DOI:10.23888/PAVLOVJ2019274451-457

ПРОБА С ВНЕШНЕЙ ПЕРИФЕРИЧЕСКОЙ СОСУДИСТОЙ ОККЛЮЗИЕЙ В ОЦЕНКЕ ЭРГОРЕФЛЕКСА У БОЛЬНЫХ С ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНЬЮ ЛЕГКИХ

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Цель. Оценить изменения на кардиоинтервалограмме (КИГ) при проведении пробы с внешней периферической сосудистой окклюзией у больных с хронической обструктивной болезнью легких (ХОБЛ) и лиц без заболеваний респираторной системы.

Материалы и методы. Обследовано 105 мужчин, из них 64 пациента с ХОБЛ (возраст 64,98±8,67) и 41 доброволец без заболеваний респираторной системы (возраст 61,68±9,21). Исследование вегетативного статуса и оценку изменений на КИГ при проведении пробы с окклюзией осуществляли на оборудовании аппаратно-программного комплекса «Варикард» (ООО «Рамена», Россия).

Результаты. Получены данные, отражающие вегетативный дисбаланс с преобладанием активности симпатического отдела вегетативной нервной системы (ВНС) у пациентов с ХОБЛ в сравнении с группой контроля ($p<0,05$). Изучение эргорефлекса посредством анализа изменений на КИГ показало снижение активности симпатического отдела ВНС в ответ на пробу с внешней периферической сосудистой окклюзией у лиц без заболеваний респираторной системы. В группе больных с ХОБЛ изменения КИГ при проведении пробы были менее выражены и не всегда достигали статистически значимого уровня ($p>0,05$).

Заключение. Различия результатов пробы с внешней периферической сосудистой окклюзией у пациентов с ХОБЛ и добровольцев без заболеваний респираторной системы обусловлены гиперактивацией эргорефлекса у больных с ХОБЛ.

Ключевые слова: *хроническая обструктивная болезнь легких; ХОБЛ; эргорефлекс; вариабельность ритма сердца; проба с внешней периферической сосудистой окклюзией.*

TEST WITH EXTERNAL PERIPHERAL VASCULAR OCCLUSION IN EVALUATION OF ERGOREFLEX IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Aim. To evaluate changes in the cardiointervalogram (CIG) in the test with external peripheral vascular occlusion in patients with chronic obstructive pulmonary disease (COPD) and in individuals without diseases of the respiratory system.

Materials and Methods. The study included 105 men, of them 64 patients with COPD (age 64.98±8.67) and 41 volunteers without diseases of the respiratory system (age 61.68±9.21). The autonomic status was examined and alterations in CIG in the test with occlusion were evaluated on Varicard hardware and software complex (OOO Ramena, Russia).

DOI:10.23888/PAVLOVJ2019274451-457

Results. The obtained data showed the autonomic imbalance with predomination of the activity of sympathetic division of the autonomic nervous system (ANS) in patients with COPD as compared to the control group ($p<0.05$). A study of ergoreflex by analysis of changes in CIG showed reduction of the activity of sympathetic division of the ANS in the test with external peripheral vascular occlusion in individuals without diseases of the respiratory system. In patients with COPD, changes in CIG in the test were less expressed and not always achieved statistically significant level ($p>0.05$).

Conclusions. Differences in the results of the test with external peripheral vascular occlusion in patients with COPD and volunteers without diseases of the respiratory system are attributed to hyperactivation of ergofeflex in patents with COPD.

Keywords: *chronic obstructive pulmonary disease; COPD; ergoreflex; heart rate variability; test with external peripheral vascular occlusion.*

COPD presents a worldwide problem nowadays. To WHO estimates, the disease is the third cause of mortality and disability [1-3]. The main symptoms of COPD are dyspnea on exercise, reduction of tolerance to exercise and cough acquiring chronic character [2,4].

Besides, an important characteristics of COPD is manifestation of systemic effects. Hypoxemia, smoking, reduction of physical activity and other factors form the basis for systemic inflammation, cachexia and dysfunction of skeletal muscles. Barreiro, et al. in their research (2016) emphasize the importance of routine evaluation of dysfunction of muscles in COPD as *a common systemic manifestation* [5]. Due to the above, patients with COPD restrict the level of physical activity, suffer from impairment of the quality of life. For evaluation of the functional condition of patients with COPD, heart rate variability (HRV) is used [6]. Method of examination of HRV permits to evaluate functioning of regulatory systems of an organism, of the activity of sympathetic and parasympathetic divisions of the autonomic nervous system (ANS) [7].

In the literature, a relationship is seen between severity of bronchial obstruction and HRV parameters in patients with bronchial asthma and COPD [8,9] which may be used for complex evaluation of the functional condition of patients.

