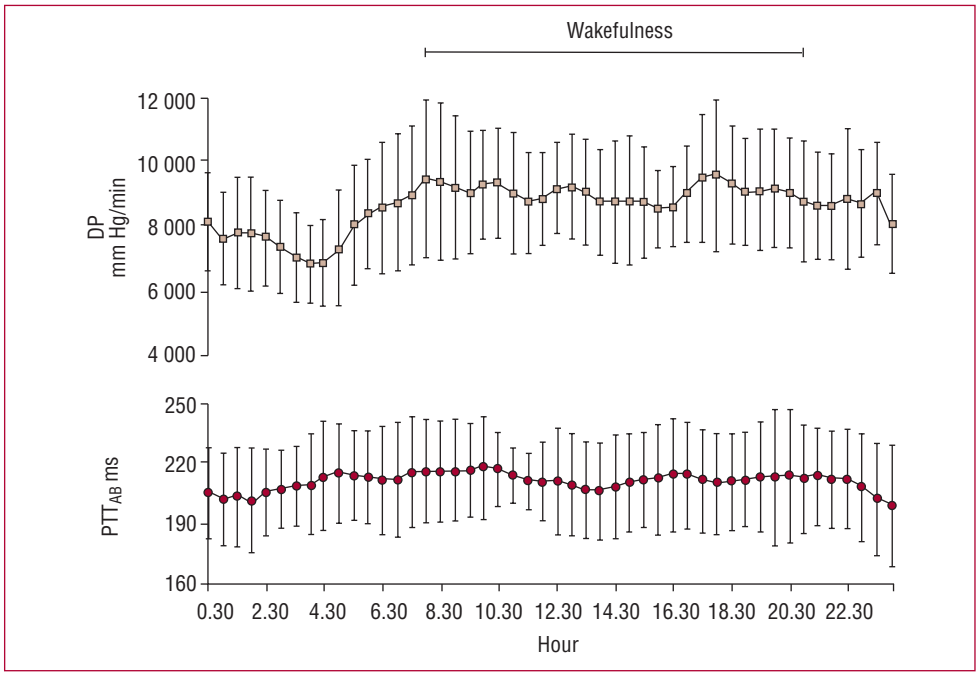

Figure. 2. Myocardial consumption of oxygen, evaluated via the double product (DP), and the transit time of the aorta-brachial pulse wave (PTTAB) obtained during 24 hours of registration of the population studied, expressed as average (standard deviation).

Registers with a minimum of 90% correct readings were considered valid. A PTTAB value was obtained for each reading, QF, SBP, diastolic blood pressure (DBP), pulse (PP=SBP–DBP) and average (MBP=DBP+PP/3), and the indexes of AS were calculated from the SBP and the DBP.

The consumption of myocardial oxygen was quantified by the product between the HR and SBP (DP).[2] The greater the DP, the greater the consumption of oxygen.

Each patient's register was adjusted by the Fourier series and re-sampled to obtain a data every 30 minutes, starting at 0.00 hour. When averaging the isochronic

samples, the 24 hour pattern of each variable for the group of individuals was obtained (Figures 1 and 2).

Arterial Stiffness

The AS was evaluated via the PTTAB and parameters calculated using the SBP and DBP.

Pulse-Wave Transit Velocity

The equipment enabled SBP, DBP, HR, and PTTAB to be measured simultaneously. The PTTAB (QKD according to other works) is the interval between the Q wave on the electrocardiogram and the last Korotkoff sound (corresponding to the BDP) registered during the deflation of the armband fitted on the left arm.[12] Consequently, the PTTAB includes the pre-ejection systolic time and the transit velocity of the pulse wave from the ascending aorta to the registration area on the left brachial artery, and its magnitude depending mainly on the velocity of the wave of the pulse of the arterial territory comprising the ascending aorta, the aortic arch, the subclavian arteries and the left humeral artery. Given that the PTTAB may be influenced by the length of the arterial segment studied, this was standardised taking into account the patient's height to reduce population dispersion and expressed as a velocity.[3,12] Lower PTTAB implied faster HR.

