Article

Autonomic Dysfunction and Comorbid Diseases in Patients with Obstructive Sleep Apnea

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Abstract: Purpose of the study. To reveal the features of heart rate variability (HRV) and comorbid pathology in patients with obstructive sleep apnea (OSA).
Material and methods. The study involved 113 patients who underwent anthropometric measurements, polysomnography, recording of heart rate variability (HRV) and questionnaires (Beck scale, HADS, Holmes-Rey stress, Spielberger-Khanin questionnaire). According to polysomnography data, 2 groups of subjects were identified: with OSA (n = 61) and without apnea (n = 52).
Results. We found that in patients with OSA, hypertension (HT) occurred in 86,9% (p=0,000), acute cerebrovascular accident (CVA) in 8,2% (p=0,035), and chronic cerebral ischemia (CCI) in 82% of patients (p=0,000). According to the results of our work, there were no significant differences in the indices of the scales of anxiety, anxiety and stress levels between the groups of examined individuals. The mean scores of asthenia on the VAS scale (p=0,001), depression on the HADS (p=0,001) and Beck (p=0,000) scales in patients with OSA were significantly higher than in the control group. Representative indicators of HRV in patients with apnea in orthostasis were low values of Cr (%), SDNN (ms), RMSSD (ms), DX (ms), CV (%) and IC (arb. units), FR (ms^2), HF (ms^2), LF (ms^2, %), VLF (ms^2), and at rest - IC (arb. units), VPP (arb. units), HF (%) and VLF (%), which were higher than in the comparison group.
Conclusion. It has been established that for patients with OSA the most common comorbid pathology is obesity, HT, CVA, CCI and depression. In patients with moderate and severe severity of OSA, the influence of the central circuit of autonomic regulation on the heart rhythm increases, the total power of HRV decreases due to the parasympathetic department and the activity of the sympathetic department predominates, which can lead to depletion of the body's regulatory systems, a decrease in the adaptation reserve and an increase in the risks of vascular diseases complications. It is necessary to continue studying the features of HRV in patients with OSA and determine the significance of changes in the autonomic nervous system (ANS) depending on the severity of apnea, as well as what place comorbid pathology and OSA occupy in ANS dysfunction.

Keywords: obstructive sleep apnea, acute cerebrovascular accident, chronic cerebral ischemia, obesity, depression, anxiety, asthenia, autonomic nervous system, heart rate variability, polysomnography.

1. Introduction

Obstructive sleep apnea (OSA) in the current international classification of diseases of the 10th revision belongs to the class of nervous diseases with code G 47.3. Currently, this pathology is one of the most common sleep disorders [1], and the number of patients suffering from it continues to increase. So, the prevalence of OSA among people older than 30 years is about 10% [2], and by the age of 70 it reaches 60% [3].

OSA pathogenesis is based on complete or partial obstruction of the upper respiratory tract during sleep (apnea or hypopnea) for at least 10 seconds [4]. Repetitive respiratory arrests cause intermittent hypoxia and hypercapnia, which in turn leads both to activation of the sympathetic division (SO) of the autonomic nervous system (ANS) and the occurrence of tachycardia, and to an increase in the work of its parasympathetic division (PO) and the appearance of bradycardia [5]. Long-term fluctuations in the activity of the ANS are the cause of depletion of the vegetative supply and a decrease in the body's adaptability to external and internal stress stimuli with the formation of a rigid reaction from the cardiovascular system, which increases the risk of vascular diseases [4, 6-8] and mental disorders [9]. In addition, physiological adrenergic activation during long-term OSA becomes pathological and can lead to an inadequate increase in blood pressure, which in itself is a risk factor for the development of vascular complications [10].

The issue of OSA and comorbid diseases deserves special attention [11]. Today, OSA is considered as a risk factor for the development of acute cerebrovascular accident (CVA) [12, 13]. A small number of studies have shown that OSA leads to increased anxiety [14] and a decrease in quality of life [15]. It has been found that any sleep disorders can potentially be chronic stress for the patient and play the role of "independent factors" in the formation of depressive disorders [16, 17].