In the context of a significant role of systemic effects of COPD, the priority task is to study functional disorders of skeletal muscles in patients with COPD and the reflex from receptors of muscle tissue of the lower limbs (ergoreflex) which is understood as *a reflex regulation of an organism in response to mechanical stretch and accumulation of metabolites in muscles* [10]. Ergoreflex may be a connective link between the autonomic imbalance, the level of tolerance to physical load and the functional status of patients with COPD.

The *aim* of study is to evaluate changes in the cardiointervalogram (CIG) in the test with external peripheral vascular occlusion in patients with COPD and in individuals without diseases of the respiratory system.

Materials and Methods

The study involved 64 patients with COPD (age 64.98±8.67 years) and 41 volunteers with no diseases of the respiratory system (age 61.68±9.21 years, $p>0.05$). Participants were also statistically comparable in gender – only men were included.

The study was approved at a meeting №3 (09.11.2016) of Local ethical committee of Ryazan State Medical University. All participants signed Informed consent.

The study included record of CIG three times: before the test, during the test with external peripheral vascular occlusion, and after the test. HRV was evaluated by R.M. Baevsky method [11], with use of Varicard hardware-software complex (OOO Ramena,

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Russia). The participants were offered to lie on the back, breathe through the nose, not to perform unnecessary movements and not to talk. For the test with occlusion, cuffs were used inflated with air and preliminarily applied on the hips of lower limbs. The activity of ergoreflex was evaluated by evidence of changes in CIG.

The results were statistically processed using application program package Excel 2010 (Microsoft Corporation, USA) and Statistica 13.0 (Stat Soft Inc., USA). Correspondence of variable to normal distribution was determined using Kolmogorov-Smirnov and Shapiro-Wilk tests. Quantitative data satisfying normal distribution are presented as mean value (M) ± standard deviation (σ). Data not satisfying normal distribution were presented as median and interquartile range: Me [Q25-Q75].

For comparison of mean values in complexes with normal distribution of a characteristic in groups, Student's t-test was used, in case of absence of characteristics of normal distribution of data, Mann-Whitney U-test was used. For comparison of parameters of dependent groups with normal distribution of a characteristic in groups, paired Student's t-test was used, with distribution different from normal – Wilcoxon paired criteria. The values were considered statistically significant at $p<0.05$.

Results and Discussion

Analysis of clinical characteristics of patients with COPD and of respondents of the control group did not show statistically significant differences in the following parameters: BMI – 27.5 [23.9;30.6] and 28.4 [26.5;29.7] kg/m^2; heart rate (HR) – 72.8±11.0 and 69.8±8.9 beat/min: respiratory rate (RR) – 15.6±4.4 and 14.8±4.3/min; index of the activity of regulatory systems (IARS) – 5.0 [4.0;6.0] and 4.0 [4.0;6.0] conv. un.; mean duration of RR interval (Mean) – 842.6±125.1 and 873.4±113.4 msec; the most common duration of RR intervals (Mo) – 838.9±117.0 and 873.7±116.6 msec, respectively (for all comparisons $p>0.05$). For other analyzed parameters statistically significant differences were obtained ($p<0.05$, Table 1).

Table 1

Comparative Analysis of Initial Parameters of Heart Rate Variability in Patients with COPD and Volunteers with no Respiratory Diseases

Parameter	Patients with COPD	Volunteers with no Respiratory Diseases	p
n	64	41	–
HR, beat./min	72.8±11.0	69.8±8.9	0.15
RR per min	15.6±4.4	14.8±4.3	0.39
IARS	5.0 [4.0;6.0]	4.0 [4.0;6.0]	0.22
RMSSD, msec	25.0 [13.0;66.0]	14.0 [10.0;25.0]	**0.001**
SDNN, msec	30.0 [19.0;55.0]	23.0 [17.0;31.0]	**0.028**
CV, %	3.5 [2.3;5.7]	2.6 [2.0;3.6]	**0.007**
Mean, msec	842.6±125.1	873.4±113.4	0.20
Mo, msec	838.9±117.0	873.7±116.6	0.14
TP, msec^2	595.1 [226.5;1796.9]	344.4 [185.8;825.2]	**0.047**
PHF, %	46.3 [29.0;66.5]	29.7 [14.5;46.4]	**0.0003**
PLF, %	27.7 [16.8;39.7]	34.4 [25.3;42.3]	**0.044**
PVLF, %	20.0 [7.8;31.0]	27.9 [19.8;47.6]	**0.001**
LF/HF	0.6 [0.3;1.2]	1.4 [0.6;2.8]	**0.0004**
IC	1.2 [0.5;2.5]	2.4 [1.2;5.9]	**0.0003**

