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FEATURES OF NIGHT PULSE OXIMETRY IN PATIENTS WITH ARTERIAL HYPERTENSION AND OBSTRUCTIVE SLEEP PNOEA / HYPOPNEA SYNDROME

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Abstract

Recent investigations confirmed close and complex relations between the arterial hypertension and sleep-disordered breathing, especially, obstructive sleep apnea syndrome (OSAS). This study was aimed to reveal features of pulse oximetry and heart rate (HR) variables in hypoxic episodes during sleep in patients with arterial hypertension. Thirty-three patients with sleep-disordered breathing underwent polysomnography; later patients with proven OSAS diagnosis and patients without this condition were exposed to pulse oximetry monitoring. Visual expert analysis of desaturation episode curves has been performed and helped to determine characteristic patterns of the curve and variables, as well as types of HR reactions. Analysis of obtained results confirmed that both the rate and degree of desaturation highly correlate with heart rate maximal variables. The duration of desaturation episodes is also directly dependent on the initial oxygen saturation.

Keywords: obstructive sleep apnea, night pulse oximetry, arterial hypertension, heart rate.

Introduction

In recent years, many studies were aimed to prove the hypothesis on close relationship between arterial hypertension (AH) and sleep-disordered breathing (SDB) and, especially, obstructive sleep apnea/hypopnea syndrome (OSAHS) and upper airway resistance syndrome (UARS) [*Vein A.M., 1992; Pankow W. et al., 2000; Peppard P. et al., 2000; Zelveian P.H. et al., 2001; Teramoto S. et al., 2001Krieger J. et al., 2002; Shamsuzzaman A. et al., 2003; Quan S., Gersh B., 2004; Robinson G. et al., 2004;*]. AH is diagnosed in 40-90% of patients with OSAHS. There is also evidence of opposite relation – OSAHS is revealed in 30% of AH patients and, furthermore, prevalence of combined OSAHS and AH reaches 3-7% in general population [*Babak S.L., et al., 1996; Zelveian P.H. et al.,. 2001; Chasova I.E., Litvin A.Yu., 2002; Van Houwelingen K. et al., 1999; Williams A. et al., 1985*]. Several investigators propose that SDB is the cause of AH in a certain patient category and in this case the latter is considered as a secondary form [*Gulleminault C., Dement W., 1978; Gulleminault C., Lugaressi E., 1983; Stradling J., 1995; Zelveian P.H. et al., 1997; Van Houwelingen K. et al., 1999*]. Blood pressure (BP) lowering effect of OSAHS pathogenetic treatment supports this concept [*Hla K. et al., 2002*].

Current diagnostic assessment of SDB includes polysomnographic study, which is relatively expensive, complex and not always applicable.

In recent 10-15 years, a new non-invasive method of hemoglobin saturation assessment in arterial blood, pulse oximetry (PO), has become

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widely used. It has a high degree of precision and measurement stability [*Netzer N. et al., 2001*]. It has been shown to be an adequate method for quantitative assessment of hypoxic episodes. PO can be used for risk group stratification and for SDB screening [*Duchna H. et al., 1995; Yamashiro Y., Kryger M. 1995; Chiner E. et al., 1999*]. According to literature data, PO appears to be the most widely used screening tool for OSAHS [*Cooper B. et al., 1991; Williams A., Stein M., 1992; Gyulay S. et al., 1993; Duchna H. et al., 1995; Ryan P. et al., 1995; Buniatian M.S. et al. 2002; Hussain S., Fleetham J., 2003; Magalang U. et al., 2003; Zamarron C. et al., 2003*]. This is explained by desaturation frequently seen in apneic episodes. After restoration of upper airway patency and due to hyperventilation following the apneic episode, hemoglobin saturation is finally restored to its baseline and higher levels (resaturation). Thereby, episodes of apnea have a quite characteristic pattern of hemoglobin saturation changes. Different authors suggested various methodological approaches in diagnosing OSAHS using PO. These include: 1) detection and quantitative evaluation of desaturation episodes; 2) detection and quantitative evaluation of resaturation episodes; 3) assessment of arterial blood hemoglobin oxygen saturation (ABHOS) variability; and 4) identification of periodic components of ABHOS changes.

The Aim of this study was to assess pulse oximetry and heart rate (HR) changes during hypoxic episodes in sleep among patients with AH and to develop a panel of measures for their qualitative and quantitative assessment.

Sample and Methods:

We obtained data on ABHOS and HR changes in 33 AH patients with I and II stages (32 males and 1 female) aged 22-77 years (mean age: 45±13 years), with mean BMI=30±3 kg/m^2 and with mean respiratory disturbance index (RDI) of 31±30 *episodes/h*. Patients were divided into two groups according to polysomnography (PSG) data: 1) with OSAHS (18 males and 1 female aged 24-65 years; mean age: 47±12 years; mean BMI 31±3 kg/m^2 and mean RDI 51±25 *episodes/h*) and 2) without OSAHS (14 males aged 22-70 years, mean age 42±14 years, mean BMI 28±3 kg/m^2, mean RDI 5±5 *episodes/h*).

