Study of Regulatory Mechanisms of Activity of Cardiovascular System by Method of Mathematical Analysis of Heart Rhythm in Workers of Chemical Manufactures

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Abstract. The article presents the results of the study of heart rate variability indices of workers engaged in the production of phenol-formaldehyde plastics and plastics at the «Karbodin» plant. 112 people aged from 20 to 50 years were studied: control group-workers with experience up to 1 year, practically healthy (n = 30), 1 group-workers with work experience up to 5 years (n = 40), 2 group workers with work experience from 5 to 10 years (n = 42). As a result of the study, violations of the functioning of the heart regulation system were revealed, depending on the length of employment. The effectiveness of the method for studying the regulation of the physiological functions of the circulatory system as well as the early diagnosis of occupational pathology has been established.

Introduction

Ecological problems, currently of global social nature, are most pronounced in the chemical industry, which is one of the leading sources of stationary emissions of harmful substances into the environment. At the same time, the air of the working area is exposed to pollutants, which is a priority environment for occupational risk assessment.

The quality of the workers' health is not only a prerequisite for high labor productivity and consequently improving welfare, but it is also a guarantee of sustainable social and economic development of the countries of the world. Specific features of the environment, technology, procurement of raw materials and production of finished products create a unique set of working conditions in the chemical industry that directly affect health. At the same time, the factors of the work environment and the characteristics of labor require an integrated approach to solving the problem of improving working condition.

Studying the features of the development of occupational diseases, using the achievements of modern science in the study of various physiological mechanisms of the vital activity of the human body, its adaptive compensatory and pathophysiological reactions, occupational pathology, occupational hygiene, physiology have made their significant contribution to understanding the general biological regularities of general pathology.

For the modern stage of development of hygienic and physiological disciplines is characterized by an isolated or combined effect of professional factors of low intensity in combination with mental and emotional stress, hypokinesia or monotonous work. This leads to the development of erased forms of occupational diseases with small clinical symptoms of their manifestation, which makes diagnosis difficult and requires in-depth knowledge of various areas of medical and biological science. The introduction of modern types of energy, chemicals, synthetic materials into the industry, intensification of labor, the growth of information loads create conditions for the development of new forms of occupational diseases.
Industry, rapid technical progress, the emergence of complex types of work have changed the habitual rhythm of life, which cannot but affect the human body, its health. These conditions have a significant impact on the working capacity and health of the worker. The unfavorable influence of the nature of labor or the production environment on human health indicates the presence of harmful production factors in the production. A harmful and dangerous production factor is a factor, the impact of which on the worker leads to significant violations of the regulation of the basic physiological functions of the organism.

Indicator of the functional state and adaptive reactions of the body can rightly be called the cardiovascular system. The functional state of the organism in the process of adaptation to environmental conditions has two limiting values: health and disease, norm and pathology. Between these values are various donorological conditions, differing in the degree of tension of regulatory systems, the degree of adaptation [1, 2]. The cardiovascular system with its neurohumoral mechanism of control and self-regulation reacts to the slightest changes in individual organs and systems and ensures the coordination of blood flow in them with hemodynamic parameters at the organism level [3].

The pathology of the cardiovascular system is a serious problem, as it is one of the most common causes of disability and deaths of a significant number of people. In Russia, mortality from circulatory system diseases has remained the highest in the world in the last two decades.

A new methodology for studying the processes of regulation of physiological functions, where the circulatory system is considered as an indicator of adaptive reactions of the whole organism, is the analysis of heart rate variability (HRV) [4, 5, 6]. The pathology of the cardiovascular system is a serious problem, as it is one of the most common causes of disability and deaths of a significant number of people. In Russia, mortality from circulatory system diseases has remained the highest in the world in the last two decades. A new methodology for studying the processes of regulation of physiological functions, where the circulatory system is considered as an indicator of adaptive reactions of the whole organism, is the analysis of heart rate variability (HRV) [4, 5, 6].

