DOI 10.1007/s11055-021-01180-5
Neuroscience and Behavioral Physiology, Vol. 51, No. 9, November, 2021

Characteristics of Emotional Status and Autonomic Regulation in Patients with Ischemic Heart Disease and Sleep Disorders

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Translated from Zhurnal Nevrologii i Psikhiatrii imeni S. S. Korsakova, Vol. 121, No. 1, Iss. 1, pp. 21–25, January, 2021. Original article submitted March 17, 2020. Accepted May 6, 2020.

Objectives: To study the features of emotional status and autonomic regulation in patients with ischemic heart disease and sleep disorders. **Materials and methods.** A total of 244 patients with functional class II–IV effort angina aged 36–72 (mean 56.9 ± 0.5 years) were studied. Emotional status was evaluated on the Hospital Anxiety and Depression Scale (HADS), the Beck Scale, and the Spielberger Scale. Autonomic status was assessed in terms of heart rate variability using 5-min cardiointervalogram traces at rest, Ewing cardiovascular tests, and an autonomic disorders questionnaire. Patients were divided into two groups depending on the severity of sleep impairments. **Results.** A total of 62 patients in the study cohort (25.4%) had no significant sleep impairment (≥22 points on the sleep quality questionnaire; these patients constituted group 2); 113 patients (46.3%) had severe sleep impairments (≤18 points on the sleep quality questionnaire; these patients constituted group 1); 69 patients (28.3%) had minor sleep impairments (19–21 points on the sleep quality questionnaire). Levels of anxiety and depression on the HADS were 9.2 ± 0.4 and 7.7 ± 0.4 points in group 1, compared with 5.9 ± 0.4 and 3.9 ± 0.4 points in group 2 ($p < 0.001$). Clinically marked autonomic disorders were seen in 100% of patients in group 1 and 75.8% of those in group 2 ($p < 0.001$). Mean scores on the autonomic impairments questionnaire were 41.8 ± 1.2 in group 1 and 25.6 ± 1.6 in group 2 ($p < 0.001$). **Conclusions.** Patients with sleep disorders had higher levels of anxiety, depression, and autonomic impairments, as well as lesser heart rhythm variability, which are unfavorable prognostic signs. This requires improvements in therapeutic and rehabilitation measures in this category of patients.

Keywords: ischemic heart disease, anxiety, depression, sleep disorders.

Emotional disorders such as anxiety and depression are a current problem in patients with ischemic heart disease (IHD), as they affect mortality and the course of illness in this category of patients [1, 2]. Epidemiological investigations provide evidence that anxiety and depression can be risk factors for IHD. Chronic anxiety can degrade the course of IHD, stimulating progression of atherogenesis and promoting fatal coronary events: arrhythmia, plaque, coronary artery spasm, and thrombosis [3]. Patients with signs of anxiety and depressive disorders have lower heart rate variability, which can increase the risk of death linked with coronary pathology and arrhythmia. Impairments to regulation of cardiac activity by the autonomic nervous system (ANS) may be one of the pathogenetic links between emotional disorders and cardiac pathology.

Changes in the emotional domain are accompanied by sleep disorders, which can in turn exacerbate the course of IHD.

The prevalence of sleep disorders in the population is up to 10% and can reach 44% among cardiology patients [4]. Patients with sleep disorders have worse prognoses, increased numbers of acute cardiac events, and increased mortality [5].

However, there is still insufficient study of the pathogenetic mechanisms of sleep disorders in IHD and the relationship between emotional impairments and autonomic regulation of heart rhythm.

The aim of the present work was to study the characteristics of emotional state and autonomic regulation in patients with IHD and sleep disorders.

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Materials and Methods. A total of 244 patients with functional class II–IV effort angina took part in the study; patients were 36–72 (mean 56.9 ± 0.5) years old. Sleep disorders were investigated using a sleep quality questionnaire at the Department of the Autonomic Nervous System, Sechenov First Moscow State Medical University (Sechenov University) [6]. Scores of 22 points were taken as sleep without significant impairments, while scores of 19–21 points corresponded to mild sleep impairment and scores of ≤18 points indicated clinically significant sleep disorders. In the cohort studied here, 62 patients (25.4%) had no significant sleep impairments, while 69 (28.3%) had minor sleep impairments and 113 (46.3%) had severe sleep impairments. Patients with severe sleep impairments comprised group 1 (n = 113), while those without sleep impairments constituted group 2 (n = 62).