ABHOS and HR monitoring was performed using "NONIN 8500M" pulse oximeter (NONIN Medical, INC, USA) in ambulatory settings. ABHOS monitoring was being started 30 *min* before the onset of sleep and stopped 15 *min* after awakening in the morning. The device detects ABHOS (% SaO_2) by measuring pulse changes in red (Red-660 *nm*) and infrared (IR-925 *nm*) light spectrum absorption by tissues. The ratio of signals derived from both light spectrums defines blood oxygen saturation. The following formula is used to calculate ABHOS:

$$SaO_2 = f * \{[\ln(max/min)Red]/[\ln(max/min)IR]\}$$

A flexible reusable sensor designed for adult patients (Flex 8000J, NONIN Medical, INC, USA) was used to obtain measurements in conditions of moderate motor activity and/or long-term monitoring. Flexible pulse-oximetric sensor was fixed to index or middle fingers of hand free of BP monitor pneumocuff. A light-emitting diode was placed from nail side and a detector – from the opposite side. "3-M-Micropor" band recommended by the manufacturer was used for fixation.

ABHOS measurement ranges from 0 to 100% and precision of measurements comprises ±2% for the range of 70-100%. ABHOS data is saved in memory every 4 seconds. Value increment in memory is 1% in the range of 0-100%.

The review of scientific literature and systematization of ABHOS assessment, visual evaluation of ABHOS and HR (~150 studies) and the pattern of their changes allowed us to use the following methods for the assessment of ABHOS, considering episodic and dynamic characteristics and the hypoxic load. Data were analyzed by "ARM-SaO2–2" program, developed during this study [*Badikov D.N. et al, 1999*].

Variables characterizing ABHOS episodic changes:

An algorithm using the average value of ABHOS "stable" part as baseline saturation was developed and used. Parts not exceeding 3 *minutes* in duration with ABHOS standard deviation

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not exceeding 1% of mean value were considered as baseline or stable. Desaturation episode (DE) was defined as a decrease of ABHOS level by more than 4% compared to baseline level. Close episodes were considered separate, if the time between the end of the first and beginning of the second episode exceeded 12 sec (Figure 1). The following variables were automatically calculated according to the study results (Figure 2):

- Minimal ABHOS values for total duration of monitoring – SaO_2 min;
- Total episodes of 4% desaturation – DE;
- Index of 4% desaturation episodes – DE/monitoring time ratio (oxygen desaturation index, ODI);
- Desaturation rate (DR) – the difference between ABHOS values at the start of episode and at the minimum point divided by their respective time difference;

