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Study of Volatile Metabolites Biogenic Amines in Myocardial Infarction

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Abstract: *Studying the content of volatile metabolites of biogenic amines in exhaled air (BB) in patients with myocardial infarction (MI) and the relationship of their disorders with the functional activity of the sympathetic-adrenal system (SAS) and to develop a new gas-analytical diagnostic method for this pathology. In the study of QMI patients (25 people), a significant increase in the daily urinary excretion of catecholamines (CA) and DOPA was found on the first day of admission to the hospital. In the study of patients with NQMI, we noted a statistically significant increase in the excretion of A, NA, DA and DOPA in the daily urine.*

Keywords— exhaled air, coronary heart disease, diethylamine, gas analysis, volatile metabolites of biogenic amines.

1. INTRODUCTION

The great damage caused to human health by cardiovascular diseases (CVD) poses serious problems for both clinicians and public health professionals. In many countries of the world, heart and artery diseases are the cause of death for more than one third of the male population [1]. As a result of epidemiological and clinical observations conducted in our country and abroad, it was shown that among CVD in recent years, coronary heart disease (CHD) is one of the main causes of early disability, disability and mortality of the population [2].

As you know, in most cases, CVD develops latently, their clinical signs appear at a late stage. Often patients are unaware of the presence of the disease and die suddenly; it is extremely rare for a clinician to have the opportunity to examine the patient before his cardiovascular system is seriously affected [1, 3]. It follows that only therapeutic measures can not solve the problem of death from CVD [4].

The main mechanism of occurrence of coronary insufficiency in morphologically unchanged vessels is arterial spasm. Disorders of neurohumoral regulatory mechanisms, which are currently relatively poorly understood, lead to spasm. The development of coronary insufficiency is facilitated by nervous and (or) physical stress, which causes an increase in the activity of the sympathetic-adrenal system (SAS). Due to the increased production of catecholamines (CA) by the adrenal glands and postganglionic endings of sympathetic nerves, an excess of these biologically active substances accumulates in the myocardium [5, 6]. Strengthening the heart, in turn, increases the need for oxygen in the myocardium. The activation of the blood coagulation system under the influence of increased activity of SAS, as well as the inhibition of its fibrinolytic activity and changes in platelet function, exacerbate coronary insufficiency and myocardial ischemia [6, 7, 8].

There is a need to make significant changes in research methods, despite the fact that they are based on clinical methods [5, 9]. Invasive methods of research, which are more or less pronounced inconveniences, and in some cases a danger to the life of the patient, forced scientists to look for alternative (non-invasive) ways to diagnose diseases of various organs and systems.

It is known that early diagnosis of CHD increases the effectiveness of its treatment and prevents the development of various complications. One of the methods of early diagnosis is the analysis of exhaled air (BB) [10, 11].

As you know, there is a constant gas exchange between the body and the environment, the supply of oxygen and the removal of carbon dioxide and many organic compounds. Carbon dioxide is easy to detect, since its content in the exhaled air (BB) reaches 5%. Other volatile components of explosives are, unfortunately, significantly smaller concentrations of the order of 10-6 or even lower. Very sensitive equipment is needed to detect such minute compounds. Mass spectrometry solves this problem, however, due to the complexity of the equipment, its use is currently limited to scientific centers. Therefore, it became necessary to develop a new sensitive and simple technique for analyzing explosives [12, 13].

Breath analysis has become a promising branch of medical technology in recent years. Doctors began to use this analysis to diagnose an ever-expanding range of diseases without the negative consequences of invasive procedures. The problem of detecting volatile organic substances in explosives has a long history. Since the time of Hippocrates, doctors have known that the smell of explosives can serve as a key in the diagnosis of diseases. In many methods of IV analysis, the patient is expected to receive an appropriate dose of the precursor of the substance being determined. The presence of abnormal amounts of decay products in the BB may indicate a disease [6, 14].

In modern medicine, the analysis of explosives is also used in the diagnosis of diseases of the stomach, liver, and intestines.

IV analysis is an expressive method that has a high specificity, low cost of research, does not require surgical intervention (implemented in an outpatient setting), and mass testing is also possible. When examining patients, the transfer of infection from the patient to the service personnel is excluded. The atraumatic and harmless nature of the study allows for dynamic observation.

In available literature we found a single work devoted to the analysis of EXPLOSIVES [7, 15] and the total lack of work on the study of volatile metabolites of biogenic amines in BB CHD patients, as well as parallel and simultaneous study and qualitative evaluation of the functional state of the SAS. Often, the state of CAC was not studied in a complex: only individual fractions of CA were studied, or the content of CA and their decay products in patients with CHD. The study of the functional state of CAC by the level of excretion of all CA fractions with a parallel study of them in the composition of explosives has not been previously conducted. As is known, the most adequate method of assessing the state of CAC is the study of CA in the urine.