HR Indexes Derived From SBP and DBP

Based on the SBP and DBP values, the systolic/diastolic ratio (SBP/DBP), and fractioned pulsatility (PP/MBP) were calculated. The higher the value of the quotients, the greater the BP.[13,14] Schematically, both indexes are based on a similar philosophical base. The ejection of blood in the aorta generates a pressure wave that travels through the arteries. Each pressure wave can be broken down into a pulse component (PP) and a stationary component (MBP). When the AS is low, in the pressure range in which the arteries work the changes in SBP and DBP occur in a parallel manner. On the other hand, as AS increases, the pressure waves generated by each cardiac ejection shows higher SBP and lower DBP. In other words, as the HR increases the SBP/DBP or PP/MBP ratio increases. Circadian variations in AS could determine variations in the SBP/DBP and/or PP/MBP ratios. Consequently, it is possible to use these indices to indirectly evaluate the AS.[13,14]

Statistical Analysis

The values were expressed as an average value (standard deviation) (AV [SD]). The periods were compared using the Student *t* test for paired data. The waking period was taken to be between 8.00 and the 21.00 and the sleeping period between 23.00 and 6.00. The sleeping-waking transition periods were studied, considering a timetable before (20.00) and afterwards (2.00) during which the person slept, and the sleeping-waking period, considering an earlier timetable (6.00) and after (10.00) when the person woke up and started his daily activities.[5] The Pearson lineal correlation coefficients were calculated for associating the changes in AS and changes in SBP, HR and DP during the sleeping-waking transition periods (from 20.00 to 2.00) and sleeping-waking (from 6.00 to 10.00). A *P* value less than .05 was considered significant.

The haemodynamic variables SBP, DBP, and HR showed a characteristic circadian pattern, describing a decrease at night and an increase in the morning (Figure 1). The DP and the PTTAB, obtained for the entire population between 0.30 and 24.00, can be seen in Figure 2. It can be seen that the greatest (night) and lowest (day) AS values coincide temporarily with the lowest and highest values of DP, respectively.

During the sleep period, the SBP, DBP, MBP, HR, and DP were lower than during the waking period ($P<.05$) (Table 2). PTTAB was lower during sleep, which is indicative of a higher HR during this period ($P<.05$). Furthermore, the SBP/DBP and PP/MBP quotients indicated higher AS during sleep ($P<.05$).

RESULTS

During the waking-sleeping transition (Table 3) the SBP, DBP, MBP, PP, HR, and DP decreased and AS increased (decrease of the PTTAB and increase in SBP/DBP and PP/MBP) ($P<.05$). To the contrary, during the sleeping-waking transition (Table 4) an increase in blood pressure figures and DP were seen and AS decreased (increase in the PTTAB and reduction in SBP/DBP and PP/MBP) ($P<.05$).

The ratio between the changes in AS (evaluated as the inverse of PTTAB) and the changes in the myocardial consumption of oxygen (evaluated via the DP) during the transition periods presents a negative correlation ($DP=-4.2\times10^6\times AS+2.8\times10^4$; $R=0.76$; $P<.05$) (Figure 3). In addition, There were negative correlations between the AS and the SBP ($SBP=-3.6\times10^4\times AS+2.9\times10^2$; $R=0.71$; $P<.05$) and AS and the HR ($HR=-1.4\times10^4\times AS+1.4\times10^2$; $R=0.62$; $P<.05$) during the transition periods.

DISCUSSION

The main results of this work were that in the population of normotensive dipper individuals in cardiovascular risk factors, the AS presented significant differences between the sleeping and waking periods, with lower AS during waking, in spite of the higher values for blood pressure, HR and DP. Secondly, the night time drop in blood pressure and HR is accompanied by an increase in AS, while the morning increase in pressure and HR is accompanied by a reduction in AS. Finally, the morning

TABLE 2. **Parameters Obtained Through the Entire Registration Period (From 0.30 to 24.00) and the Sleeping Periods (of 23.00 to 6.00), and Waking (From 8.00 o 21.00)**

	Total Registered	Waking	Sleeping
SBP, mm Hg	116 (9)	121 (10)	108 (9)[a]
DBP, mm Hg	78 (6)	81 (6)	71 (6)[a]
SBP, mm hg	91 (7)	94 (7)	85 (7)[a]
SBP, mm Hg	39 (6)	40 (6)	37 (6)[a]
HR, lat/min	73 (8)	76 (9)	69 (9)[a]
DP, mm Hg×min	8543 (1024)	9030 (1116)	7603 (1086)[a]
PTTAB, ms	211 (21)	212 (22)	209 (22)[a]
Height, cm/PTTAB, s	823 (85)	823 (85)	832 (87)[a]
SBP/DBP	1.5 (0.08)	1.49 (0.07)	1.52 (0.11)[a]
PP/HBP	0.42 (0.05)	0.41 (0.05)	0.44 (0.07)[a]

DP indicates double product; HR, heart rate; DBP, diastolic blood pressure; MBP, average blood pressure; SBP, systolic blood pressure; PP, pulse pressure; PTTAB, aorta-brachial pulse-wave transit time.
[a]*P*<.05 between the waking and sleeping periods. The data expresses average (standard deviation).