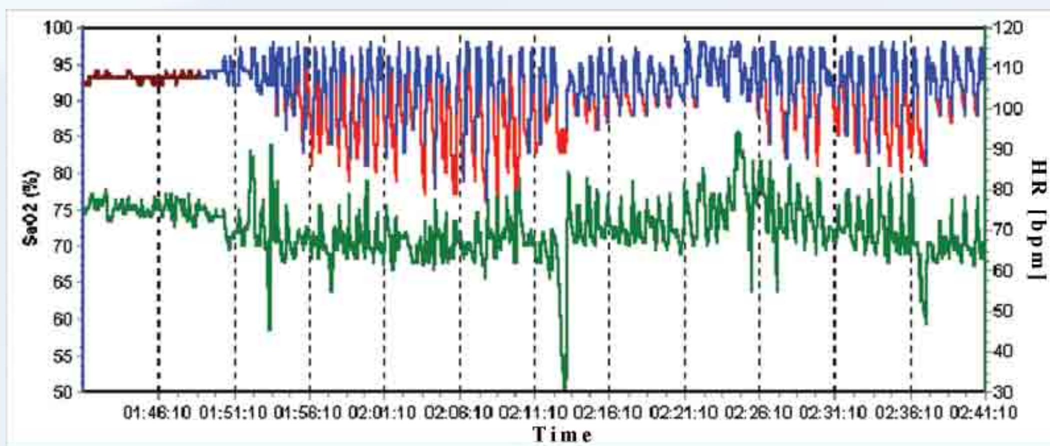

Figure 1. *Scheme for desaturation episode determination using "stable" part.*

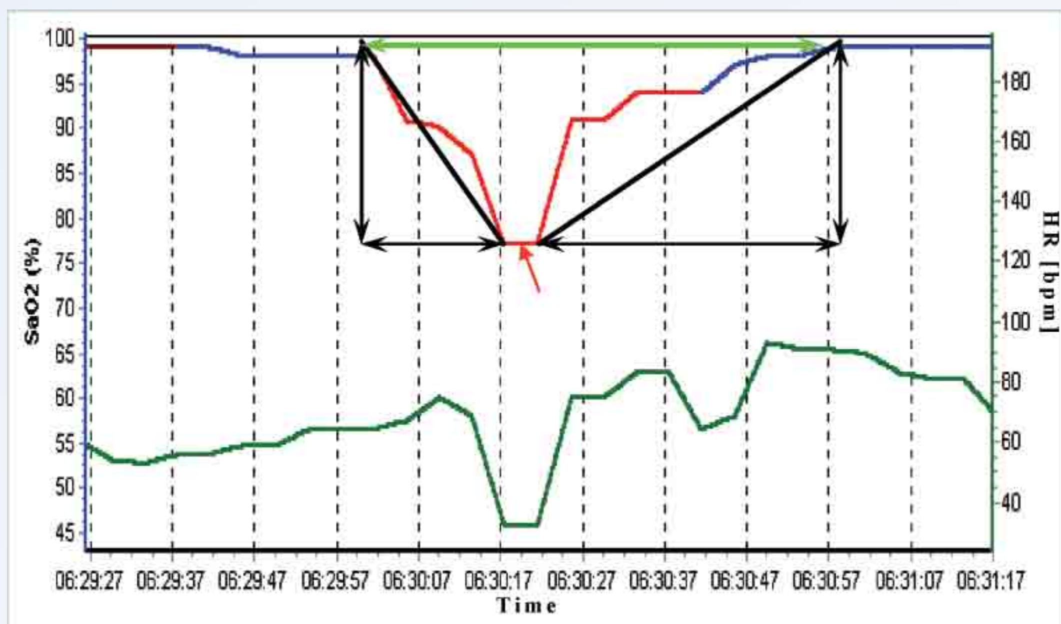

Figure 2. *Variables, characterizing ABHOS periodic changes.*

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- Resaturation rate (RR) – difference between ABHOS values at the end of episode and at minimum point divided by their respective time difference;
- Mean Desaturation Rate (MDR) – mean DR value of all episodes for total duration of monitoring;
- Mean Resaturation Rate (MRR) – mean RR value of all episodes for total duration of monitoring;
- Desaturation Episode Duration – DED;
- Initial ABHOS value before its decrease during desaturation episode – IDE;
- Final ABHOS value after its maximal increase in resaturation – FDE.

Variables characterizing ABHOS dynamic changes:

- $VAR1SaO_2$ – ABHOS standard deviation during monitoring;
- $VAR2SaO_2$ – standard deviation of differences between ABHOS sequential values;
- $VAR3SaO_2$ – ABHOS standard deviation during monitoring except stable parts, i.e. parts with the most probable DEs of different severity.

Variables characterizing hypoxic load:

- Percent of time with ABHOS lower than 90% of total monitoring time (time index, TI) – $TISaO_2<90\%$;
- Mean ABHOS value for total monitoring period – Mean SaO_2

Variables characterizing HR changes:

Six thousand nine hundred and six desaturation episodes were viewed for analysis of HR variability pattern in DE and the following HR variables were calculated:

- Mean HR value for total time of monitoring – MeanHR;
- Minimal HR value in DE - MinEpHR;
- Mean value of minimal HR in DE - MinEpMeanHR;
- Maximal HR value in DE – MaxEpHR;
- Mean of maximal HR values in DE - MaxEpMeanHR;
- VAR1HR – HR standard deviation during total time;
- VAR2HR – HR standard deviation in stable parts;
- DeltaHR – mean HR reaction value (absolute difference of maximal HR and minimal HR) for DE-s during total monitoring time.

SPSS version 14 was used for statistical analysis. Paired non-parametric method by Wilcoxon for intergroup difference evaluation and sign test were used. Spearman's and Pearson's correlation coefficients were also calculated. The differences were considered as significant at P-values below 0.05.

Results:

On the initial stage of the study a visual expert evaluation of PO curves was performed. In OSAHS patients ABHOS curves appeared stable enough in time (standard deviation 1.6±0.6%) with mean ABHOS value 94±2%, rare DEs, frequently characterized as single, rarely cyclic (wave-like periodic ABHOS changes with more than 3 episodes coupled in time) with small number of episodes. In contrary, in OSAHS patients ABHOS changes looked predominantly cyclic with varying total duration of 30 *min* and longer (Figure 3). DEs were saw-like sharp-end shaped episodic in nature with sudden increase of ABHOS level after respiratory restoration. Respiratory restoration leaded to more stable ABHOS curves with low amplitude episodic changes until next wave-like DE-s.

Expert evaluation of the above-mentioned DE-s revealed that single DEs were accompanied by the following types of HR reactions: «tachy» – pulse rate increase with normalization (45%) (Figure 4), «brady» – pulse rate decrease with normalization due to ABHOS restoration (12%) (Figure 5), «brady-tachy» – bradycardia changing into tachycardia with normalization (27%) (Figure 6) and «tachy-brady» – tachycardia changing into bradycardia with normalization (16%) (Figure 7). The so-called cyclic episodes were encountered most frequently among OSAHS patients. HR changes in them had mostly unidirectional nature (Figure 8), which allowed referring 86% of such episodes to «tachy-brady» type.

Relationship between different desaturation characteristics: A close relationship between the above-mentioned episodic variables with ABHOS dynamic variability and hypoxic load was revealed when correlation analysis was performed.

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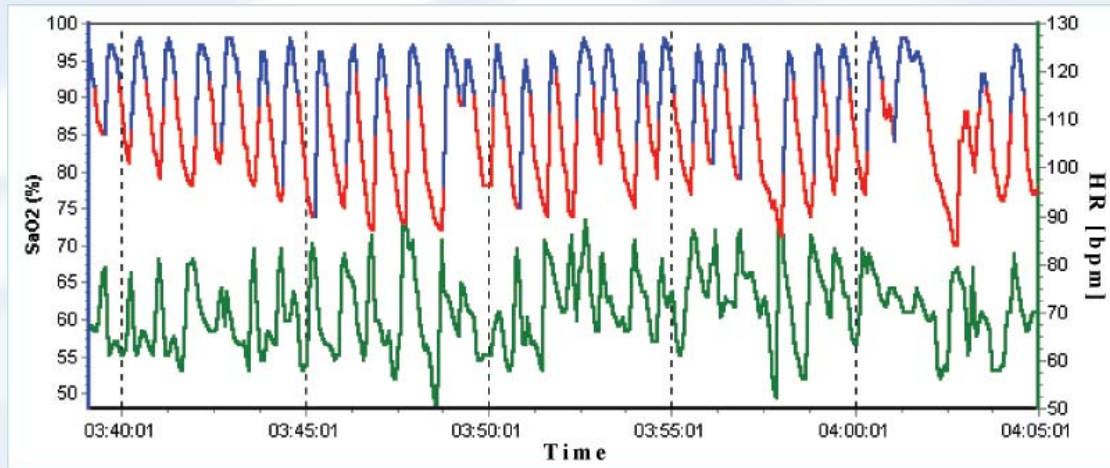