Currently, HRV analysis is recognized as the most informative non-invasive method for quantifying vegetative regulation of heart rhythm. The HRV analysis method is a nonspecific diagnosis of cardiovascular pathology with an assessment of the state of peripheral vegetative and humoral-metabolic regulation of pacemaker activity in the sinoaureicular node of the heart, based on a high-resolution analysis of wave multifrequency variations in the duration of inter-cystolic intervals (the so-called RR intervals) of an electrocardiogram. Decrease in HRV values precedes haemodynamic,metabolic, energy disorders and is the earliest prognostic sign of the patient's unhappiness [7, 8, 9, 10].

The mechanisms of heart rate variability have not been fully deciphered and are still in the literature. To date, there is no accurate interpretation of the results of HRV analysis, and there is no HRT under different production conditions. Therefore, the introduction of a new method for studying the influence on the vegetative and humoral metabolic regulation of the selective effect of harmful production factors.

There remain many unresolved problems in the study of HRV, which require careful study and therefore research in this area must necessarily continue. In connection with this, the purpose of this work is to study the regulatory mechanisms of heart activity in workers of the «Karbodin» plant in Orekhovo-Zuyevo, Moscow Region, using the analysis of heart rate variability. To achieve this goal, the following tasks must be accomplished:

1. To study statistical and index indicators of heart rate variability in the study groups of workers.
2. To study the parameters of the spectral analysis of heart rate variability in the study groups of workers.
3. Determine the effect of harmful and dangerous production factors on the state of the heart's regulatory systems in the employees of the enterprise, depending on the length of service.
Materials

112 people aged 20 to 50 years were studied, and the subjects were divided into three groups:

- control group, which includes employees who have recently arrived at the enterprise (up to 1 year), without significant bad habits and almost healthy (30 people).

And two experimental groups of workers in the production of chemical plastics. The total number of 82 people. The considered groups of workers were ranked according to the duration of work at the enterprise:

- with a work experience of up to 5 years
- with a work experience of 5 to 10 years.

A 5-minute ECG recording was performed in a quiet separate room, with a constant temperature (C). The period of adaptation to the study conditions (horizontal position of the body) was 10 min. Registration of cardiointervals was carried out with the help of hardware and software complex "Varicard" with subsequent processing of the received material under a special program.

Statistical processing of data was carried out with the help of: a statistical package STATISTICA 6.

In the time domain, the statistical characteristics of the dynamic series were calculated:

- mean value of the cardio interval (R-R).
- standard deviation of the average NN intervals computed over 5-minute time intervals (low-frequency components of the HRV) - SDNN.
- rms deviation of absolute increments of cardiocycle durations, (high-frequency components of HRV) - RMSSD.
- Percentage of cardiocycles, the duration of which differs from the previous one by more than 50 milliseconds - pNN50%.

The parameters of variation pulsometry were estimated:

- mode values (Mo, ms) - the most frequently encountered in this dynamic range is the value of the cardiointerval
- Amplitude mode - (AMO,%) - percentage of R-intervals that entered the modal class with a width of 50 milliseconds, characterizing the measure of the influence of the sympathetic department of the ANS [3].

The obtained data allow to determine the stress index (IN), which characterizes the degree of functional tension of the regulatory mechanisms of the circulatory system:

In the frequency range of cardiac rhythm variability in stationary intervals, cardiointervalograms were determined:

- TP - total power of all normal intervals R-R (ms²), reflecting the total effect of all regulatory systems on the heart rhythm.
- Spectral power densities in the very low frequency range - VLF (ms²) - the effect of thermoregulatory and peripheral motor systems and inter-system integration at the higher brain level, emotional and psychogenic effects on HRV.
- power in the low frequency range - LF (ms²) - reflecting sympathetic and parasympathetic cardiac and vasomotor influences.
- power in the high frequency range - HF (ms²) characterizing the parasympathetic cardiac effects caused by the respiratory waves.
- LF / HF index, reflecting the balance of sympathetic and parasympathetic influences on ANS.