Emotional state in patients was assessed using questionnaires: levels of trait and reactive anxiety were assessed on the Spielberger scale, anxiety and depression levels were evaluated on the Hospital Anxiety and Depression Scale (HADS), the total number of life events (perceived as stressful) was evaluated on the Holmes and Rahe Inventory, and the severity of autonomic impairments was assessed using a questionnaire for autonomic disorders at the Department of the Autonomic Nervous System, Sechenov University. Pain was evaluated quantitatively using a visual analog scale (VAS).

Autonomic status was evaluated by analysis of heart rate variability using 5-min cardiointervalogram traces in the state of relaxed waking in the supine position after a 15-min adaptation period, and in the orthostatic and clinostatic tests. Time and frequency analysis of traces used R–R intervals with computation of mean static heart rate (HR_{mean}), mean square (standard) deviation of R–R intervals (SDNN) (msec), the percentage of measured R–R intervals differing from the previous by more than 50 msec (pNN50%), the power of frequency components in the high-frequency range (0.15–0.4 Hz) (HF) ($msec^2$), the power of frequency components in the low-frequency range (0.04–0.15 Hz) (LF) ($msec^2$), the power of frequency components in the very low-frequency range (0.003–0.04 Hz) (VLF) ($msec^2$), total spectral frequency component power (TP) ($msec^2$), and the ratio of power in the low-frequency range to power in the high-frequency range (LF/HF) as a measure of the balance between the sympathetic and parasympathetic compartments of the ANS. A predominance of parasympathetic tone (parasympathotonia) was diagnosed at LF/HF <1.5; a balanced ANS state was identified at LF/HF 1.5–2.0; a predominance of sympathetic tone (sympathotonia) was diagnosed at LF/HF >2.0. Cardiovascular tests were performed using the Ewing method for quantitative assessment of sympathetic and parasympathetic influences on the cardiovascular system on loading. The following tests were performed during ECG recordings: a) the "six breaths a minute" test, with computation of the coefficient (C_{6b}) as the ratio of the maximum R–R interval on exhalation to the minimum on inhalation; b) the "30:15" test, with computation of the 30:15 coefficient as the ratio of the 30th R–R interval to the 15th from the start of rising to standing ($C_{30:15}$); c) the Valsalva test with computation of the Valsalva coefficient ($C_{Valsalva}$) as the ratio of the maximum R–R interval during the relaxation period after loading to the minimum during the period of loading; d) the 3-min orthostatic test with determination of the difference between systolic arterial blood pressure (SBP) initially in the supine position and that at the end of the third minute of the test; e) the isometric test with isometric tensioning and assessment of the increase in diastolic arterial blood pressure (DBP) during squeezing of a dynamometer at 30% of maximal force for 3 min as compared with initial DBP at rest. The first three tests assessed the influence of parasympathetic activity on the cardiovascular system and the latter two assessed the effects of sympathetic activity [8].

Results were analyzed statistically. Results are presented as $M \pm m$ where M is the arithmetic mean and m is the error of the arithmetic mean. Significant differences between groups were identified using the two-tailed Student's t test or, where necessary, the Mann–Whitney test; interactions between features were identified by computing the Spearman correlation coefficient in Excel 2013 and Statistica 6.0. Differences were taken as statistically significant at $p < 0.05$.

Results and Discussion. There were no between-group differences in the functional class of angina or treatment.

Levels of reactive and trait anxiety in group 1 were 47.1 ± 1.0 and 49.9 ± 0.9 points, respectively, corresponding to high levels of anxiety; levels in group 2 were 40.4 ± ± 0.9 and 42.0 ± 0.9 points ($p < 0.001$), corresponding to intermediate levels of anxiety. Anxiety and depression levels on the HADS in group 1 were 9.2 ± 0.4 and 7.7 ± 0.4 points, respectively, while those in group 2 were 5.9 ± 0.4 and 3.9 ± 0.0.4 points, respectively, ($p < 0.001$). The number of life events assessed by patients as stressful on the Holmes and Rahe Inventory was higher in group 1 at 655.2 ± ± 29.3 points than in group 2 at 431.4 ± 26.5 points ($p <$ < 0.001). The overall indicator of sleep quality in group 1 was 15.5 ± 0.2 points, compared with 23.0 ± 0.1 points in group 2 ($p < 0.001$).