Figure 3. *"Significant" desaturation episodes (episodes of critical ABHOS decreases).*

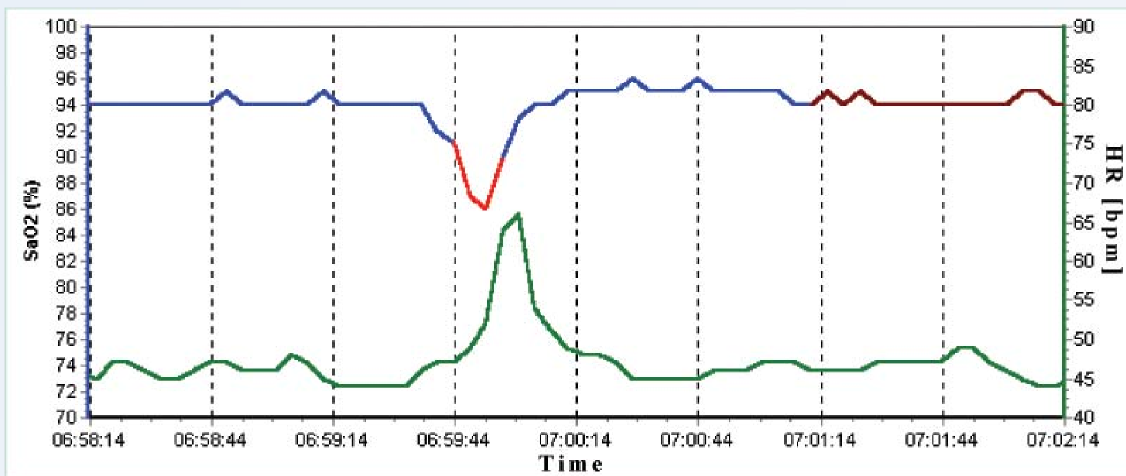

Figure 4. *Character of heart rate changes in a «tachy» type single desaturation episode.*

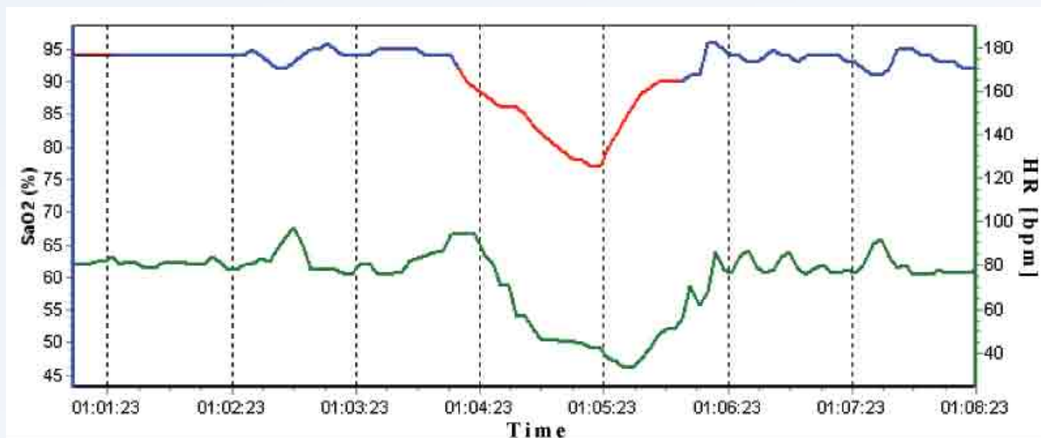

Figure 5. *Character of heart rate changes in a «brady» type single desaturation episode.*

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Thereby, largest and statistically significant correlations were revealed between ODI with $VAR1SaO_2$ and $VAR3SaO_2$; $MinSaO_2$ and $VAR2SaO_2$; DR and RR with $VAR1SaO_2$ and $VAR3SaO_2$; DED and $MeanSaO_2$ (Table 1).

Analysis between ABHOS variables and HR variability revealed significant relationships for VAR1HR and $VAR2SaO_2$, RR, DR, ODI, $MinSaO_2$, while VAR2HR had tendency to have significant correlation with RR and $VAR2SaO_2$ (Table 2).

We analyzed correlations between variables for duration and severity of 6106 DE-s, of which 5985 – in patients with OSAHS (group I) and 121 – patients without OSAHS (group II).

Distribution analysis for most of parameters showed inconsistency with normal distribution; therefore we computed Spearman's correlation coefficients. In OSAHS patients the minimal ABHOS value during DE, which expresses the rate of desaturation, highly correlated with both ABHOS values and HR. (Figure 9, Table 3); similar results were obtained for DR (Figure 9, Table 4). Coefficients for SaO2MinEp-HRMaxEp correlation were significantly higher than for SaO_2MinEp-HRMinEp (-0.56 and -0.31 respectively, $p=0.008$). Similar tendency was found for DR, however it was not statistically significant (0.44 and 0.37 respectively, $p=0.37$).