The most accurate method for diagnosing OSA is stationary polysomnography [18]. To study the autonomic balance in patients with OSA, it is recommended to use the method of recording heart rate variability (HRV) [19, 20]. Analyzing HRV indicators, one can not only assess the functional state of the body, but also monitor it in dynamics up to revealing a high probability of death [21]. Currently, this technique is used to predict the course of the disease, stratify the risk of cardiovascular complications [22], optimize the therapy taking into account neurohumoral regulation, and clarify the rehabilitation potential of the examined patients [23, 24].

Despite the rich experience in studying patients with OSA, it is necessary to continue studying the activity of the ANS in them, taking into account comorbid pathology to assess the indicators that are most significant in the development of complications.

Purpose of the study - to reveal the features of heart rate variability and comorbid pathology in patients with obstructive sleep apnea.

2. Materials and Methods

The work was carried out in accordance with the ethical standards of the Declaration of Helsinki of the World Medical Association "Ethical principles for conducting research involving humans" (as amended in 2013). The study protocol was approved by the ethics committee of the Tver State Medical University of the Ministry of Health of Russia (protocol № 4 09.03.2023). All subjects signed an informed voluntary consent. A cross-sectional study of a series of cases was performed.

Exclusion criteria: mild OSA, acute infectious and respiratory, oncological and mental diseases.

Patients were assessed for a history of hypertension (HT), smoking, and stroke. The diagnosis of chronic cerebral ischemia I-II (CCI) was established on the basis of criteria accepted in Russia [25].

Patients were measured weight (kg), height (cm), neck volume (cm). To calculate the body mass index (BMI), we used the formula proposed in the middle of the 19th century by the Belgian mathematician and sociologist Adolphe Quetelet: body weight in kilograms divided by body height in meters squared (kg/m²). The norm was BMI 18,5-24,9 kg/m², overweight - 25-29,9 kg/m², obesity of the 1st degree - 30-34,9 kg/m², 2nd degree - 35-39,9 kg/m² and 3 degrees with a BMI greater than 40 kg/m².

To identify OSA and assess the vegetative status, the subjects underwent polysomnography and registration of HRV using the Neuron-Spectrum NET program (OOO «Neurosoft», Ivanovo, Russia). The severity of OSA was determined according to the classification proposed by the Russian Society of Somnologists [26].

HRV was recorded at rest “lying down” (rest) and under orthostatic load (orthostasis) [27]. The following indicators were evaluated: the minimum value of the R-R interval (R-R min., ms), the maximum value of the R-R interval (R-R max., ms), the reaction coefficient (Cr, %), the standard deviation of the values of the R-R intervals (SDNN, ms), square root of the average of the squared differences in the values of successive pairs of NN intervals (RMSSD, ms), coefficient of variation (CV, %), variational range (DX, ms), vegetative rhythm index (VPR, conv. units), autonomic equilibrium index (IVR, conv. units), power of high-frequency (respiratory waves, HF, ms2, %), low-frequency (slow waves of the 1st order, LF, ms2, %), very low-frequency oscillations (slow waves of the 2nd order, VLF, ms2, %), absolute total power of the spectrum (TP, ms2), centralization index (IC, conv. units).

The level of reactive or situational (RT) anxiety as a condition, and personal (LT) as a stable characteristic of a person, was assessed using the Spielberger-Khanin questionnaire, and the level of anxiety and depression using the Hospital Anxiety and Depression Scale (HADS) [28]. The Beck scale made it possible to screen and determine the severity of the depressive state [28]. Using the Holmes-Ray stress scale [28], the level of social adaptation (stress) was assessed. To quantify the subjective severity of the patient's condition, a visual analogue scale (VAS) of asthenia was used from 0 to 10 points.

For statistical data processing, the IBM SPSS Statistics 23 program was used. The normality of the distribution of variables was assessed by the Kolmogorov-Smirnov criterion. With an abnormal distribution, medians (Me), quartiles (Q25; Q75) and percentiles (P25, P75) were used to describe the data obtained, and with a normal distribution, the mean ± standard deviation was used. Qualitative variables are presented as absolute value and percentage. To compare the two samples, non-parametric statistics methods were used - the Mann-Whitney test, parametric statistics - Student's t-test. To analyze the statistical significance of relationships between qualitative traits, we used Fisher's exact test. Differences were considered significant at p<0.05. Correlation was assessed using Spearman's coefficients for abnormal and Pearson's coefficients for normal distribution of the studied parameters.

