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№ 3549

Studying Nocturnal Blood Pressure Patterns and Levels and Obstructive Sleep Apnea: Clinical Implications and Technical Solution

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June 3, 2020

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Abstract.*Background:* Beside specific consequences, obstructive sleep apnea (OSA) has been described as a novel and major risk factor of high blood pressure (BP), cardiovascular complications and organ damage. Ambulatory blood pressure monitoring (ABPM) is now considered as part of standard of care in management of hypertension. The study aims to initially describe possible association between BP levels and patterns, especially nighttime BP, and OSA.
Methodology: The study was conducted on both inpatient and outpatient subjects who have clear or dim notion of fluctuating clinical or self-measured home BP. Cardiorespiratory polygraphy indicated, when appropriate, led to the identification of two subgroups (with or without OSA). The 24-hour ABPM was then indicated to perform on subjects of both subgroups. Both exploratory techniques are non-invasive and have their own indication in clinical contexts.
Results: In two subgroup of 12 and 19 patients with or without OSA respectively, ABPM reported initially a higher proportion of isolated nocturnal hypertension, non-dipper nocturnal BP patterns or nighttime BP surges in subgroup of patients with OSA compared that recorded in non-OSA control subgroup.
Conclusion and Discussion: Initial study results suggest the patterns of nocturnal BP in patients with- and without OSA. Nocturnal BP level and pattern, which could only be achieved for now by ABPM holter systems, appear to have increasing importance and link to OSA. Clinical implications issue of high nocturnal BP may set needs for technical works of combination that enables simultanous analyses of both patient's nocturnal BP and sleeping state.

Keywords: Nocturnal BP, non-dipping BP, OSA, integrating technical work

1 Background

In the context of increasing non-communicable chronic diseases related to environmental pollution and unhealthy habits, in addition to diabetes, chronic lung disease and cancer, cardiovascular diseases and related pathologies are rising as the main disease group with high disease burden and mortality. Some diseases such as hypertension, diabetes, lipid disorders on one hand are pathologies have their own risk factors,they are on their turn considered as risk factors for a chain of diseases. Cardiovascular disease can lead to ultimate consequences of heart failure, major cardiovascular events and death.

In addition to paying attention to primary risks, attention paid to secondary risk factors by proper awareness, management and good treatment of conditions such as hypertension, diabetes, blood lipid disorders, overweight/obesity servesnot only to these specific conditions but also have important effects for preventable secondary events.

Hypertension (or high BP) is defined with defining levels of blood pressure which were varied a little bit according to office/clinic, ambulatory or home BP measurement, and to major professional societies. Hypertension is a common medical condition, easy to diagnose, having effective interventions and treatment, but there still remain many challenges. The first challenge for hypertension comes from the condition itself, the number of sufferers, its rising trend, the heavy consequences and dangerous complications of hypertension, the low rate of diagnosis (roughly only one out two), treated and controlled rates are also low (roughly only one out ten). [1-4]Besides cardiovascular risks, hypertension has also been identified as the most common risk factor for chronic kidney disease.[5]The mortality rate associated with hypertension increases exponentially with the increase in blood pressure levels in hypertensive patients.[6,7]This fact increases the challenge when placed alongside with evidence of a very clear effect of treatment and tighter control of blood pressure reduces mortality by cardiovascular events such as stroke, ischemic heart diseases [6,8-10], when the key points in the recommendations for diagnosis, treatment and management of hypertension, built from research evidence, are reaching agreement.[11,12] There is still the critical problemsassociated with ambulatory blood pressure measurement,nocturnal hypertension and masked hypertension[13-15]

The current indications of polysomnography or cardiorespiratory/respiratory polygraphy are focused on a number of clinical features that are often associated with obstructive sleep apneasyndrome (OSA, OSAS). However, the combination of obstructive sleep apnea and hypertension suggest an appropriate practical attitude is to prescribe this exploratory examination for diagnosed or suspected hypertension and in the reverse direction, ambulatory blood pressure monitoring by a holter system is indicated in case the OSAS was identified. Drager's research showed that the presence of metabolic syndrome (MetS) is a more important hint over suggestive signs of obstructive sleep apnea. [16]

