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Non-dipping blood pressure in normotensive patients with Obstructive Sleep Apnea

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أسباب عدم هبوط ضغط الدم في الليل عند مرضى انقطاع التنفس الإنسدادي أثناء النوم

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خلاصة : يهدف هذا البحث إلى دراسة تغيرات ضغط الدم اليومية في مرضى انقطاع التنفس الإنسدادي أثناء النوم وعلاقته بالعلامات المختلفة لهذا المرض وكذلك بقياسات البطين الأيسر للقلب . تمت دراسة ٢١ مريضاً من الذكور بضغط دم عادي (أقل من ١٤٠ / ٩٠ م م زئبق) وقد تم اختيار المرضى من شريحة متقاربة في السن والوزن وكلهم من ذوي الشخير العالي وقد تم تخطيط مؤشرات ومراحل النوم وتسجيل ضغط الدم لمدة ٢٤ ساعة وتصوير القلب بالموجات فوق الصوتية . أظهرت النتائج أن ٩ من المرضى لا يهبط ضغط الدم عندهم أثناء النوم وعند مقارنتهم بالمرضى الذين يهبط ضغطهم وجدنا أنه لا يوجد اختلاف بين نتائج مؤشرات ومراحل النوم وكمية الأوكسجين في الدم في المجموعتين ولكن وجدنا أن حجم مقاسات البطين الأيسر المختلفة في المرضى الذين لا يهبط ضغط دمهم أثناء النوم تفوق مقاسات المجموعة الأخرى بكثير . وقد لاحظنا في هذه الدراسة المبدئية أن عدم هبوط ضغط الدم أثناء النوم لهؤلاء المرضى لا يمكن أن ينسب إلى مؤشرات هذا المرض لوحدها كما ذكرت بعض الدراسات . وقد خلصت هذه الدراسة إلى أن تضخم البطين الأيسر الذي ينتج عادة عن ارتفاع ضغط الدم قد يكون بحد ذاته السبب في ارتفاع ضغط الدم أثناء النوم في هذه الحالات وهذا عكس العرف العلمي السائد .

ABSTRACT: To investigate circadian blood pressure profiles in normotensive patients with moderate to severe obstructive sleep apnea (OSA), in relation to their apnea indices and left ventricular parameters, we studied twenty one male patients with clinic blood pressures of < 140/90 mmHg. They were matched for age and body mass index (BMI) and all were heavy snorers. They underwent overnight polysomnography, 24 h non-invasive arterial blood pressure monitoring (ABPM) and echocardiography. Patients with a nocturnal reduction in average daytime systolic and diastolic blood pressure of less than 10% were considered non-dippers. Nine patients were non-dippers and 12 were dippers. In the non-dipper group asleep systolic and diastolic blood pressure were significantly higher than in the dipper group, ($P< 0.0001$ and $P<0.01$ respectively). There were no significant differences between the apnea/hypopnea (AHI) and the oxygen desaturation (ODI) indices of the dipper and the non-dipper groups. However, left ventricular parameters were significantly higher in the non-dipper than in the dipper group: left ventricular mass index (LVMI, $P<0.001$), posterior wall thickness (PWT, $P<0.001$), interventricular septal thickness (IVST, $P<0.001$) and relative wall thickness (RWT, $P<0.01$). In this preliminary study an absent or reduced blood pressure fall during sleep in normotensive patients with moderate to severe OSA cannot be explained by the severity of the apnea alone. Left ventricular hypertrophy, though may be a sequel to the non-dipper situation may also be the cause of it.

Keywords: Normotensive non-dippers, sleep apnea, left ventricular hypertrophy

Hypertensive patients who are non-dippers have a higher incidence of target organ damage score than those who are dippers (Pickering, 1990). Systemic hypertension occurs in about half the patients with Obstructive Sleep Apnea (OSA; Strading, 1989) and its severity is related to the apnea severity (Lavie et al., 1993). Nocturnal systolic and diastolic blood pressures were significantly higher in patients with OSA than in hypertensive controls (Strading, 1989) and in snoring patients with OSA than in snoring controls (Hoffstein and Mateika, 1992). In a recent study 50% of normotensive and 43% of hypertensive patients with OSA were found to be non-dippers (Suzuki et al., 1996).

Hypertensives who are non-dippers had greater left ventricular mass index (LVMI) than hypertensive dippers, and that LVMI and other parameters correlated more closely with night-time than daytime blood pressure (Fagard, Staessen and Thijs, 1995). Studies on left ventricular mass in patients with OSA were contradictory. Some studies showed a larger left ventricular mass in normotensive patients with OSA than in control subjects (Hadner, Ejnell and Caidahl, 1990; Davies et al., 1994). However, a better controlled study failed to show any difference in left ventricular size between snorers and patients with OSA (Hanley et al., 1992).