The aim of the study was to study the content of volatile metabolites of biogenic amines in BB in patients with MI and the relationship of their violation with the functional activity of SAS and to develop a new gas-analytical diagnostic method for this pathology.

2. MATERIALS AND METHODS OF RESEARCH.

We observed 45 male patients aged 31 to 68 years suffering from coronary heart disease. The duration of the disease is from 3 to 20 years. The patients were hospitalized in the cardiology department of the Andijan branch of the Center for Emergency Emergency Care.

45 patients were randomized into 2 groups, taking into account the diagnosis. 25 patients were diagnosed with IHD QMI (aged 31 to 68 years); 20 men were diagnosed with IHD NQMI (35 to 60 years).

The diagnosis in all examined patients is based on the data of clinical observation, laboratory analysis and functional diagnostics. For many years – from 3 to 20, patients underwent inpatient and outpatient treatment for CHD. The patients we observed with acute myocardial infarction received traditional treatment.

The control group consisted of 20 patients aged 30 to 55 years.

IV samples for analysis in patients with myocardial infarction were taken on the first day of admission to the hospital, on the 7th-8th day and on the 12th-14th day of the disease.

When selecting patients for the analysis of BB, the pathology of the respiratory organs was excluded.

Determination of epinephrine, norepinephrine, dopamine and DOPA in daily urine was performed by trioxyindole fluorimetric method [8].

The results of clinical studies were processed with the help of applied programs of statistical processing of Excel, as well as by the method of variation statistics according to Fisher using t-criteria of Student tables. The arithmetic mean values (M) and the average errors of the arithmetic mean (m) are indicated. The differences between the arithmetic mean values were considered statistically significant at $p<0.05$ (G. G. Avtandilov, 1990). To determine the strength of the relationship between the indicators, we used correlation analysis using Excel statistical processing programs.

3. THE RESULTS OF THE RESEARCH.

When examining patients with QMI in the first days of admission to the hospital, an increased content of volatile amines in the BB was noted. And if patients with NQMI on the 1st day increased the level of biogenic amine metabolites by 412.1%, then in patients with QMI increased by 11.8 times compared to healthy ones. On day 7-8, the content of amines in IV in QMI patients decreased to 582±27.29 10-9 g / l, which was 7.8 times higher than in healthy patients. On day 12-14, there was a significant decrease in the content of amines in IV in QMI patients to 301±17.91 10-9 g / L, which is 4 times higher than the control group (Table 1).

Table 1
The level of volatile metabolites of biogenic amines in BB in patients with QMI and NQMI

Groups	When you receive $\times 10^{-9}$ g/l	7-8 days $\times 10^{-9}$ g/l	12-14 days $\times 10^{-9}$ g/l
I Healthy, n=20	74±0,74		
II QMI, n=20	879±54,6	582±27,29	301±17,91
II NQMI, n=20	379±12,14	301±11,55	207±10,84
P_{1-2}	P<0,001		
P_{1-3}	P<0,001		

Examination of patients with NQMI was carried out at admission, then on 7-8 days of stay and on 12-14 days. On the first day, there was a significant increase to 379±41 10-9 g / l of volatile metabolites of biogenic amines in the BB, which is 5.1 times higher than the control indicator (P<0.001). On the 7-8 day of the disease, a slight decrease in the metabolites of biogenic amines was observed to 301±49 10-9 g / l, which is 4 times higher than the indicator of the healthy group (P<0.001). And on 12-14 days, the level of diethylamine descends to 207±47 10-9 g / l, which is 2.7 times higher than the control level (P<0.001) (Table 1).

Table 2
Content of volatile metabolites of biogenic amines in exhaled air and daily excretion of catecholamines in healthy patients with NQMI and QMI

№	GROUPS	Catecholamines				Amines in BB $\times 10^{-9}$ g/l
		A total (mkg/day)	NA total (mkg/day)	DA total (mkg/day)	DOPAMINE (mkg/day)	

1	Healthy	7,3±0,2	16,4±0,3	282,8±6,2	47,9±1,0	74±0,7
2	QMI	17,6±1,1	36,0±2,4	256,6±32,4	23,9±5,1	379±12,1
3	NQMI	11,1±0,7	26,5±1,9	252,9±11,3	22,2±1,7	879±54,6
P_{1-2}		P<0,001	P<0,001	P>0,05	P<0,001	P<0,001
P_{1-3}		P<0,001	P<0,001	P>0,01	P<0,001	P<0,001

In the study of QMI patients (25 people) on the first day of admission to the hospital, a significant increase in the daily urinary excretion of catecholamines (CA) and DOPA was found (Table 2).