3. Results

We have identified 2 groups of subjects (table 1).

Table 1. General characteristics of the groups of examined persons

Indicators	The main group, n = 61	The comparison group, n = 52	P
Age, years	56,13±10,28	55,40±7,71	0,676
Men, n (%) Women, n (%)	35 (57,40) 26 (42,60)	20 (38,50) 32 (61,50)	0,059 0,059
BMI, kg/m2 Norm, n (%) Overweight, n (%) Obesity 1 st., n (%) Obesity 2 st., n (%) Obesity 3 st., n (%)	37,86±7,83 1 (1,60) 10 (16,40) 10 (16,40) 18 (29,50) 22 (36,10)	32,66±4,10 2 (3,80) 10 (19,20) 25 (48,10) 11 (21,20) 4 (7,70)	0,000*
Neck volume, cm	45,00 (41,05; 47,00)	39,50 (37,00; 42,50)	0,000*
AHI, per hour	42,27 (22,50; 67,63)	3,39(1,90; 4,40)	0,000*
Saturation, %	93,00 (90,00; 95,00)	96,00 (95,00; 96,00)	0,000*
Desaturation, per hour	32,93 (17,35; 54,20)	1,40 (0,40; 2,39)	0,000*
HT, n (%)	53 (86,90)	26 (50,00)	0,000*
Smoking, n (%)	24 (39,30)	14 (26,90)	0,167
CVA, n (%)	5 (8,20)	0 (0,00)	0,035*
CCI, n (%)	50 (82,00)	20 (38,50)	0,000*

Note. * - significant differences in values between the main and comparison group at p ‹0,05.

The main group consisted of patients with OSA, and the comparison group consisted of patients without apnea. The subjects of both groups were comparable in age and the number of smokers. The prevalence of OSA among men was higher, but at the trend level. The following significant differences were established in these groups. Mean BMI and neck circumference were higher in patients with sleep apnea. The average saturation level was higher in the comparison group, and the desaturation index was higher in the main group. We found an average negative relationship between the saturation level and BMI (r=-0,683, p=0,000), neck volume (r=-0,379, p=0,003) and AHI (r=-0,581, p=0,000). HT was more common in patients with OSA and correlated with neck volume (r=0,343, p=0,007). According to the anamnesis, stroke was detected only in the main group in 8,2% of cases, and CCI in 82% of this category of patients (p=0,000). It should be noted that CCI correlated with BMI (r=0,277, p=0,030) and HT (r=0,323, p=0,011).

According to the results of our work, there were no significant differences in the indices of the scales of anxiety, anxiety and stress levels between the groups of examined persons (table 2).

Table 2. Values of indicators of emotional status in groups of examined persons

Indicators	The main group, n = 61	The comparison group, n = 52	P
Beck depression scale, n (%)	43 (70,5%)	16 (30,8%)	0,000*
Beck Depression Scale, scores Me (25%; 75%)	12,00 (8,00;17,00)	7,00 (5,00;11,00)	0,000*

HADS (depression), n (%)	20 (32,8%)	4 (7,7%)	0,001*
HADS (depression), scores Me (25%; 75%)	6,00 (4,00;8,50)	4,00 (2,00;4,00)	0,000*
HADS (anxiety), n (%)	18 (34,6%)	21 (34,4%)	0,983
HADS (anxiety), scores Me (25%; 75%)	6,00 (4,00;9,00)	5,50 (2,00;9,00)	0,408
Spielberger-Khanin RT scale, scores, Me (25%; 75%)	53,00 (38,00;58,00)	51,00 (34,00;59,00)	0,867
Spielberger-Khanin LT scale, scores, Me (25%; 75%)	40,00 (31,00;50,00)	34,50 (29,00;48,00)	0,213
Holmes-Reay stress scale, scores Me (25%; 75%)	136,00 (72,50;187,00)	107,50 (82,00;176,00)	0,963
VAS "Astenia" Me (25%; 75%)	6,00 (5,00;7,00)	5,00 (3,00;6,00)	0,001*

Note. * - significant differences in values between the main and comparison group at p ‹0,05.