Clinically marked autonomic disorders were seen in 100% of patients in group 1 and 75.8% of those in group 2 ($p < 0.001$). Mean scores on the autonomic disorders questionnaire were 41.8 ± 1.2 points in group 1 and 25.6 ± 1.6 points in group 2 ($p < 0.001$).

The severity of pain on the VAS did not differ between groups, at 4.82 ± 0.2 points in group 1 and 4.7 ± 0.3 points in group 2, though the duration of angina attacks was significantly greater in patients with IHD and sleep disorder – 8.8 ± 0.5 min, as compared with 6.78 ± 0.6 min in group 2 ($p < 0.05$).

Values in the 30:15 test, reflecting the state of the parasympathetic compartment of the ANS, were within normal limits in both groups. Values on the 6 breaths per minute test

TABLE 1. Autonomic Test Results in IHD Patients ($M \pm m$)

Indicator (test)	Group 1 (n = 113)	Group 2 (n = 62)	Different between groups 1 and 2
6 breaths per min	1.20 ± 0.01	1.18 ± 0.01	1.7%
Valsalva	1.31 ± 0.02	1.35 ± 0.01	–3.7%
30:15	1.15 ± 0.01	1.19 ± 0.03	–15.8%
Isometric test, mmHg	12.7 ± 0.7	15.4 ± 1.1*	–17.4%
Orthostatic test, mmHg	–7.3 ± 1.2	–7.3 ± 1.9	0%

*$p < 0.05$

TABLE 2. Measures of Heart Rate Variability in IHD Patients in the Orthostatic Test Depending on the Severity of Sleep Disorders

Test	HR, bpm	SDNN, msec	pNN50%, %	TP, msec^2	HF, msec^2	LF, msec^2	VLF, msec^2	LF/HF
Group 1 (baseline)								
$M \pm m$	63.7 ± 1.1	27.4 ± 1.3	6.1 ± 1.3	731.2 ± 93.7	190.1 ± 30.1	180.6 ± 21.7	361.6 ± 56.9	1.7 ± 0.2
% comparison	4.5	–19.5†	–12.6	–34.3	–39.2	–39.1†	–28.3	–27.6
Orthostatic test								
$M \pm m$	72.6 ± 1.6	24.6 ± 1.3	2.6 ± 0.8	589.4 ± 72.2	96.4 ± 15.1	163.2 ± 20.4	329.8 ± 40.4	3.2 ± 0.4
% comparison	9.1†	–10.2	52.1	–4.3	15.2	–9.3	–6.4	–11.3
% baseline	14.0*	17.95*	–56.9*	–19.4*	–49.3*	–9.7	–8.8	86.3*
Rest after orthostatic test								
$M \pm m$	62.3 ± 1.1	35.1 ± 1.7	7.7 ± 1.4	997.9 ± 92.9	250.6 ± 36.3	260.6 ± 29.8	329.8 ± 40.4	1.8 ± 0.2
% comparison	8.2	3.0	19.9	7.3	–7.5	–4.9	26.4	14.7
% baseline	–2.3	27.9*	26.1	36.5*	31.8*	44.3*	34.6*	6.5
Group 2 (baseline)								
$M \pm m$	60.9 ± 1.2	34.0 ± 2.3	7.0 ± 2.0	1113.5 ± 176.5	312.0 ± 100.2	297.0 ± 46.1	504.8 ± 73.9	2.3 ± 0.3
Orthostatic test								
$M \pm m$	66.6 ± 1.2	27.2 ± 1.2	1.7 ± 0.5	616.1 ± 65.0	83.7 ± 12.1	179.9 ± 23.4	352.4 ± 39.5	3.5 ± 0.5
% baseline	9.2*	–20.2*	–75.2*	–44.7*	–73.2*	–39.4*	–30.2*	52.1*
Rest after orthostatic test								
$M \pm m$	57.5 ± 1.2	34.0 ± 2.2	6.5 ± 1.5	930.2 ± 108.2	270.8 ± 43.9	274.3 ± 39.9	385.1 ± 42.8	3.2 ± 0.4
% baseline	–5.6	–0.1	–8.1	–16.5	–13.2	–7.7	–23.7	–32.8*