There was a statistically significant increase in the excretion of free epinephrine (A) compared to healthy people by 1.7 times (P<0.001). Compared with the control, the excretion of conjugated A was 3.1 times greater (P<0.001). Accordingly, the coefficient of increase in the content of total A in daily urine in relation to the control value was equal to 2.6 (P<0.001) (P<0.001).

The excretion of all fractions of norepinephrine (NA) was also statistically significantly higher than the control level. There was an increase in free NA in comparison with the control by almost 2 times (P<0.001). The increase in conjugated NA in daily urine exceeded the control level by 2.4 times (P<0.001). Accordingly, the indicator of increased excretion of total NA was 2.2 in relation to the control (P<0.001).

The excretion of free, conjugated and total dopamine (DA) in patients remained relatively lower than in healthy patients and was statistically unreliable. The excretion of free, conjugated and total dopamine in healthy subjects was 141.4 7.6 mcg/day; 141.4 7.6 mcg/day; 282.8 10 mcg/day, respectively (see Table 3.9). The level of DOPA excretion in QMI patients on day 1-2 of the disease was significantly lower (P<0.001) than in healthy patients and amounted to 23.9 1.9 mcg/day, and in healthy patients the DOPA excretion was 47.9 2 mcg / day (Table 2).

The correlation coefficient between volatile amines and total A at QMI was -0.13, which indicates a weak inverse relationship. When determining the correlation of diethylamine with a total ON the direct relationship (coefficient =+0,03), with YES – feedback (-0,44), with DOPA – also feedback (coefficient = -0,05).

In the study of patients with NQMI we noted a statistically significant increase in excretion AND NA, and DOPA in the urine daily.

Daily excretion of free A in patients with NQMI compared with healthy individuals increased by 22.6% (P<0.05), conjugated by 84.1% (P<0.001) and total by 52.3% (P<0.001).

Daily urine excretion in NQMI patients was statistically significantly higher than the control level. The excretion of free NA increased by 55.1% (P<0.01), conjugated by 68.5% (P<0.01) and total by 62.2% (P<0.001).

The decrease in the daily excretion of all DA fractions compared to healthy ones, free by 17.9% (P<0.05), conjugated by 3.3% was statistically unreliable.

The level of DOPA excretion was statistically significantly reduced by 2.2 times (P<0.01).

Thus, the values obtained by us indicate a statistically significant increase in the excretion of KA, in particular NA and A, and a decrease in DOPA in the daily urine of NQMI patients.

When determining the correlation between the content of volatile metabolites of biogenic amines in BB and the excretion of A, a weak direct relationship was determined (the correlation coefficient is + 0.12). When correlating with the total output of NA, a weak direct relationship was found (coefficient +0.21), with the total output of DA – a strong inverse correlation (-0.77), with DOPA – an inverse relationship (coefficient = -0.62).

Calorimetric and fluorimetric studies have shown that the functional activity of the sympathetic-adrenal system in patients with myocardial infarction is increased. This was manifested by a statistically significant increase in the daily urinary excretion of catecholamines compared to healthy people.

4. DISCUSSION OF THE RESULTS.

In the course of our work, interesting and important data were obtained that open up certain prospects for further research. Volatile metabolites of biogenic amines in BB were detected by gas-analytical method and the daily excretion of CA in the urine of MI patients and clinically healthy people was studied in parallel.

The results of our research led to the development of a new method of examination, which is convenient, does not pose a danger to the patient's life and is fast in execution. Volatile metabolites of biogenic amines in BB in patients with CHD were studied for the first time. The proposed method is based on the use of modern methods of physical electronics and gas analysis. For the first time, a surface-ionization sensor with high sensitivity and selectivity to amines was used for medical diagnostics. On the basis of clinical studies, new ways of amine formation in BB in patients with acute MI were identified.

BB analysis is a non-invasive diagnostic method and will provide important new approaches to elucidating the biochemical functions of the body. Also, a clinical trial of the amine gas analyzer was conducted on the basis of the Department of Faculty Therapy of ASMI for the examination of patients with coronary heart disease. In recent years, the rise in interest in explosives research has been driven by advances in analytical technology that have made it possible to identify a rapidly growing number of substances in explosives. Our clinical studies using advanced methods of gas analysis have shown that the presence of biogenic amine metabolites in IV will help early diagnosis of CHD and the choice of treatment tactics, as well as prevent the development of complications. This method of diagnosis

without the negative consequences of invasive procedures has become a promising branch of medical technology.