TABLE 3. **Parameters Obtained for the Transition Between Waking (at 20.00) and Sleeping (at 2.00)[a]**

	20.00	2.00
SBP, mm Hg	123 (15)	106 (12)[a]
DBP, mm Hg	81 (9)	67 (8)[a]
SBP, mm Hg	95 (11)	81 (7)[a]
SBP, mm Hg	43 (14)	39 (12)
HR, lat/min	75 (13)	71 (11)
DP, mm Hg×min	9141 (1879)	7573 (1780)[a]
APTTAB, ms	213 (34)	204 (26)[a]
Stature, cm/PTTAB, s	821 (120)	853 (110)[a]
SBP/DBP	1.53 (0.19)	1.6 (0.23)[a]
PP/MBP	0.45 (0.14)	0.49 (0.14)[a]

DP indicates double product; HR, heart rate; DBP, diastolic blood pressure; MBP, average blood pressure; SBP, systolic blood pressure; PP, pulse pressure; PTTAB, aorta-brachial pulse-wave transit time.
[a]*P*<.05 between both states.
The data expresses average (standard deviation).

TABLE 4. **Parameters Obtained for the Transition Between Sleeping (at 20.00) and Waking (at 10.00)[a]**

	6.00	10.00
SBP, mm Hg	112 (13)	121 (8)[a]
DBP, mm Hg	76 (9)	82 (8)[a]
SBP, mm Hg	88 (10)	95 (8)[a]
SBP, mm Hg	37 (11)	40 (8)[a]
HR, lat/min	75 (13)	77 (13)[a]
DP, mm Hg×min	8539 (1573)	9324 (1723)[a]
PTTAB, ms	210 (17)	218 (18)[a]
Stature, cm/PTTAB, s	820 (62)	794 (63)[a]
SBP/DBP	1.51 (0.18)	1.47 (0.12)[a]
PP/MBP	0.43 (0.12)	0.41 (0.09)[a]

DP indicates double product; HR, heart rate; DBP, diastolic blood pressure; MBP, average blood pressure; SBP, systolic blood pressure; PP, pulse pressure; PTT_{AB}, aorta-brachial pulse-wave transit time.
[a]*P*<.05 between both states.
The data expresses average (standard deviation).

changes in the AS figures would not be contributing to the morning time increase in blood pressure. On the contrary, the changes existing in blood pressure during the sleeping-waking transition would be minimised by the reductions in AS.

Methodological Considerations

Different methods for recording and biomechanical parameters are used to characterise AS.[2,3] At present, the approaches to evaluating AS can be divided into systemic, regional, and local, according to the vascular territory studied.[3] Traditionally, the systemic AS has been evaluated via the quotient between the systolic volume and the medial brachial PP.[2,3] The low sensitivity for early detection of arterial changes and identifying focalised changes (eg, in bifurcations) has determined that it is currently not recommended for the diagnosis of vascular disease. On the other hand, there has been an increase in the use of registration methodologies and biomechanical parameters that have proven appropriate for determining regional and/or local AS in a direct, non-invasive manner.[3] In the analysis of the regional AS, the standard is the measurement of velocity of the pulse wave.[3] This parameter is obtained by calculating the transit time of the pulse wave between 2 separated arterial segments or between the QRS and the register of the pulse wave in the arterial site of interest.[3] Knowing the transit time and the distance between the 2 measurement sites enables the pulse propagation velocity to be calculated. The higher the propagation speed the greater the AS.[3] For studying local AS, methods are used that relate the instantaneous or systolic and diastolic changes in the pressure waves and arterial diameter obtained using applanation tonometry and ultrasound, respectively.[3] Based on the pressure/diameter ratio different parameters can be obtained that enable the AS to be characterised (eg, distensibility and elasticity). The measurement of the