Table 1.

Correlation between ABHOS episodic change variables and integral variables characterizing dynamic ABHOS changes and hypoxic load

	$SaO_{2\ mean}$	$TISaO_2$ <90%	$VAR1SaO_2$	$VAR2SaO_2$	$VAR3SaO_2$
ODI	-0.63	0.71	0.86	0.83	0.86
$SaO_{2\ min}$	0.49	-0.55	-0.64	-0.8	-0.66
DED (in sec)	0.35	-0.30*	-0.23*	-0.25*	-0.16*
DR	-0.46	0.53	0.72	0.67	0.73
RR	-0.61	0.7	0.86	0.83	0.86

* - $p<0,001$

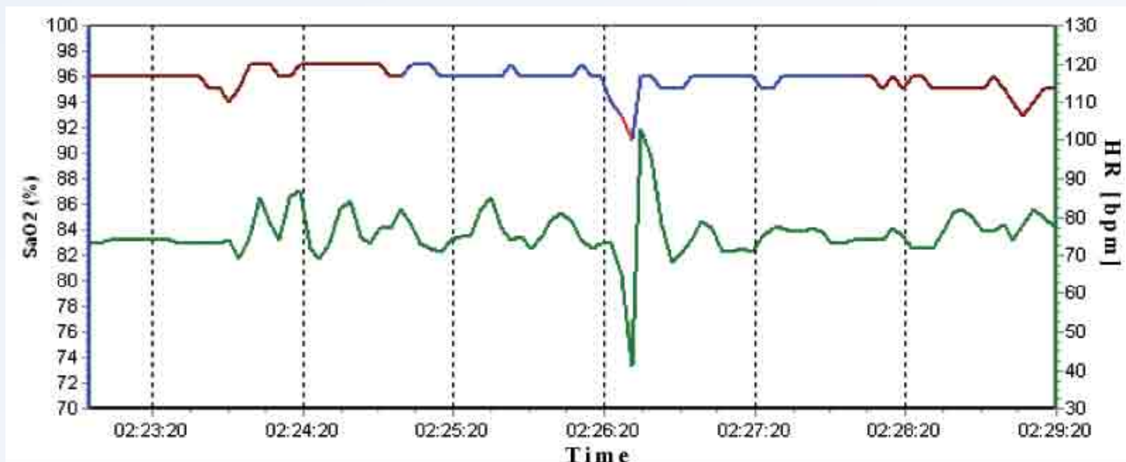

Figure 6. *Character of heart rate changes in a «brady-tachy» type single desaturation episode.*

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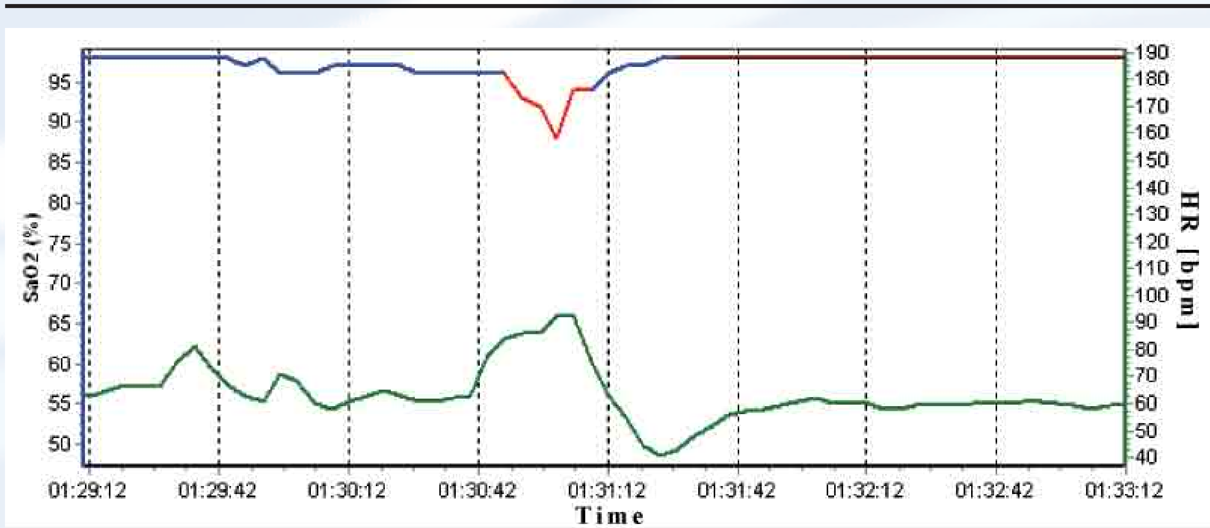
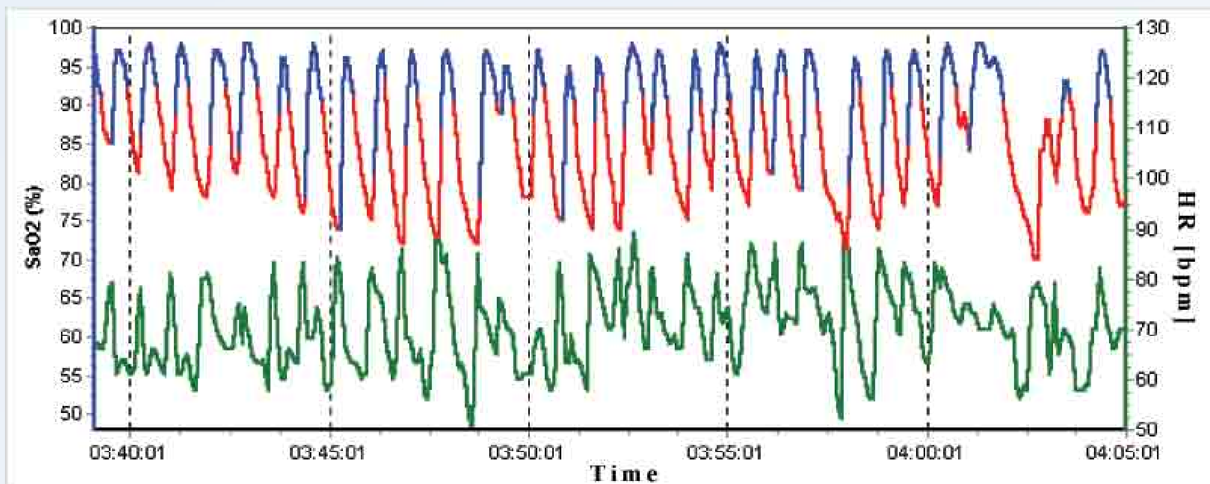