*Statistically significant within-group differences between baseline values in the orthostatic test and after the orthostatic test ($p < 0.05$); †statistically significant between-group differences, $p < 0.05$; % comparison – difference in values in group 1 as compared with group 2 (%); % baseline – differences in within-group value from baseline (%).

and the Valsalva test, reflecting the state of the parasympathetic compartment of the compartment of the ANS, were on the margin between normal and peripheral autonomic insufficiency in both groups. Values in the orthostatic test, reflecting the state of the sympathetic compartment of the ANS, were normal in both groups, while values on the isometric test were on the margin between normal and peripheral autonomic insufficiency in both groups (Table 1).

Analysis of heart rate variability revealed the following changes. At rest, initial HR in group 1 was not significantly different from that in group 2, wile SDNN was decreased in both groups; in group 1, SDNN was significantly reduced by 19.5% (Table 2). TP was 34.3% lower in group 1 than group 2. pNN50% and HF were lower in group 1. Power in the range of the baroreflex component of the spectrum of heart rate variability (LF) was significantly lower in

group 1, by 39.2%, than in group 2. VLF was 28.3% lower in group 1 than group 2, though this did not reach statistical significance ($p > 0.05$). The LF/HF ratio in group 1 was significantly lower and corresponded to the level of eutonia, while in group 2 at rest the value was shifted towards a predominance of sympathetic tone (see Table 2).

The orthostatic test increased HR in group 1 and significantly reduced SDNN, pNN50%, TP, and HF, while LF and VLF decreased insignificantly, autonomic balance tending towards predominance of activity in sympathetic tone. In group 2, the orthostatic test increased HR; SDNN, pNN50%, TP, HF, LF, and VLF significantly decreased and autonomic balance shifted further towards predominance of sympathetic tone.

After the orthostatic test at rest, autonomic balance in group 1 returned to initial, i.e., eutonia, while that in group 2 remained at a high level of predominance of sympathetic nervous system activity.

Correlation analysis showed that the extent of sleep disorder showed strong negative correlations with the level of autonomic impairments ($r = –0.42$, $p = 0.000018$), the level of trait anxiety ($r = –0.35$, $p = 0.00042$), the severity of depressive impairment on the Beck scale ($r = –0.34$, $p = 0.00068$), the level of anxiety on the HADS ($r = –0.24$, $p = 0.028$), the level of depression on the HADS ($r = –0.22$, $p = 0.048$), and the level of reactive anxiety ($r = –0.21$, $p = 0.034$), as well as positive correlations with the result of the 30:15 test ($r = 0.23$, $p = 0.031$) and high-frequency power HF ($r = 0.21$, $p = 0.049$), which reflects the activity of the parasympathetic compartment of the ANS. In addition, there was no link between the extent of sleep disorders and the functional class of angina, age, or number of life events experienced as stressful.

Changes in the emotional domain can be accompanied by changes in sleep quality, while sleep disorders can lead to changes in psychological status, increased levels of anxiety, depression, autonomic impairments, and endocrine shifts in the body. Chronic psychological tension produces rearrangement of central neurochemical mechanisms, which is accompanied by autonomic impairments, changes in the activity of the hypothalamo-hypophyseal-adrenal and sympathoadrenal axes and the whole hormonal profile of the body, changes in electrolyte, protein, and lipid metabolism, impairments to endothelial and immune system functions, and procoagulatory changes in hemostasis, which can lead to the onset or progression of existing atherosclerosis [9], this in turn being able to promote the development of IHD or to aggravate its course. Furthermore, sleep disorders were also linked with increased levels of inflammatory markers in the systemic circulation, such as C-reactive protein and interleukin-6, which are associated with cardiovascular disorders [10, 11]. These mechanisms can explain the negative influences of insomnia on the development and course of cardiovascular diseases [12].

Thus, patients with sleep impairments showed higher levels of anxiety, depression, and autonomic impairments, as well as lower heart rhythm variability, which are unfavorable prognostic signs. This needs to be considered in designing therapeutic and rehabilitation measures in this group of patients.

The authors declare that they have no conflicts of interests.

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