The mean scores of asthenia on the VAS scale (p=0,001), depression on the HADS (p=0,001) and Beck (p=0,000) scales in patients with OSA were significantly higher than in the comparison group. The mean Beck depression score in sleep apnea patients correlated with BMI (r=0,307, p=0,016). In addition, in patients with OSA, a positive relationship was found between depression on the Beck scale (n, %) and HADS (mean score) and CCI (r=0,351, p=0,006 and r=0,284, p=0,026, accordingly). We also found a negative mean relationship between sex and depression on the Beck scale (n, % and mean score) (r=-0,340, p=0,007 and r=-0,328, p=0,010 female and male, respectively), a positive mean relationship between obesity and depression on the Beck scale (mean score) (r=0,359, p=0,004).

As can be seen from table 3, depression in patients with OSA was most often mild, less often severe and correlated with BMI (r=0,312, p=0,014).

Table 3. The value of indicators of the severity of depression (Beck scale) in the groups of examined individuals, n (%)

Severity of depression	The main group, n = 61	The comparison group, n = 52
norm (0-9 scores)	18 (29,50%)	36 (69,23%)
light (10-15 scores)	24 (39,34%)	12 (23,07%)
mild (16-19 scores)	8 (13,11%)	0 (0,00%)
severe (20-29 scores)	9 (14,75%)	2 (3,84%)
heavy (30-63 scores)	2 (3,27%)	2 (3,84%)

So, changes in the emotional sphere in patients with OSA are due to depression, while the severity increases with increasing BMI.

Table 4 presents the average values of the studied HRV indicators.

Table 4. The value of heart rate variability in the examined groups, Me (25%; 75%)

Indicators	State	The main group, n = 61	The comparison group, n = 52	P

Cr, %	rest	62,43 (32,93;73,59)	60,18 (32,99;72,97)	0,818
	orthos-tasis	16,17 (11,90;22,78)	20,39 (17,89;33,42)	0,000*
SDNN, ms	rest	59,00 (34,00;86,50)	54,50 (35,00;91,00)	0,931
	orthos-tasis	22,00 (17,00;31,00)	29,50 (23,00;41,00)	0,001*
RMSSD, ms	rest	56,00 (23,50;80,00)	52,50 (35,00;80,00)	0,612
	orthos-tasis	12,00 (8,00;18,00)	16,00 (11,00;25,00)	0,012*
CV, %	rest	6,70(4,56;10,60)	6,43 (4,36;10,60)	0,782
	orthos-tasis	3,05 (2,20;4,23)	4,43 (3,27;5,28)	0,000*
TP, ms^2	rest	2228,00 (775,00;6017,50)	2625,00 (1146,00;8316,00)	0,274
	orthos-tasis	458,00 (304,00;875,50)	751,00 (468,00;1562,00)	0,005*
LF, ms^2	rest	570,00 (176,50;1791,00)	734,50 (255,00;2283,00)	0,302
	orthos-tasis	90,00 (45,50;217,00)	199,50 (108,00;363,00)	0,001*
LF, %	rest	25,50 (18,45;38,20)	29,25 (22,10;37,10)	0,351
	orthos-tasis	19,80 (13,15;30,40)	29,70 (21,50;40,70)	0,022*
HF, ms^2	rest	621,00 (159,00;1617,00)	1039,50 (438,00;2218,00)	0,035*
	orthos-tasis	39,00 (20,00;90,00)	83,00 (38,00;179,00)	0,001*
HF, %	rest	22,90 (12,45;39,50)	25,95 (19,70;52,90)	0,043*
	orthos-tasis	8,90 (4,85;18,75)	12,40 (7,30;23,30)	0,167
VLF, ms^2	rest	682,00 (378,50;2815,00)	824,00 (364,00;3194,00)	0,604