In hypertension, a number of issues have been being reconsidered, from the most basic issues such as determining the threshold values for determining hypertension (systolic blood pressure repeated consistently at $\geq$ 140 mmHg and/or diastolic blood pressure $\geq$ 90 mmHg with blood pressure measured in hospitals (clinic/office BP), the use of automated measuring devices at hospitals, clinics and ambulatory, at home. As of 2013, blood pressure measurements at clinics or hospitals are considered as the standard for screening, diagnosis, and follow-up of treatment for hypertension. However, measurement of blood pressure at a clinic or hospital does not generally allow the identification of white-coat hypertension, masked hypertension or nocturnal hypertension, nor can it help to determine with certainty whether the treatment currently being applied in the patient provides good blood pressure control. [17,18]Since evidence confirms that recording blood pressure at a hospital or clinic is not a highly reliable method, the diagnosis of hypertension requires blood pressure readings to be reconfirmed, preferably with blood pressure measured outside clinic or hospital, at home or ambulatory. Standardized electronic blood pressure devices that automatically perform 3 measurements and calculate the average results are recommended

for use (should be preferred than traditional devices) in clinical practice.[19,20] At the same time, the measurement and recording with out-of-hospital ambulatory mobile blood pressure (self-measurement and home-based recording are formally recommended to perform in priority in confirming the diagnosis of hypertension as well as in titrate of medication treatment for appropriate dose in clinical practice as well as in providing a reliable basis for remote treatment counseling. [12]Ambulatory blood pressure monitoring is recommended and encouraged to used widely for all patients requiring hypertension screening or in diagnostic purpose; considered in a reasonable exploratory examination, which should be paid for (by Health Insurance) in the management of hypertension. Diagnosis of hypertension through ambulatory or home BP recording is based on lower blood pressure thresholds (130/80 mmHg for outpatient ambulatory blood pressure recording and 135/85 mmHg for home blood pressure monitoring). Monitoring of blood pressure at home has also been found to be beneficial in improving attention, accountability, and, as a result, blood pressure control rates. [21]In addition to helping to determine the diagnosis of hypertension reliably, blood pressure levels in patients also help determine the overall cardiovascular risk level.

Obstructive sleep apnea (OSA) and hypertension have a special link where OSA have been described and suggested, in both observational and prospective studies, as a novel and major risk factor of high blood pressure.[22-24] This study was carried out to explore the potential link between OSA and masked hypertension withits clinically relevant BP variability patterns.

Methodology

The study was conducted on both inpatient and outpatient subjects who have vague notion of fluctuating clinical or self-measured home BP. Respiratory polygraphy indicated, when appropriate (cases of presumed arterial hypertension), led to the identification of two subgroups (with or without OSA). The 24-hour ABPM was then indicated to perform on subjects of both subgroups. The obstructive sleep apnea was diagnosed using Philips Respironics Alice NightOne device and its software. [25]The patient's 24-hour-blood pressure was measured and recorded by ASPEL HolCARD CR-07 Ambulatory Blood Pressure System, analysed with HolCARD CR-07 software.[26]Both exploratory techniques are non-invasive and have their own indication in clinical contexts. The diagnosis of obstructive sleep apnea(OSA) was made by ambulatory or in-hospital seven-channel cardio-respiratory polygraphy using reliable and easy-to-use home sleep testing Alice NightOne device. 'Manual' scoring analysis was assisted by the native Alice software. An AHI of less than 5 (events per hour) is considered normal (non-OSA). OSA with AHI ≥ 5 and < 15 is classified as mild; AHI ≥ 15 and < 30 as moderate and an AHI more than 30 characterizes severe OSA.[27]