Results and Discussion

Our analysis of statistical and index indicators of heart rate variability revealed that the workers of the study groups statistically significantly differ in heart rate indicators, which indicates differences in the functioning of their cardiovascular system and regulatory systems in general. The average values of the working indicators are given in Table 1 (the mean values and standard deviations are indicated).
### Table 1

| Indicator | Control        | Group 1        | Group 2        |
|-----------|----------------|----------------|----------------|
| R-R , ms  | 876.00±126.01  | 928.44±234.6   | 698.73±65.32   *** |
| SDNN, ms  | 58.12±26.12    | 49.87±15.62    | 40.63±20.76   *** |
| RMSSD, ms | 52.18±31.59    | 51.67±23.64    | 39.17±25.90   *** |
| pNN50, %  | 38.60±17.57    | 32.59±14.32    | 22.32±12.44   *** |
| Mo, ms    | 710.12±32.12   | 660±25.44      | 590±21.45     *** |
| AMo, %    | 39.1±3.41      | 42.4±2.92      | 53±3.95       *** |
| Indicator | 117.26±32.12   | 201.52±54.05   | 252.98±46.25  |

* ** - differences between groups are statistically significant at p≤0.01
  *** - differences between groups are statistically significant at p≤0.001

The mathematical expectation (mean value of the RR-interval) reflects the result of all regulatory influences on the heart and the circulatory system as a whole. The indicator has the smallest variability among all medical and statistical indicators, and its deviation from the individual norm usually signals an increase in the load on the circulatory system or the presence of pathological abnormalities. In our studies it was shown that the average value of the RR-interval is within the limits of the norm for workers of the first group, with an increase in the length of service from 5 to 10 years (group 2), the value of the RR-interval significantly decreases by 20.2% (p≤0.01) in comparison with the value of this indicator of the control group.

The mean square deviation (SDNN) is extremely sensitive an indicator of the state of the mechanisms of regulation of the heart rhythm. A decrease in the index is associated with an increase in sympathetic regulation, which enhances the activity of the autonomous circuit. Our studies show that the SDNN value of the workers of the first group differed insignificantly from the SDNN values of the control group and was less by 14.2% with an increase in work experience from 5 to 10 years (group 2) there is a significant decrease in the parameter compared to the control group by 30.1% (p <0.001).

The RMSSD indicator reflects the activity of the autonomous regulation loop. The higher the value of RMSSD, the more active the link of parasympathetic regulation. In the case of workers in Group 1, this was lower than in the control group, but there was no significant difference. With an increase in the length of service from 5 to 10 years (group 2), there is a significant decrease in the parameter compared to the control group by 25.1% (p <0.001).

pNN50% - gives information similar to RMSSD, but since only difference values above 50 ms are taken into account here, this index is more sensitive to high-frequency, respiratory vibrations of the heart rhythm and, therefore, better reflects the activity of the autonomous regulation loop. From the values of pNN50, one can judge the relative predominance of the parasympathetic or sympathetic link of regulation. In the case of workers in Group 1, this was lower than in the control group, but there was no significant difference. With an increase in the length of service from 5 to 10 years (group 2), there is a significant reduction in the parameter compared to the control group by 31.5% (p <0.001).

MS - indicates the dominant level of functioning of the sinus node. In the first group, the Mo value is at the lower limit of the norm and 7.4% lower than in the control group. In group 2, the value of Mo decreases reliably by 16.9% (p<0.01).

Based on the data obtained, it can be said that most of the workers in the 2nd group are sympathicosotonics, i.e. characterized by increased activity of the sympathetic department of the autonomic nervous system.

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The amplitude of the MS (mode) - reflects the effect of the stabilizing influence of the sympathetic nervous system on the cardiorhythm. The conditional norm of AMo is 32-41% (eutonium).
A decrease in AMO below 32% indicates vagotonia; an increase of more than 41% - about sympathicotonia.

The mean values of AMO in group 1 are near the upper limit of the norm, and do not differ significantly. In group 2, the AMO value increases significantly by 26.4% (p≤0.001).

The stress index (IN), proposed by R.M. Bayevsky, is an integral indicator designed to evaluate the "degree of stress of regulatory mechanisms." The higher it is, the higher the "activity of the sympathetic regulation channel," and the lower, the lower the "activity of the humoral and parasympathetic channels," that is, the increase in IN indicates on the "tension of adaptation", and its decrease indicates a stable adaptation to the effects of various environmental factors. A small load (physical or emotional) increases the IN 1.5 - 2 times. According to our data, the IN of the workers of the 1st group was 201.52 ± 54.05, which is 1.72 higher than in the control group. With an increase in the length of service from 5 to 10 years, ID was 252.98 ± 46.25, which is 1.26 ± 0.05 times higher than in the first group and 2.16 ± 0.05 times higher than in the control group.