	orthos-tasis	266,00 (156,50;503,50)	311,50 (235,00;724,00)	0,035*
VLF, %	rest	43,50 (27,35;59,00)	33,20 (24,80;50,10)	0,042*
	orthos-tasis	63,80 (41,05;77,75)	53,00 (35,00;71,80)	0,252
IVR, conv. units	rest	102,80 (50,10;59,20)	91,95 (54,20;210,20)	0,963
	orthos-tasis	450,70 (290,70;673,60)	329,80 (179,70;396,10)	0,003*
VPR, conv. units	rest	1,96 (1,24;3,99)	1,92 (1,14;3,83)	0,035*
	orthos-tasis	10,33 (6,13;13,92)	8,64 (3,86;11,45)	0,423
DX, ms	rest	672,00 (327,00;869,00)	674,50 (316,00;905,00)	0,704
	orthos-tasis	132,00 (103,00;194,00)	148,00 (139,00;307,00)	0,005*
IC, conv. units	rest	3,48 (1,53;7,05)	2,85 (0,89;4,07)	0,036*
	orthos-tasis	269,19 (167,96;506,73)	313,34 (236,44;727,12)	0,036*

Note. * - significant differences in values between the main and comparison group at p ‹0,05.

For analysis, we selected indicators of time and frequency analysis of HRV in patients with OSA, which have significant differences with the comparison group (table 4).

We found that the indicators of time analysis: Cr (%), SDNN (ms), RMSSD (ms), DX (ms), CV (%) and IC (conv. units) were lower, and IVR (conv. units) is higher in patients with OSA in orthostasis than in the comparison group. At rest, differences were revealed only when analyzing such temporal indicators as IC (conv. units) and VPR (conv. units), which turned out to be higher in patients with apnea than in the comparison group.

There was a correlation in orthostasis between Cr (%) and asthenia according to VAS (r=0,289, p=0,024), RMSSD (ms) and desaturation index (r=0,294, p=0,021), CV (%) and AHI (r=0,258, p=0,045), as well as between IC (conv. units) and AHI (r=0,303, p=0,018) and IC (conv. units) and Beck depression (n, %) (r=0,303, p=0,018). In addition, we established a correlation in orthostasis between the male sex and the following HRV indicators: Cr (%) (r=0,358, p=0,005), CV (%) (r=0,340, p=0,007) and DX (ms) (r =0,303, p=0,018).

Spectral frequency analysis indicators: TP, (ms^2), HF (ms^2), LF (ms^2), LF (%), VLF (ms^2) in patients with orthostatic apnea were lower, and HF (%) and VLF (%) at rest higher than in the comparison group. We found a positive relationship in orthostasis between TP (ms^2) and AHI (r=0,288, p=0,024), VLF (ms^2) and AHI (r=0,280, p=0,029), VLF (ms^2) and Beck depression (n, %) (r=0,287, p=0,025), as well as between LF (%) and saturation (%) (r=0,276, p=0,031), LF (%) and male gender (r=0,316, p=0,013). At rest, a correlation was found only between HF (%) and neck volume (r=-0,333, p=0,009).

So, in patients with OSA, most of the indicators of time and frequency analyzes of HRV were lower, except for IVR (conv. units) in orthostasis and IC (conv. units), VPR (conv. units), HF (%) and VLF (%) at rest, which are higher than in the comparison group.

4. Discussion

Our results of anthropometric features in patients with OSA are consistent with the results of studies that show that obesity and neck volume are risk factors for apnea [11, 29].

The high level of desaturation revealed by us in the main group is probably due to a more severe degree of the disease. At the same time, the level of saturation in patients with OSA decreases with an increase in BMI, neck volume and AHI, which shows a negative effect of the severity of apnea on blood oxygen saturation. R. V. Buzunov et al. [30] noted that chronic hypoxemia adversely affects the functioning of all organs and systems of the body.

Analyzing the relationship between OSA and comorbid pathology, we have established an association of this pathology with HT, CVA, CCI, and depression, which is consistent with the results of studies by some authors [11, 12, 13, 16, 17].

It should be noted that HT in patients with sleep apnea may progress with an increase in neck volume. Considering that OSA is considered a risk factor for obesity [29], it can be assumed that excessive fat deposition in the parapharyngeal tissue is an additional extravasal factor affecting the carotid sinus node, the irritation of which can contribute to the development and progression of HT.