Thresholds or cut-off valuesused for the definition of hypertensive entities were 130/80mmHg for 24-hABPM*(≥130 mm Hg systolic or 80 mm Hg diastolic)*, 135/85 mmHg for daytime ABPM and home BP, 120/70 mmHg for night-time BP.Isolated nocturnal hypertension was defined as a night-time blood pressure of ≥120/70 mm Hg and a daytime blood pressure <135/85 mm Hg; isolated daytime hypertension as a daytime blood pressure of ≥135/85 mm Hg and a nighttime blood pressure <120/70 mm Hg; sustained hypertension as a nighttime blood pressure of ≥120/70 mm Hg and a

daytime blood pressure of ≥135/85 mm Hg. Ambulatory normotension is defined as a nighttimeblood pressure <120/70 mm Hg and a daytime blood pressure <135/85 mm Hg.[11,13,17,18]The BP dipping patterns, which were determined by systolic nighttime to daytime BP ratio. Non-dipping pattern (or reduced nighttime dip) is described as the ratio > 0,9; the ratio > 1 will be described as reverse-dipping pattern.

Results

The essential patient's characteristics of two study subgroups were presented in *Table 1*.The patients of two study groups differ in some key anthropometric parameters, namely BMI, waist circonfrence (WC) and the WC-to-height ratio (WHtR).

Althrough patients enrolled in this study have a vague notion of hypertension, neither of them had documentedly diagnosed or were currently treated. The confirmation of systemic hypertension by ABPM helped diagnose the masked hypertension in 10 (out 12), and in 11(out of 19) in patients with- and without OSA respectively. The study also characterized, among those with masked hypertension (demasked and confirmed by ABPM), some nocturnal BP patterns, including nocturnal hypertension, non-dipping nocturnal BP and night-time reverse-dipping, and revealed initially a higher proportion of these patterns insubgroup of patients with OSA compared to that recorded in non-OSA control subgroup.

Table 1. Characteristics of patients in two subsets.

Patient's characteristics		**OSA (+)***(12)*	**OSA (-)***(19)*	p
Demographic	Age (rang)	61,5 (47-78)	64,7 (34-84)	
	Malegender (%)	10 (83,3)	9 (47,4)	0.0493
Anthropometric	BMI (kg/m2)	30,1	24,0	**<0.0001**
	WC (cm)	109,25	87,9	**<0.0001**
	WHtR	0,67	0,55	**<0.0001**
	AHI (events/h)	17,8	1,8	
24-H ABPM	sBP (mmHg)	**136,5**	**133,3**	0.4322
	dBP (mmHg)	81,3	79,7	
Nocturnal ABPM	sBP (mmHg)	**130,6**	**121,8**	**0.0367**
	dBP (mmHg)	75,1	69,7	
Diurnal ABPM	sBP (mmHg)	**140,4**	**140,2**	0.3060
	dBP (mmHg)	88,9	85,2	
Dipping pattern	sBP N/D	**0,96**	**0,87**	**0,0127**

AHI: Apnea-hypopnea index; sBP: systolic BP; dBP: diastolic BP; N/D: Daytime to nighttime sBP ratio

There are significative differences in absolute mean values of BMI, waist circonfrence (WC), waist-to-height ratio, nocturnal systolic BP and reduced nighttime BP dip between two subgroups of patients with and without OSA*(Table 1)*. In this study, ABPM revealed a masked hypertension in 88,33 and 57,89 % respectively. In the patients with OSA, nocturnal hypertension was determined in 10/12 patients, roughly double in proportion determined in the subgroup of patient without OSA (8/19).