Figure 7. *Character of heart rate changes in a «tachy-brady» type single desaturation episode*



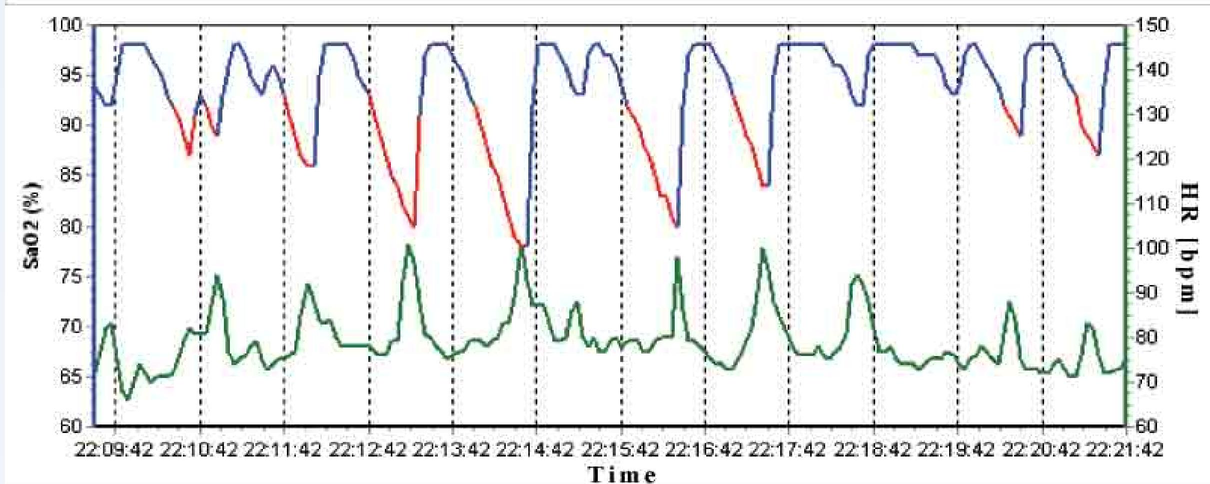


Figure 8. *Monodirectional character of HR changes during cyclic desaturation episodes*

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Table 2.

Correlation between HR variability and ABHOS integral variables

	SaO_2 min	SaO_2 mean	ODI	DR mean	RR mean.	VAR1 SaO_2	VAR2 SaO_2	VAR3 SaO_2	TI SaO_2<90%	DED
VAR1 HR	-0.36	-0.26	0.40	0.41	0.53	0.36	0.55	0.36	0.27	-0.21
p	0.04	0.15	0.02	0.02	0.001	0.04	0.001	0.04	0.13	0.25
VAR2 HR	-0.06	0.13	0.15	0.26	0.30	0.02	0.30	0.03	-0.11	-0.13
p=	0.73	0.48	0.42	0.15	0.09	0.91	0.09	0.85	0.56	0.48

Table 3.

Correlation between desaturation degree and rate, resaturation rate, ABHOS values in the beginning and the end of desaturation episode, variables characterizing HR changes

$SaO_{2\ min.ep.}$	DR	RR	IDE	FDE	MinEp HR	MaxEp HR	delta HR
Group I.	-0.73	-0.79	0.61	0.59	-0.31	-0.56	-0.44
p<	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Group II	-0.13	-0.30	0.61	0.48	-0.12	-0.08	0.04
p=	0.16	0.001	0.001	0.001	0.21	0.39	0.68

Table 4.

Correlation between desaturation rate and degree, resaturation rate, ABHOS values in the beginning and end of desaturation episode, variables, characterizing HR changes.

DR	SaO_2 min.ep.	RR	IDE	FDE	MinEp HR	MaxEp HR	delta HR
I гр.	-0.73	0.62	-0.46	-0.47	0.37	0.44	0.2
p<	0.001	0.001	0.001	0.001	0.001	0.001	0.001
II гр.	-0.13	0.31	0.04	0.11	0.15	0.01	-0.18
p=	0.2	0.001	0.69	0.25	0.10	0.90	0.05

Table 5.