Note: RMSSD – root-mean-square difference between duration of neighboring RR intervals; SDNN – standard deviation of NN intervals, reflects the total effect of autonomic regulation of heart rhythm; CV – coefficient of variation; TP – total power of spectrum; PHF – relative power of high-frequency oscillations; PLF – relative power of low-frequency oscillations; PVLF – relative power of 'very' low-frequency oscillations; LF/HF – proportion between sympathetic and parasympathetic influence on the heart rhythm; IC – index of centralization

DOI:10.23888/PAVLOVJ2019274451-457

The activity of ergoreflex was evaluated by comparison of CIG parameters in three stages of the research: initial HRV, during test with occlusion and immediately on completion of the test. The results of research for patients with COPD are given in Table 2.

Table 2

Comparative Analysis of Parameters of Heart Rhythm Variability in Evaluation of Ergoreflex in Patients with COPD

Parameter	Patients with COPD (n=64)		
	Initially	In the test	After the test
HR, beat/min	72.8±11.0*	72.6±10.8**	71.6±10.5
RR per min	15.6±4.4	15.8±4.6	15.9±4.4
IARS	5.0 [4.0;6.0]	6.0 [4.0;6.5]**	5.0 [4.0;6.0]
RMSSD, msec	25.0 [13.0;66.0]	27.0 [12.0;57.0]	27.5 [13.5;60.5]
SDNN, msec	30.0 [19,0;55.0]	27.0 [18.5;49.5]	33.0 [23.0;52.5]
CV, %	3.5 [2.3;5.7]	3.4 [2.4;5.8]	4.0 [2.9;5.8]
Mean, msec	842.6±125.1*	843.7±119.6**	854.5±121.2
Mo, msec	838.9±117.0*	843.4±117.2**	854.9±111.6
TP, $msec^2$	595.1 [226.5;1796.9]	483.0 [211.3;1828.6]	815.9 [299.6;1739.3]
PHF, %	46.3 [29.0;66.5]	51.3 [29.9;68.6]	47.2 [27.0;69.3]
PLF, %	27.7 [16.8;39.7]	27.9 [17.4;41.9]	28.8 [16.9;39,7]
PVLF, %	20.0 [7.8;31.0]	14.2 [7.6;30.3]**	22.7 [11.4;34,9]
LF/HF	0.6 [0.3;1.2]	0.6 [0.3;1.4]	0.7 [0.3;1.2]
IC	1.2 [0.5;2.5]	1.0 [0.5;2.4]	1.1 [0.4;2.7]

Note: * – p<0.05 in comparison of initial data with period of recovery; ** – p<0.05 in comparison of the data during the test and in the period of recovery, *Note*: RMSSD – root-mean-square difference between duration of neighboring RR intervals; SDNN – standard deviation of NN intervals, reflects the total effect of autonomic regulation of heart rhythm; CV – coefficient of variation; TP – total power of spectrum; PHF – relative power of high-frequency oscillations; PLF – relative power of low-frequency oscillations; PVLF – relative power of 'very' low-frequency oscillations; LF/HF – proportion of sympathetic and parasympathetic influence on the heart rhythm; IC – index of centralization

Statistically significant differences were obtained in the group of patients with COPD in HR, Mean and Mo parameters in the initial period and the period of recovery. Here, in the studied period HR decreased, while Mean and Mo, on the contrary, showed a statistically significant growth (p<0.05). Comparison of the parameters in the test and in the period of recovery showed buildup of Mean, Mo and power of 'very' low frequency range (PVLF). HR and IARS values in the analyzed period decreased (p<0.05). No statistically significant changes were noted in comparison of the initial parameters and those recorded during the test.

To compare changes between CIG parameters in the test with external peripheral vascular occlusion in patients with COPD and control group (volunteers without respiratory diseases), these parameters were also analyzed in the control group (Table 3).

Comparison of data between the initial period and the period of recovery showed statistically significant decrease in HR, IARS, power of high-frequency range (PHF). The parameters of the total effect of the autonomic regulation (SDNN), coefficient of variation (CV), Mean, Mo, total power of spectrum (TP), power of low-frequency range (PLF), index of centralization (IC) showed a statistically significant increase (p<0.05). According to the data of R.M. Baevsky, the obtained changes are *explained by reduction of sympathetic and growth of parasympathetic influence in the regulation of the heart rhythm* [7,11].