Workers engaged in the production of phenol-formaldehyde plastics and plastics showed significant changes in the parameters of spectral analysis of heart rate variability (Table 2)

| Indicator | Control | Group 1 | Group 2 |
|-----------|---------|---------|---------|
| TP, ms²   | 4196±328.21 | 3554.44±234.61 | 6814±324.12*** |
| VLF, ms²  | 1356±323.23 | 923±245.25*** | 1860±299.38*** |
| LF, ms²   | 1443±417.2 | 1534±245.28 | 3520±299.32*** |
| HF, ms²   | 1397±523.7 | 1097±232.29 | 1434±299.3*** |
| (LF/HF)   | 1.03±0.85 | 1.36±0.36 | 2.45±0.36*** |

** - differences between groups are statistically significant at p≤0.01
*** - differences between groups are statistically significant at p≤0.001

Thus, the total power of the spectrum (TP, ms²) for workers in the first group differed insignificantly from the values (TP, ms²) of the control group and was less by 15.3%. With an increase in the length of service from 5 to 10 years (group 2) TP (6814±324.1 ms²) compared with the control group by 32.5% (p <0.001).

When studying the ultra-low-frequency component of the spectrum responsible for the humoral-metabolic effects of the heart rhythm, it is noted that workers with a small amount of work experience decrease the VLF value as compared to the control group. Thus, in group 1 the index of the ultra-low-frequency component of the spectrum is 923±245.2 ms², which is 31.9% lower than the practically healthy control group (p <0.001).

In the second experimental group, the VLF (1860±299.3 ms²) increased by 29.8% (p<0.001) compared to the control group.

The LF index, which characterizes the maximum power of low frequency waves, reflecting the activity of the sympathetic centers of the medulla oblongata (cardiostimulating and vasoconstrictor) in workers of the first group increases insignificantly as compared to the control group. For example, in group 1, LF is 1534±245.2 ms², which is 6% higher than the practically healthy control group - 1443±417.2 ms². In the second group, the LF (3520±299.3 ms²) increases significantly compared to the control group.

The high-frequency component of the HF spectrum is associated with respiratory movements and reflects the vagal control of the heart rhythm (fluctuations in the parasympathetic part of the autonomic nervous system). In the first group, at the beginning of the labor activity there is a slight decrease in the HF index. So, in the 1st group the HF index is 1097±232.2 ms², which is 14.3% lower than the practically healthy control group.

In workers of the second group, the HF index (1434±299.3 ms²) slightly increased compared to the same indicator of the control group (1397±523.7 ms²) by 4%.
The sympathetic-vagal index (LF / HF) conditionally characterizes the percentage contribution of sympathetic and parasympathetic influences to autonomic regulation of the heart rhythm. Its increase indicates a sympathetic regulation of the heart rate, a decrease - about the opposite effect. In the first group of workers, the value of this index was slightly shifted towards the predominance of the influence of the sympathetic department of the autonomic nervous system (1.36 ± 0.36), while in the control group this index was 1.03 ± 0.85 (p <0.05).

With the increase in the length of employment in Group 2, there is a significant increase in the sympathetic-vagal balance in the direction of the predominance of sympathetic influences, which indicates an increased tension in the mechanisms of regulation of cardiac activity. For example, in group 2 the indicator (LF / HF) is 2.45 ± 0.36, which is 1.8 times higher than the indicator (LF / HF) of practically healthy control workers.

Conclusion

Our studies have revealed the negative impact of harmful factors of production on the system of regulation of cardiac activity. Workers engaged in the production of phenol-formaldehyde plastics and plastics, regardless of the length of service, there are changes in the statistical parameters of the heart rate. Thus, in both groups of workers, the reduced RR-interval, SDNN, RMSSD, pNN50%, Mo mode are noted, which reflects an increased tone of the sympathetic part of the autonomic nervous system. In workers of the 2nd group, these indicators decrease reliably, which reflects the increased tension of the mechanisms of regulation of cardiac activity. The values of the index of vegetative tension, the adequacy of regulatory processes, the vegetative index of the rhythm are significantly higher in workers of the 2nd group, which indicates a higher activity of the sympathetic department of the autonomic nervous system. As noted in the literature, the indicators SDNN and RMSSD, pNN 50% change unidirectionally, as shown in our experiment.