It is known that CCI is one of the most common diagnoses in our country [31], however, in modern foreign literature and neurological practice, instead of the term CCI, they use “vascular cognitive disorders”, which are regarded as the main manifestation of chronic cerebrovascular disease [32]. It has been shown that obesity and HT are risk factors for cognitive impairment [33]. According to our study, it seems logical that CCI correlates with BMI in patients with sleep apnea and with hypertension. It is likely that cerebral ischemia is due to chronic intermittent hypoxia against the background of respiratory arrest, and obesity and HT may be additional risk factors or an independent cause contributing to the progression of CCI in patients with OSA. The relationship between the risk of developing vascular complications and the duration of the course of OSA against the background of an inadequate increase in blood pressure has also been shown [10]. A similar relationship between apnea, CCI and HT may indicate common pathogenetic mechanisms.

The revealed changes in the emotional sphere in patients with OSA are due to depression, which is consistent with the literature data [17]. We found an increase in the severity of depression with an increase in BMI, which is probably associated with more significant disturbances in the composition of blood gases against the background of worsening OSA. The negative mean correlation between sex and depression indicates more pronounced shifts in the emotional sphere in females. The low rate of saturation and high level of desaturation obtained by us in patients with apnea, apparently, are the cause of depressive disorders as a result of dysregulation in certain brain structures. In the work of E.I. Schwartz et al. [34] obtained data demonstrating that desaturation in patients with OSA may put the prefrontal cortex, hippocampus, and amygdala at risk. The established positive relationship between depression and CCI in patients with OSA is probably also due to low saturation.

We have studied the indicators of time and frequency (spectral) analyzes of HRV, assessed the effect of ANS departments on the heart rhythm in the examined individuals. According to R.M. Baevsky and G.G. Ivanov [8], the current activity of the ANS is the result of a systemic reaction of the mechanisms of multi-loop and multi-level regulation.

In our study, it was found that most of the indicators of the time analysis of HRV in orthostasis are lower in patients with OSA than in the comparison group.

So, we received Cr equal to 16,17% in patients with apnea, corresponds to the category of reduced response to orthostasis, which, according to E. A. Berezny et al. [35] characterizes the deterioration of the functional state of the organism. The revealed positive relationship between Cr (%) and asthenia according to VAS, apparently reflects the degree of functional state decrease.

The low values of SDNN (ms), RMSSD (ms), DX (ms), CV (%) established by us indicate the dominance of SO, which is consistent with the data obtained by G. N. Khodyrev et al. [36]. It can be assumed that the positive relationship between RMSSD (ms) and the desaturation index indirectly reflects the effect of the degree of apnea on the increase in SO activity. This can also be judged by the correlation of CV (%) with AHI.

A positive average correlation in orthostasis in patients with OSA between Cr (%), CV (%), DX (ms), LF (%) and gender shows that in males the values of these indicators are higher than in women.

IC is an integral indicator of involvement of suprasegmental ergotropic mechanisms in heart rate control [37]. The IC gives a quantitative characteristic of the state of the segmental-suprasegmental connection: the higher the values, the less the connection between the central and autonomous circuits of autonomic regulation [38]. Taking into account the above interpretation, low values of IC (conv. units) in orthostasis in patients with OSA, identified in our work, may indicate a high value of the central contour of autonomic regulation. According to E. V. Kuryanova et al. [39], a decrease in IC reflects the restriction of the flow of information to the pacemaker from the central nervous system and various reflexogenic zones, which confirms the high significance of extracardiac cholinergic and adrenergic regulatory influences. We have established an average positive relationship of IC (conv. units) in orthostasis with AHI and depression according to the Beck scale (n, %). It can be assumed that with an increase in the severity of OSA, the influence of the central circuit on the heart rhythm increases. The connection of IC with depression is probably due to general disorders in the work of the hypothalamic-limbic brain structures against the background of desaturation in patients with OSA [34].

In our study, VPR (conv. units) and IVR (conv. units) in patients with apnea were higher than in the comparison group, which shows the dominant effect of SO on the heart rhythm and is consistent with the data of G.Kh. Khodyreva et al. [36].

Along with time indicators, the analysis of the spectral structure of the rhythm was carried out. The TP indicator reflects the total activity of regulatory systems [40], while an increase in the activity of SO ANS leads to its decrease [41]. We found that TP (ms^2) at rest in patients with OSA tended to be lower than in the comparison group and was significantly lower in orthostasis. The decrease in TP in patients with apnea is apparently associated with dysfunction of β2-adrenergic receptors of the heart and is consistent with the opinion of I.M. Voronin [42]. The positive relationship established by us between TP (ms^2) and AHI indicates the influence of the severity of OSA on the total power of the spectrum. A more pronounced severity of apnea probably leads to the depletion of the body's regulatory systems and a decrease in the adaptation reserve.