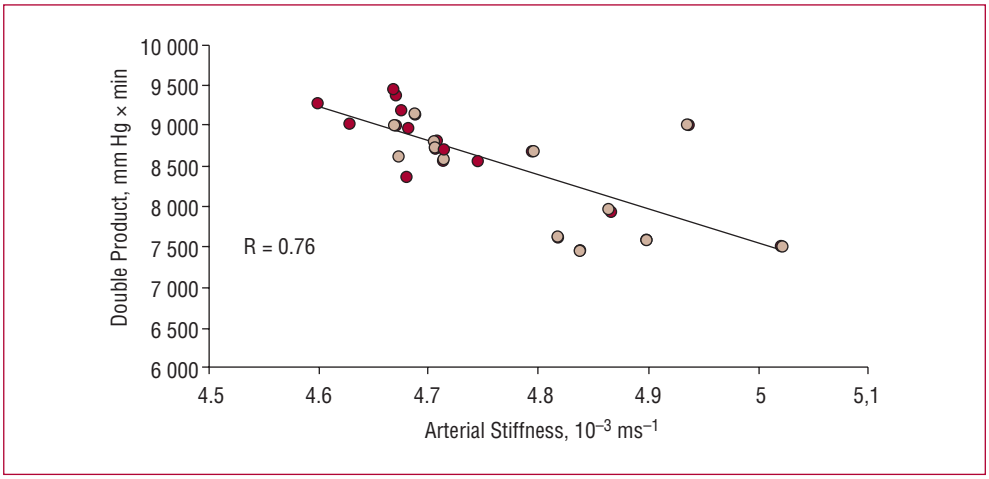

Figure. 3. Correlation between the double product (DP) and arterial stiffness (AS), evaluated as the inverse of the transit time of the aorta-brachial pulse wave (PTTAB), during the transition period waking-sleeping (beige circles) and sleeping-waking (maroon circles).

regional mechanical and/or local properties with the methods and parameters described require specific equipment and trained staff, and do not enable the outpatient measurement of AS.[3,14] For this purpose, it is of great interest to generate equipment and methodologies for evaluation which, although those used at the surgery can present have limitations, they have the advantage of enabling AS to be evaluated in an outpatient setting.[3,12] In this work we evaluate AS in an outpatient setting and in a non-invasive manner by quantifying the PTTAB and rates of fractional pulsatility (SBP/DBP and PP/MBP). The PTTAB (or QKD) has the limitation of being a parameter dependent on pressure and HR, meaning it influences the both intrinsic stiffness of the materials making up the arterial wall and the external variants of this (such as SBP and HR). This limitation is also suffered by the pulse wave velocity. Moreover, the quantification of PTTAB is supported by the identical base theory that measuring the velocity of the pulse wave, the current most frequently-used and accepted by everyone for the non-invasive characterisation of AS.[3] In this respect, the information that the PTTAB provides should not be undervalued.

In our work, the results obtained were not determined by the variations in the SBP and HR. If the changes seen in the AS, evaluated as the inverse of the PTTAB , had been determined by changes in these variables, the variations in AS would have been the opposites to those found. During the night, the descent in SBP and HR were not accompanied by a descent in the AS, but, on the contrary, the AS increased. In addition, during awakeness the SBP and HR increased but the AS reduced.

Physiological Considerations

In this work it was seen that, in contrast to the increase in blood pressure and HR, during the waking period the values of AS reduced (Table 2). Furthermore, when the subjects got out of bed in the morning, at the same time as SBP, HR, and DP increased there was a reduction in AS (Table 4, Figure 3). The opposite occurred when the individuals passed from a waking state to sleep (Table 3, Figure 3). Consequently, in individuals without risk factors, an increase in the AS did not appear to be among the factors contributing to the circadian pattern of cardiovascular vulnerability.

Our results coincided partially with those obtained by Kool et al[15] in healthy subjects, but in non-physiological study conditions (recorded over 24 hours taken with the person lying down, and waking them up to take ultrasound readings). These authors found that the AS was greater during the night, and attributed this finding to arterial dilation found during this period. In this respect, in spite of the night reduction in arterial pressure would imply a smaller arterial diameter, the authors found larger diameters, and attributed the increased AS to an increase in slipping of the arterial pressure/diameter ratio towards the right, which determines increased collagen uptake at any pressure. In these authors' opinion, the night time reduction in the activity of the sympathetic nervous system would be the cause of the arterial dilatation. In our opinion, this phenomenon may also be underlying our results. However, it is evident that this explanation may cause serious controversy, as reductions in the activity of the sympathetic nervous system are generally associated with arterial dilatation and the simultaneous decrease in AS, or to the contrary, the increased activity in the sympathetic system is associated with smooth muscle constriction and an increase in AS. However, it must be taken into account that our groups' work[8] and those of other authors[9] have shown that the activation of the smooth arterial muscle determines a reduction (isobaric or absolute) in AS, in spite of increases in blood pressure. In this respect, for any pressure, having a larger arterial diameter implies that a larger quantity of collagen fibres are stretched. The latter determines whether the artery is found to be working in a steeper area of the pressure/arterial diameter ratio, ie, in the area where the

arterial wall is stiffer. Therefore, for a given pressure, an increase in smooth muscle tone causes less stretching of the collagen fibre and, consequently, a reduction in AS. With regard to our results, the night time reduction in smooth arterial muscle tone could be the cause of an increase in AS.[8,9]