Our studies have revealed a negative effect of the harmful. In both groups, as the intensity of the adaptive processes increases, along with a decrease in the RR-interval, SDNN, RMSSD, pNN50%, Mo, AMo and IN indicators increase, which confirms the consistency of changes in the heart rhythm, indicates centralization of control heart rate and increased sympathetic effects.

When considering the wave characteristics of HRV in the company's employees, we come to a conclusion about the negative impact of harmful factors of production on the system of regulation of cardiac activity. Workers engaged in the production of phenol-formaldehyde plastics and plastics, regardless of length of service, observe a change in the overall power of neurohumoral regulation associated with the mobilization of functional reserves. The total power of the spectrum of neurohumoral regulation in cardiac rhythm modulation among workers in group 1, at the beginning of work, changes in the direction of decline, i.e. a decrease in the regulatory capacity of the body, with increasing length of service, activation of the lower levels of control is observed. This jump in the total power of the spectrum for workers with a work experience of 5-10 years can characterize the displacement of the pacemaker (within the zone of the sinus node).

When studying very low-frequency oscillations of the spectrum, there is a significant change associated with the work experience of workers. Workers of the first group have a decrease in humoral metabolic and cerebral ergotropic influences in modulation of the heart rhythm, as evidenced by a change in VLF. The obtained data indicate that the response of the regulation channel depends on the initial voltage of the tone of vegetative innervation of the heart.

Workers of Group 2 show a significant increase in VLF, which indicates activation of the superregemental structures of the brain, and this change indicates the transition of the regulation of the heart rate from the reflexive vegetative control level to the humoral metabolic, which is unable to provide homeostasis quickly.

According to some authors, the arrhythmia, tachycardia, diencephalic pathology, autonomic dysfunction, asthenic syndrome of vegetative dystonia, and damage to the peripheral nervous system are observed among workers in the chemical industry, as well as working with formaldehyde resins [11,12].
The magnitude of LF in the work of group 1 tends to increase, indicating an increase in the influence of the sympathetic vascular center. As the work experience increases, the activity of the sympatho-adrenal system in workers of the 2nd group increases significantly.

Sympathetic-parasympathetic equilibrium among workers of the 1st group was slightly shifted towards the predominance of the sympathetic department of the autonomic nervous system. As the work experience increased in Group 2, a reliable shift of the sympathetic balance to the predominance of sympathetic influences was observed, indicating an increased tension of the regulatory mechanisms cardiac activity.

Thus, with prolonged stays in unfavorable working conditions, persistent changes in physiological functions are possible, accompanied by a disruption in the function of the cardiovascular system [12]. In the case of an extreme force of influence or a long duration of production factors, a pronounced tension of the regulatory systems arises that is required to mobilize the body's functional reserves and to include the appropriate adaptive reactions necessary to maintain and preserve homeostasis. Mobilization of functional reserves can be considered as one of the results of regulatory systems to protect the body from adverse effects or to adapt it to new conditions of existence.

**Recommendations**

Based on the data obtained during the study, it is possible to recommend:

1. The introduction of high-resolution ECG diagnostics into practice (HRV analysis) will allow to identify early professional pathology (at the level of the donorosis state).
2. The method can be used for mass preventive examinations of the working population (as a method of additional diagnosis of cardiovascular pathology with an assessment of the state of peripheral vegetative and humoral-metabolic regulation of pacemaker activity of the sinus node of the heart).
3. The use of this methodology will allow under the conditions of production to assess the vegetative regulation of cardiac activity in healthy people and in workers with various pathologies.
4. Use of this technique will allow to predict the current functional state and state of physiological systems of the body during professional selection, and the definition of occupational fitness.
5. The obtained data can be used in the planning of preventive measures, adequate monitoring of the health status and prescription of drug therapy.
6. These materials can be used for lecture materials and sanitary and industrial research by the department of industrial ecology and labor protection.

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