It is known [27, 40] that HF (ms^2, %) is an indicator of software activity. In our work, we obtained reduced HF (ms^2, %) at rest and HF (ms^2) in orthostasis in patients with OSA than in the comparison group, which demonstrates a weakening of the effect of PO and/or an increase in the effect of SO on heart rate. The correlation relationship established by us between HF (%) at rest and neck volume reflects the reciprocal relationship between this HRV indicator and the volume of body fat in the projection of the neck.

It is known that LF (ms^2, %) reflects SO activity [43]. However, M. Ahmed et al. [44] believe that it is impossible to assess SO activity using this indicator, since, according to their data, β-adrenergic receptor agonists did't cause unidirectional changes in low-frequency oscillations in volunteers. Therefore, the question of interpreting changes in this indicator remains open. The low LF values obtained by us (ms^2, %) do not contradict the idea of an increased effect of SO on the heart rhythm [45]. It can be assumed that the weak positive relationship between LF (%) and saturation (%) in patients with orthostasis apnea that we have established indicates the importance of hypoxia in reducing the effect of this HRV indicator on heart rhythm.

Such an indicator of HRV as VLF (%) reflects the activity of cerebral ergotropic and humoral-metabolic mechanisms of heart rate regulation [46]. According to our data, VLF (%) in patients with OSA was higher at rest, and significantly decreased during exercise. The correlation in orthostasis established by us between VLF (ms^2) and AHI, as well as depression on the Beck scale (n, %), reflects the probability of a decrease in this HRV indicator against the background of an increase in the severity of apnea. Low VLF values (ms^2) may also affect the development of depression.

We believe that some of the considered parameters of HRV may be markers of depletion of the body's regulatory systems, a decrease in the adaptation reserve and the likelihood of developing vascular complications in patients with moderate and severe OSA and, especially, in men with a neck volume of more than 45 cm, obesity of the 2nd and higher severity, AHI more than 42 episodes per hour, saturation less than 93% and desaturation index more than 32 per hour. An increase in AHI and desaturation index causes a transition to the central regulation circuit and an increase in the influence of SO ANS on the heart rhythm. Representative indicators of HRV in patients with apnea in orthostasis were low values of Cr (%), SDNN (ms), RMSSD (ms), DX (ms), CV (%) and IC (conv. units), TP (ms^2), HF (ms^2), LF (ms^2), LF (%), VLF (ms^2), and at rest - IC (conv. units), VPR (conv. units), HF (%) and VLF (%), which were higher than in the comparison group.

5. Conclusion

As a result of the study, it was found that for patients with OSA in neurological practice, the most common comorbid pathology is obesity, HT, CVA, CCI, and depression. At the same time, CCI is caused by intermittent hypoxia against the background of respiratory arrest, and obesity and hypertension may be additional factors contributing to the progression of this disease. The severity of depression increases with an increase in BMI, severity of OSA, and a decrease in saturation.

The results of the analysis of the autonomic balance in patients with OSA showed that apnea is an additional factor in the development of autonomic disorders and, as a result, the occurrence of stroke and CCI. Patients with OSA are characterized by a decrease in most indicators of time and frequency analyzes of HRV, which indicate the dominant influence of SO ANS on the heart rhythm. An increase in such indicators as VPR (conv. units) and IVR (conv. units) in patients with OSA also reflect an increased effect of SO. With an increase in the severity of OSA, the influence of the central circuit of autonomic regulation on the heart rhythm increases, the overall power of HRV decreases, which can lead to depletion of the regulatory systems of the body, a decrease in the adaptation reserve and an increase in the risk of vascular complications.

It is necessary to continue to study the features of HRV in patients with OSA and determine the significance of changes in the ANS depending on the severity of apnea, as well as the place occupied by comorbid pathology and OSA in the dysfunction of the ANS.

Application of artificial intelligence:

The article is written without the use of artificial intelligence technologies.

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