Correlation between duration of desaturation episode and desaturation degree, desaturation rate, resaturation rate, ABHOS values in the beginning and the end of desaturation episode, variables, characterizing HR changes

DED	SaO_2 min.ep.	DR	RR	IDE	FDE	Min EpHR	Max EpHR
Group I.	0.13	-0.57	-0.22	0.50	0.45	-0.36	-0.22
p<	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Group II.	-0.04	-0.78	-0.37	0.12	0.02	-0.12	0.05
p=	0.69	0.001	0.001	0.17	0.8	0.19	0.57

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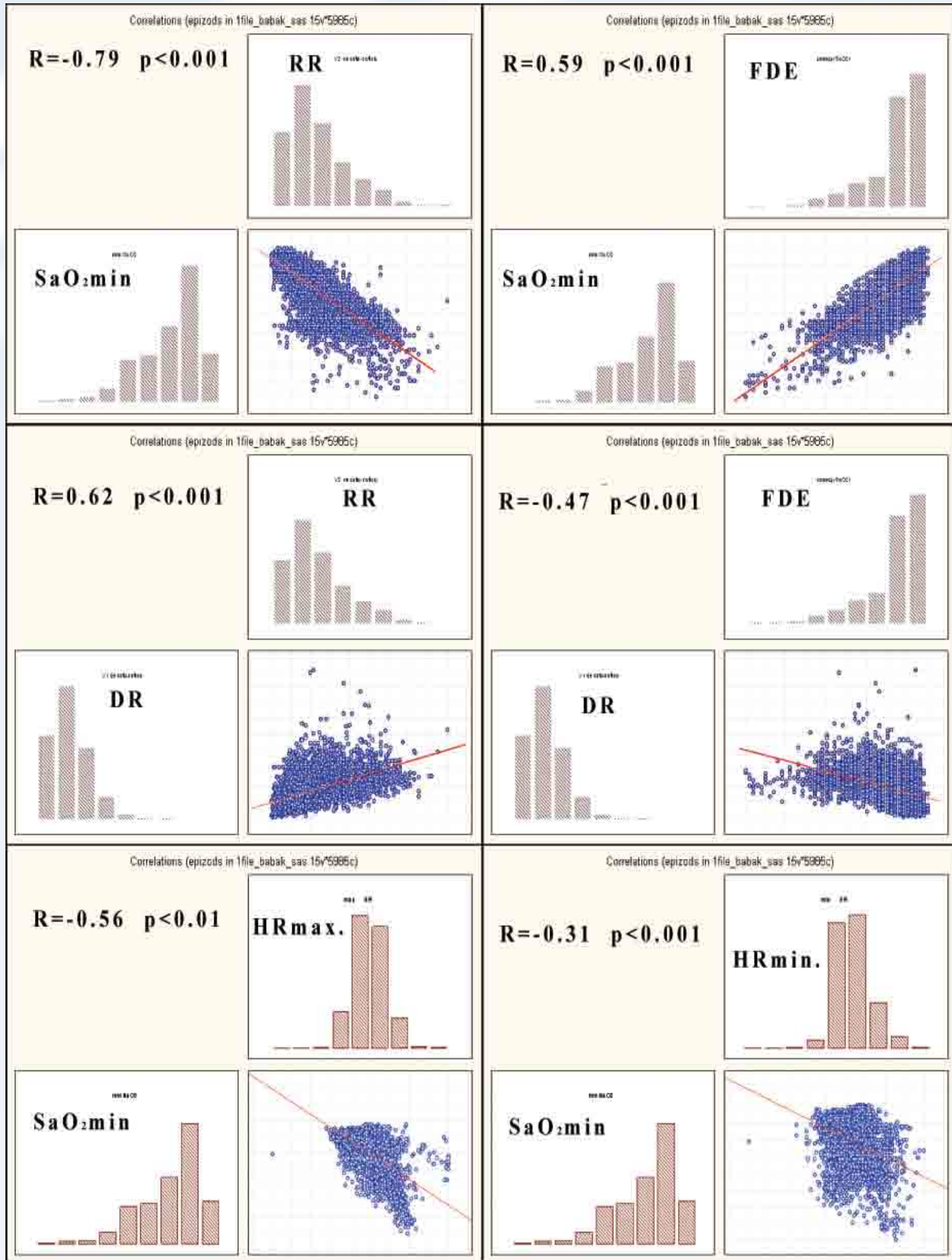

Figure 9. *Correlation of ABHOS minimal values (SaO2 min) and desaturation rate with ABHOS and HR values in PSAHS patients.*

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Although duration of DE strongly and significantly correlated with all variables characterizing ABHOS and HR changes during DE, the strongest correlations were seen with DR, IDE, FDE and the weakest with SaO2MinEp (Table 5).