Our work was not intended to determine the mechanisms that cause the changes in AS. However, our results could be explained by circadian variations in the activity of the autonomous nervous system and/or in the concentration of circulation hormones. As we mentioned, the night time reduction in the sympathetic activity and its morning time increase could determine changes in smooth muscle tone that condition the increase in the AS at night and the changes observed during the transition periods. In addition, although in our work, hormones in plasma were not determined, earlier works have shown that the main hormones with constrictive action on the vascular smooth muscle present their lowest values during the night and increase and decrease during the earlier hours of the morning and the final hours of the evening, respectively.[1,16,17] In particular, earlier works have shown that, with regard to the daytime waking hours, during the night there are lower plasma concentrations of cortisol, plasma prorenin, angiotensin II, vasopressin, and catecolamines.[1,16,17]

It is important to analyse the changes in the AS in the context of the circadian changes of haemodynamic variables. Previous works showed that during the night the reductions in HR determined a reduction in cardiac output, in spite of remaining unchanged or only slightly reduced systolic volume. During the night, the reduction in cardiac output, together with the descent in the circulating plasma volume and the redistribution of blood volume, determine reductions in blood pressure, partially offset by increases in peripheral vascular resistance.[18,19] These increases in vascular resistance have been associated with vasoconstriction existing in the different tissues that, during the night, reduce their blood flow (self-regulation of flow), secondary to have reduced its metabolism.[19] Early in the morning, when getting up, the subject undergoes an increase in HR that determines the increase in cardiac output and then blood pressure.[19] Consequently, it could be postulated that the vascular system would respond via 2 mechanisms that would allow the increases in pressure existing during the day to be lessened. Firstly, as our results show, AS would be reduced, which would lessen the abrupt increase in blood pressure and minimise the DP. Furthermore, there would be a reduction in peripheral resistance (vasodilation)[18,19] that would permit blood flow to increase to the tissues, reducing the reflections of waves and attenuate the increase in blood pressure.

Clinical Implications

AS is the greatest determinant factor of dynamic ventricular afterloading.[2] In the light of our results it could be postulated that the reduction in AS observed during the waking period (Table 2), and specifically the opposite changes in SBP and HR and in AP during the waking-sleeping transitions (Table 3) and sleeping-waking (Table 4), would be part of the homeostatic mechanism that allows the ventricular work to remain lower. In this respect, during the waking period—a situation in which *a*) the demands of the cardiovascular system are higher than those during the sleeping period (greater DP) (Table 2) and *b*) the cardiovascular system must be in a condition to enable it to make great adjustments (changes) in cardiac output (as it must go quickly from the resting to isotonic exercise, such as running)— the arterial system shows higher distensibility as a way of reducing the work of the heart and allow variations in the systolic volume without increasing the AS excessively. On the contrary, during sleep, a state in which the cardiovascular system does not undergo great demands nor face great variations, the control systems for AS can "rest" and therefore the active minimisation of the AS reduces.

Further studies are necessary to analyse whether the circadian pattern or sleeping-waking pattern of the AS and/or changes in AS during the waking-sleeping pattern show changes in subjects with cardiovascular risk factors, and whether these are associated with the circadian pattern of cardiovascular events. In this respect, studies by our group (unpublished data) indicate that hypertensive subjects would have a diminished capacity to reduce the AS during the morning when the SBP and HR increase. The earlier studies described that the rates of change and/or the mechanisms for homeostatic control of blood pressure are changed in subjects with cardiovascular disease, deterioration in the reduction of AS during the morning could be associated with risks in the probability of a cardiovascular event in subjects with cardiovascular risk factors.

CONCLUSIONS

The course of AS was characterised over 24 hours via the outpatient recording of PTTAB and 2 indices of fractionated pulsatility in healthy volunteers. During waking hours there were lower figures of AS compared to the sleeping period, in spite of higher blood pressure and HR. The drop in arterial pressure, HR, and DP during the waking-sleeping transition was accompanied by a simultaneous increase in AS. On the contrary, during the sleeping-waking transition an increase in blood pressure, HR and DP was seen, as well as a reduction in the AS.

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