Table 2. Some nocturnal BP patterns

	OSA (+)*(12)*	**OSA (-)***(19)*	p
Masked hypertension, (%)	10 (83,33)	11(57,89)	0,1465
Nocturnal hypertension(%)	10 (83,33)	8 (42,11)	0,0258
N/D sBP ratio >0,9(%)	8 (66,67)	5 (26,32)	0,0291

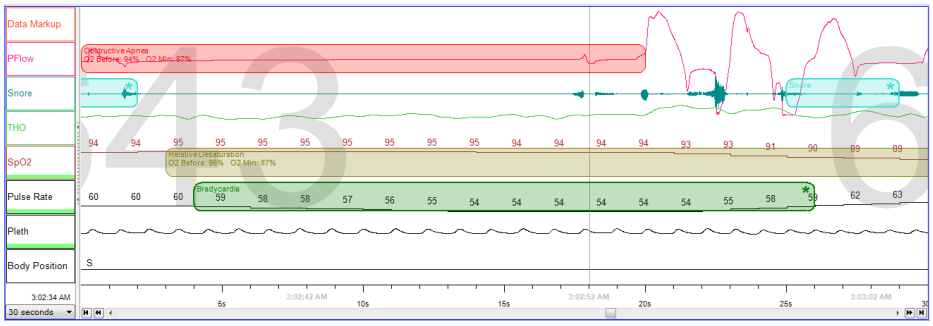

Fig. 1. Illustration of obstructive sleep apnea (OSA) event

Fig. 2. Illustration of BP dipping (A) and non-dipping (B) patterns.

Discussions

This study is directed to indicate the cardiorespiratory polygraphy in patients with suspected hypertension, and, in return, to redetermine the blood pressure status, via 24-hour ambulatory blood pressure monitoring in two sub-classified groups of patients (with and without obstructive sleep apnea). The study results continue to suggest a combination of OSA and hypertension. Although large studies have identified a causal relationship in which obstructive sleep apnea has been identified as a secondary cause of hypertension and is associated with resistant hypertension, [22,28], the relationship between OSA and hypertension continues to require epidemiological studies analyzing pathogenesis, identifying real underlying risk factors for more meaningful preventive interventions. A prospective follow-up study of middle-aged and elderly patients with OSAS without hypertension shows the important role of overweight/obesity in the formation of hypertension. as well as the predictive significance of nocturnal BP abnormalities [17,29]

In current study, nocturnal blood pressure abnormalities were not identified due to the intrinsic blood pressure abnormality in the patient or to influence of automatic blood pressure measurement during the nightthat have affected sleep and thereby affecting blood pressure(patientwhich awakened and got stressed). A valuable technical solution might be integration of BP measuring module in to polygraph device (or in reverse direction).

A prospective descriptive study found that patient' BP readings during the night were correlated with patient's subjective assessment of decrease in sleep time associated with blood pressure recording being performed automatically during the night; at the same time, the prognostic value of nocturnal blood pressure for cardiovascular outcomes and overall mortality (all causes) is lost in patients who experience a markedly reduced ($\geq$ 2 hours) of sleep time during the night[30]

Whether hypertension or masked hypertension, nocturnal hypertensionor nocturnal BP surges or reduced nighttime BP dip (non-dipping or reverse-dipping patterns)are associated with OSA, with sleep shortening or reduced sleep quality or insomnia, andthese conditions are related or independent of overweight or obesity (including normal weight obesity, NWO), cardiorespiratory polygraph indicated and performed on those with hypertension or suspected abnormal of BPdo have beneficial value especially when the test is performed simultaneously with blood pressure mornitoring. [17,18,22,31,32] This again suggests strongly a technical solution in which the blood pressure monitoring is integrated into the central processing module of cardiorespiratory polygraph.

At present, the diagnosis of arterial hypertension makes use either repeated visits for office BP measurement or out-of-officemeasurement. The ABPM could beindicated as adjunct to office BP monitoring and HBPM in casesof suspect or maskedhypertension, and to assess the nighttime BP. Along with office/clinic BP measurement and home blood pressure monitoring (HBPM), the ambulatory blood pressure monitoring (ABPM) by allowing assessment of nighttime BP, short-term BP variability provides an additive and stronger tool for diagnosis, prognosis and the follow-up. The close cooperation between clinical and BME teams might help elaborate technical projects to develop or improve the currently used devices.

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