DOI:10.23888/PAVLOVJ2019274451-457

Table 3

Comparative Analysis of Parameters of Heart Rate Variability in Evaluation of Ergoreflex in Group of Volunteers with no Diseases of Respiratory Organs

Parameter	Control Group (n=41)		
	Initially	In the test	After the test
HR, beat/min	69.8±8.9*	70.5±9.2**	68.6±8.4
RR per min	14.8±4.3	14.1 [10.8;16.8]	14.4±4.2
IARS	4.0 [4.0;6.0]*	5.0 [3.0;6.0]**	4.0 [3.0;5.0]
RMSSD, msec	14.0 [10.0;25/0]	16.0 [10.0;25.0]	14.0 [11.0;22.0]
SDNN, msec	23.0 [17.0;31.0]*^	27.0 [17.0;37.0]	27.0 [20.0;37.0]
CV, %	2.6 [2.0;3.6]*^	3.1 [2.2;4.3]	3.0 [2.1;4.1]
Mean, msec	873.4±113.4*	866.4±116.6**	887.7±112.4
Mo, msec	873.7±116.6*	865.8±118.4**	890.2±113.7
TP, msec^2	344.4 [185.8;825.2]*	451.1 [243.2;940.9]	597.3 [327.7;1051.2]
PHF, %	29.7 [14.5;46.4]*	23.6 [15.4;38.3]	24.1 [17.2;31.2]
PLF, %	34.4 [25.3;42.3]^	43.9 [28.9;52.3]	35.9 [29.0;44.2]
PVLF, %	27.9 [19.8;47.6]	26.1 [17.4;39.7]**	37.3 [32.0;49.0]
LF/HF	1.4 [0.6;2.8]	2.1 [0.9;2.7]	1.7 [1.0;2.8]
IC	2.4 [1.2;5.9]*	3.2 [1.6;5.5]	4.1 [2.2;5.6]

Note: * – p<0.05 in comparison of initial data with period of recovery; ** – p<0.05 in comparison of the data in the test and in the period of recovery, *Note*: RMSSD – root-mean-square difference between duration of neighboring RR intervals; SDNN – standard deviation of NN intervals, reflects the total effect of autonomic regulation of heart rhythm; CV – coefficient of variation; TP – total power of spectrum; PHF – relative power of high-frequency oscillations; PLF – relative power of low-frequency oscillations; PVLF – relative power of 'very' low-frequency oscillations; LF/HF – proportion between sympathetic and parasympathetic influence of the heart rhythm; IC – index of centralization

Comparison of the data of the test and of the period of recovery showed decline of HR and IARS. Mean, Mo, and also PVLF parameters increased, here, Mean, Mo showed a tendency to higher values in the period of recovery in comparison with the group of patients with COPD. Besides, in comparison of the initial data with the period of test, statistically significant increase in values SDNN, CV, PLF was obtained in participants of the control group.

Conclusion

Thus, a study of the activity of ergoreflex by parameters of CIG showed the difference between groups of patients with COPD and respondents of the control group. In the test with external peripheral vascular occlusion, changes of CIG in the control group were more expressed, and many parameters showed statistically significant changes (p<0.05). In patients with COPD, very likely due to persistent hyperactivity of ergoreflex, the changes were less expressed and not always reached statistically significant level (p>0.05).

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Дополнительная информация [Additional Info]

Источник финансирования. Бюджет ФГБОУ ВО Рязанский государственный медицинский университет им. акад. И.П. Павлова Минздрава России. [**Financing of study.** Budget of Ryazan State Medical University.]

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, о которых необходимо сообщить, в связи с публикацией данной статьи. [**Conflict of interests**. The authors declare no actual and potential conflict of interests which should be stated in connection with publication of the article.]

DOI:10.23888/PAVLOVJ2019274451-457

Участие авторов. Абросимов В.Н. – концепция и дизайн исследования, Косяков А.В. – сбор и обработка материала, написание и перевод текста, статистическая обработка. [**Participation of authors.** V.N. Abrosimov – concept and design research. A.V. Kosyakov – collection and processing of material, writing and translation of the text, statistical processing.]

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Цитировать: Косяков А.В., Абросимов В.Н. Проба с внешней периферической сосудистой окклюзией в оценке эргорефлекса у больных с хронической обструктивной болезнью легких // Российский медико-биологический вестник имени академика И.П. Павлова. 2019. Т. 27, №4. С. 451-457. doi:10.23888/PAVLOVJ2019274451-457

To cite this article: Kosyakov AV, Abrosimov VN. Test with external peripheral vascular occlusion in evaluation of ergoreflex in patients with chronic obstructive pulmonary disease. *I.P. Pavlov Russian Medical Biological Herald.* 2019;27(4):451-7. doi:10.23888/PAVLOVJ2019274451-457

Поступила/Received: 15.08.2019
Принята в печать/Accepted: 16.12.2019