Most of the studies on circadian blood pressure

variability in patients with OSA were not controlling for all the confounding factors that can affect both OSA and blood pressure. In this prospective study we have undertaken to investigate apnea indices and left ventricular parameters in obese normotensive dipper and non-dipper patients with moderate to severe OSA.

Patients and Methods

Twenty one obese male patients with a mean body mass index (BMI) of 36.3 ± SD 4.5 Kg/m² and a mean age 36.8 ± 8.3 years were selected from a larger study on circadian blood pressure and heart rate variability and left ventricular function in patients with OSA. The main selection criteria for this report were an age of < 45 years, a clinic blood pressure of <140/90, a BMI of more than 30 kg/m² and an apnea/hypopnea index (AHI) of >20 per hour of actual sleep time. All patients were admitted to hospital and all underwent echocardiography, non-invasive arterial blood pressure monitoring (ABPM) and a standard overnight polysomnography.

All the patients were snorers for more than one year and had good quality ABPM. None was on hypotensive agents, had heart failure, diabetes, renal disease, and none were alcohol users.

M-mode and two dimensional echocardiography was performed a skilled technologist, who was unaware of the purpose of the study, utilizing a Hewlett-Packard Ultrasound Imaging System (HP Sono 1000, Massachusetts USA) equipped with a 2.5 or 3.5 MHz phased-array transducer. M-mode studies of the left ventricular cavity were guided by two-dimensional echocardiography using an optimal long axis view below the tips of the mitral leaflets. Measurements were made according to the recommendations of the American Society of Echocardiography using the leading edge to leading edge convention (Sahn et al., 1978). The interventricular septum (IVS), posterior wall thickness (PWT), and left ventricular end-diastolic dimension (LVID) were measured at the onset of the QRS complex. Left ventricular mass was derived by Penn convention measurements using the anatomically validated formula (Devereux, 1987).

Left ventricular mass (g) = 0.84 ×1.04{[(LVID (cm) + PWT (cm) + IVST (cm)]³ - LVID³] }+ 0.6 LVMI (g/m²) was derived by the formula LVM / body surface area. The relative wall thickness was calculated as 2PWT/LVID. The mean of at least three measurements was calculated.

Blood pressure was recorded non-invasively on the fourth day of admission by the Oxford Medilog System (Abingdon, UK) starting at 10:00 hour recording every 30 minutes for 24 hours. Definitions of the "Awake" and the "Asleep" periods and the quality of sleep as assessed by a scoring method were described by the authors elsewhere (Hassan, Al Shafie and Johnston, 1993). The mean of the 30 minute ABPM systolic and diastolic blood pr values were calculated for the awake and the periods. Non-dippers were arbitrarily defined as who do not exhibit a reduction in mean systoli diastolic BP of at least 10% from the awake and periods.

Overnight polysomnography was performed second night of admission using the Oxford Medilo system (Abingdon U.K) starting at 20:00 hours 06:00 hours. The recordings included sleep staging, oxymetry, nasal airflow, respiratory move submental electromyography, electrooculogram an rate. For the purpose of this study, only the AHI (n of episodes >20/hour of actual sleep time and lastir seconds) and oxygen desaturation index (ODI, m minimal oxygen saturation after each event of < were considered.

Statistical Analysis

Values are expressed as means ± SD. Compa between dippers and non-dippers were made Student's unpaired t-test. Simple linear regressic applied to examine the relationships of asleep s blood pressure, AHI, ODI and left ventricular para in the two groups. A P value of < 0.05 was cons statistically significant. Analysis was performed u "STATGRAPH" statistical package.

Results

Table 1 shows the main characteristics of the patients. There were no significant differences in a BMI. Nine patients were non-dippers and 12 dippers. In the non-dipper group asleep systol diastolic blood pressure were significantly higher t the dipper group, (P< 0.0001 and P<0.01 respecti There were no significant differences between th and the ODI indices of the dipper and the non- groups. However left ventricular parameters significantly higher in the non-dipper than in the groups: (LVMI, P<0.001, PWT, P<0.001, IVST, P and RWT, P<0.01 respectively).

Table 2 shows the results of the correlation coeffici asleep systolic blood pressure, AHI and ODI w ventricular parameters. The best correlations w asleep systolic blood pressure of the non-dipper with LVMI (r = 0.58, P< 0.0001), and RWT (r = 0. 0.001), while other left ventricular parameters s less but significant correlations. In the non-dippe the AHI and the ODI showed slightly higher t significant correlations with the asleep systolic pressure.