Discussion:

For better interpretation of night PO data it is necessary to classify clearly the nature of ABHOS time changes, which have wave-like appearance in OSAHS patients. Some researchers consider that studying patterns of ABHOS changes could help in differentiating wave-like changes in apnea and hypopnea, obstructive and central apnea, Cheyne-Stokes respiration (CSR) [*Rauscher H., et al., 1991; Yeroshina V.A., Buzuov R.V. ,1999; Ross S. Et al., 2000; Buniatian M.S. et al., 2002; Zamarron C. et al., 2003*]. For example, in obstructive apnea ABHOS changes pattern presents as episodic saw-like, sharp-ended with sudden increase of ABHOS level with restoration of breathing, while in hypopnea «toothing» is not so sharp and in central apnea sometimes it is even absent. ABHOS changes in CSR have regular wave-like pattern with symmetrical decrement and increment and increase in ABHOS level, as repeated analogous breathing changes. However, in some cases central apnea changes can resemble obstructive apnea pattern. Duration of ABHOS changes can be also helpful, especially in patients with COPD, as secondary ABHOS changes are longer and slower in nature leading to total decrease of ABHOS level. Our results show strong and statistically significant relationship between frequency, depth, ABHOS decremental and incremental speed variables during episodic changes of ABHOS, ABHOS variability and hypoxic load variables. At the same time, the length of ABHOS decremental episode did not have any statistical significance, although demonstrating negative relation with variability and time index of hypoxic load. On the other hand, analysis of relationship between 4% ABHOS decrease episodes based on a large database (6106 episodes) has shown that ABHOS value after DE is associated with the baseline ABHOS level before the episode in OSAHS patients (5985 episodes). We found that the longer the DE, the slower the speed of ABHOS decrement is. Also, the lower ABHOS level changes during the episode, the higher are desaturation and resaturation rates. Resaturation rate is almost two-fold higher than desaturation rate (0.59±0.008*%/sec* and 0.32±0,004*%/sec*; $p<0.0001$). We demonstrated quantitative interrelations confirming qualitative nature of ABHOS changes in disordered breathing previously described in literature.

Apnea episode can influence cardiac rhythm in various ways: first, increasing bradycardia with subsequent tachycardia after the episode ends, and second, sinus tachycardia with subsequent bradycardia [*Guilleminault C. et al., 1984; Babak S.L. et al., 1996*]. According to C. Guilleminault and co-authors, 11% of OSAHS patients developed sinus rhythm pauses during apnea episodes, which lasted from 2.5 to 13 sec, and in 7% of cases bradycardia of less than 30 bpm was seen [*Guilleminault C. et al., 1984*]. Additionally, atrial and/or ventricular premature beats and transient atrioventricular block can be registered [*Szaboova E., et al., 1997*]. Also, cyclical variation of heart rate in patients with OSAHS was revealed, defined as characteristic sequence of increasing and decreasing respiratory sinus arrhythmia episodes with normal autonomic regulation of cardiac rhythm. According to our results, in most of cases of either single or grouped DEs HR increase was seen. Apparently, this has the following explanation: DE does not comply by phase with apnea or hypopnea episode, it rather arises with a delay and complies in time with HR increase, which follows the restoration of breathing.

Two main mechanisms explaining the emergence of bradycardia during apnea episode exist:

• First, reflex decrease of rhythm as a response to increased venous return due to the increase of negative intrathoracic pressure (chest wall movements without restoration of airway patency) and cardiac output.

• Second, this could be a result of vagal activation similar to that in diver’s reflex; in this case, bradycardia and peripheral vasoconstriction are caused by hypoxia in absence of pulmonary ventilation.

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Vasoconstriction provides redistribution of blood minute volume for brain supply. Bradycardia, in turn, prevents hypertension. Similar conditions are present in OSAHS. Studies have shown an increase of bradycardia in response to deteriorating desaturation and its disappearance with oxygen therapy and atropine injection [*Zimin Yu.B., Buzunov R.V., 1997; Shamsuzzaman A. et al., 2003; Quan S., Gersh B., 2004*]. S. Masuyama and co-authors propose that the severity of bradycardia correlates with the organism's sensitivity to hypoxia [*Masuyama S. et al., 1990*]. Primary vagotonic effect due to peripheral receptor chemosensitivity prevails over vagal activation determined by increased negative intrathoracic pressure. Peripheral vasoconstriction is seen in patients with OSAHS, which provides further support for the above-mentioned mechanism describing emergence of bradycardia [*Masuyama S. et al., 1990*].

Tachycardia following apnea episode can be determined by arousal and sympathetic activation [*Guilleminauet C. et al., 1984*]. Low-frequency (LF) component, expressing mainly sympathetic activity, increases after apnea episode in heart rate variability studies using spectral analysis. Also, LF/HF (high-frequency – expresses parasympathetic activity) ratio is increased, proving autonomous nervous system imbalance with sympathetic component being more active [*European Guidelines 1996*].

Premature ventricular beats are seen in 15% of OSAHS patients. With saturation decrease lower than 60% the number of patients with premature ventricular beats increases three-fold, ventricular tachycardia is also seen, being a consequence of cardiac electrical instability [*Szaboova E. et al., 1997*]. It is not coincidental that OSAHS was characterized by Fletcher as a "potentially lethal condition" [*Fletcher E. et al., 1985*].

In quantitative assessment of HR variability and ABHOS integral variables we found essential correlations between HR variability with $VAR2SaO_2$, RR, DR and ODI and negative correlations with SaO2Min. This confirms the impact of HR on degree, character, and number of DEs. The fact that OSAHS patients have significantly higher correlation for DR with maximal HR values during DEs than with DR showing minimal values confirms the above-mentioned presumption of sympathetic activity increase in this category of patients.

Conclusions:

Hypertensive patients with OSAHS have a characteristic pattern of desaturation episode change trends at night:

• Desaturation rate and degree are in direct relationship with resaturation rate and better correlate with maximal than with minimal HR values.

• Duration of desaturation episodes is in direct relation with initial oxygen saturation values and in inverse relation with desaturation and resaturation rates and in lesser degree relates to desaturation degree.

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