Discussion

Our limited purpose in this preliminary report is to study possible causes of the absent nocturnal blood pressure dip in some normotensive patients with OSA. A good quality ABPM in this obese sample has resulted in the small number included in the study of whom 43% were non-dippers as compared to 50% of normotensives with OSA in other studies (Suzuki et al., 1996). We have no immediate explanation as to why some of our matched patients were non-dippers and whether their left ventricular hypertrophy is the cause or the result of the non-dipper situation (Hassan, Al-Shafie and Johnstone, 1993). In OSA the non-dipper profile is attributed to arousal in response to hypoxia, hypercapnia, ineffectual inspiratory efforts (Bradley and Phillipson, 1985), increased sympathetic nervous system activity, increased left ventricular afterload (Hall and Bradley, 1995) and reduced baroreflex sensitivity (Cortelli et al., 1994). These factors however may explain some but not all the causes of the non-dipping blood pressure observed in this normotensive group. Normotensive offspring of non-dipper hypertensive parents were found to have an abnormal pattern of sleep in the form of microarousals with increased sleep blood pressure (Allemann and Weidmann, 1995) and, normotensive offspring of hypertensive parents compared with offspring of normotensive parents were found to have higher LVMI paralleled by a similar trend in blood pressure (Allemann and Weidmann, 1995). Blood pressure data of the parents of our group of patients are not available. Left ventricular hypertrophy may also develop as a primary abnormality generating higher basal blood pressure levels or higher blood pressure responses to different stimuli (Devereux,

TABLE 1

Main characteristics and comparisons of blood pressure, left ventricular parameters and OSA indices of dipper and non-dipper patients with OSA.

	Dippers	Non-dippers
Number	12	9
Age (years)	37.2 ± 6.5	35 ±11.0
BMI (Kg/m^2)	36.6 ± 3.7	35 ± 4.5
PWT (mm)**	10.3 ± 1.0	11.8 ± 3.2
IVST (mm)**	10.1 ± 0.7	13.3 ± 1.5
LVID (mm)	45 ± 4	46 ± 6
RWT*	0.33 ± 0.08	0.36 ± 0.11
LVMI (gm/m^2)**	131 ± 17	157 ± 28
Awake ASBP (mmHg)	130 ± 7	132 ± 8
Asleep ASBP***	106 ± 11	124 ± 15
Awake ADBP	79 ± 6	82 ± 6
Asleep ADBP*	69 ± 10	76 ± 11
AHI n/h	43 ± 16	46 ± 19
ODI (mean low SaO_2) %	80 ± 7	77 ± 12

Values are expressed as mean + SD. BMI, body mass index; PWT, posterior wall thickness; IVST, interventricular septal thickness; LVID, left ventricular end diastolic dimension; LVMI, left ventricular mass index: RWT, relative wall thickness; ASBP, ambulatory systolic blood pressure; ADBP, ambulatory diastolic blood pressure; AHI, apnea/hypopnea index;.ODI, oxygen desaturation index, SaO_2, oxygen saturation, *P< 0.01, **P <0.001, ***P < 0.0001.

TABLE 2

Regression coefficients of asleep systolic ambulatory blood pressure and OSA indices with left ventricular parameters in dipper and non dipper patients.

	Dippers			**Non-dippers**		
	ASSBP	AHI	ODI	ASSBP	AHI	ODI
PWT	0.181	0.050	0.076	0.369**	0.102	0.097
IVST	0.129	0.07	0.090	0.372*	0.093	0.152
LVID	-0.053	0.066	0.045	0.383*	0.020	0.095
R W T	0.120	0.03	0.087	0.465***	0.031	0.129
LVMI	0.236	0.094	0.108	0.598***	0.077	0.086
ASSBP		0.192	0.165		0.231	0.209
ASDBP		0.126	0.144		0.109	0.137

PWT, posterior wall thickness; IVST, interventricular septal thickness; LVID, left ventricular internal dimension; RWT, relative wall thickness; LVMI, left ventricular mass index; ASSBP, asleep systolic blood pressure; ASDBP, asleep diastolic blood pressure; ODI, oxygen desaturation index; AHI, apnea/hypopnea index. *P <0.01, **P<0..001, ***P<0.0001.

1990). The relationship between a non-dipper situation and the degree of left ventricular hypertrophy in hypertensives with and without OSA has already been documented in several well conducted studies (Prisant and Carr, 1990; Hanley et al., 1992). However, previous studies on normotensive patients with OSA did not control for BMI and OSA indices as is done in this study.

Irrespective of the cause of hypertension in OSA, our results have further confirmed that a large proportion of the normotensive patients with this condition are non-dippers and have left ventricular hypertrophy. These findings also may explain the increased prevalence of hypertension and its target organ damage as well as the increase in mortality in OSA described by other authors (Strading, 1989; Hall and Bradley, 1995), especially in male patients below 50 years of age (He et al., 1990).

In summary this study indicates that in this selected group of patients with OSA the AHI and the ODI do not seem to influence the overall nocturnal blood pressure as recorded by the above method. However the associated left ventricular hypertrophy, which is thought to be a sequel to the non-dipper situation, may actually precede it and both represent a continuum of cardiovascular risk. Because of the small sample size we suggest that readers should interpret these preliminary results with some caution pending our final report. Studies are also needed to elucidate the efficacy of pharmacological agents to reduce blood pressure of non-dippers in countries where other means of OSA treatment are not feasible.

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