The results of clinical studies of BB analysis reveal previously unknown mechanisms underlying the metabolism of biogenic amines in patients with coronary heart disease. As is known, CHD is accompanied by a pronounced violation of KA biosynthesis and an increase in the activity of the sympathetic-adrenal system in MI, especially in QMI. As already noted in patients with acute IHD, an increase in the excretion of A and NA in the first days of myocardial infarction was accompanied by a significant decrease in the content of DA and DOPA in the daily urine. The low content of catecholamine precursors in the daily urine in the first days of observation, apparently, is due to their accelerated transition to NA and A, as well as reflex inhibition of their formation due to excessive content of A and NA. According to the literature, it should be noted that in the future, for a long time from the onset of the disease, the level of excretion of DA and DOPA remains significantly lower than normal. Low excretion of DA and DOPA with a parallel decrease in the excretion of A and NA in the dynamics of the disease indicates the depletion of the reserve capabilities of SAS in patients with MI. This is most clearly seen in patients with MI with the Q-wave.

As already mentioned, in pathological conditions that cause the accumulation of primary amines, a channel leading to the formation of diethylamine by the above mechanism is possible. As already mentioned, the system under consideration has two outputs, the first output is associated with the urea cycle, and the second with the BB. Thus, this system is open, at the input of which oxalic acetic and ketoglutaric acids are continuously supplied, and at the output there is a continuous removal of glutamic acid and a volatile metabolite of biogenic amines – diethylamine.

The results of the research B. Askarov and his co-authors. (2013) show that the stationary concentration of diethylamine increases with an increase in the activity of ASAT, and vice versa, an increase in the activity of MAO leads to a decrease in the stationary concentration of diethylamine in the BB.

It is assumed that it is possible to determine the degree of cellular myocardial hypoxia by the content of diethylamine in the BB. Since, as a result of deamination of KA, secondary alkylamines are formed, in particular diethylamine, and a stressful situation exacerbates myocardial hypoxia.

The analysis of explosives also provides an interesting clue to the biochemical basis of many diseases, the causes of which are still unknown. The value of the information that can be obtained in the analysis of explosives is due to the fact that the contents of the alveoli of the lungs are separated from the blood in the capillaries only by a thin barrier – the alveolocapillary membrane. Like water flowing down from an elevation, volatile organic compounds can diffuse through the alveolocapillary membrane from one compartment to another, in the direction of lower vapor pressure – from the air to the blood or vice versa (M. Phillips).

A non-invasive breath test is being introduced into the practical work of individual clinical units. They carry unique information about changes in various organs, and at the molecular level. Their importance for practical health care is great.

It can be considered reasonable to believe that the introduction of non-invasive diagnostics will bring significant benefits in the recognition of a number of difficult-to-diagnose diseases, as well as significantly protect and make the process of examining patients more comfortable. Therefore, we believe that the widespread use of the method in clinical practice is not only justified, but is already becoming mandatory.

Early diagnosis of coronary heart disease, as well as other pathological conditions and syndromes, such as the severity of oxidative stress in diseases of internal organs in general, will allow us to develop earlier criteria for diseases and justify their differentiated treatment using both drug and non-drug effects.

The results obtained by us, taking into account the data of literature sources, indicate the need to monitor the state of SAS in patients with MI. This is not only theoretical, but also of great practical importance for the diagnosis, prediction, and determination of the tactics of rational MI therapy and prevention of complications.

5. CONCLUSIONS:

1. A new additional method for the diagnosis of coronary heart disease carried out by an amine gas analyzer has been developed. Due to its high sensitivity, the amine gas analyzer allows you to solve the problem of diagnosing myocardial infarction. The obtained data on the volatile metabolites of biogenic amines in exhaled air can be used as additional diagnostic criteria.
2. This method of diagnosis for complete safety, expressiveness, lack of necessary surgical intervention can be implemented in an outpatient setting, as well as for mass testing, the impossibility of transmitting infection from patient to staff, low cost of study allows to implement in practical health care.
3. A significant increase in the yield of volatile metabolites of biogenic amines with exhaled air was found in patients with myocardial infarction, Q Q, which is of great interest in identifying the mechanism of development of myocardial infarction.
4. A comprehensive study of the sympathetic-adrenal system and the metabolism of biogenic amines in patients with ischemic heart disease showed that in acute myocardial infarction, there is a pronounced violation of catecholamine biosynthesis, which is manifested by an increase in

urinary excretion of free and conjugated forms of epinephrine and norepinephrine.

5. A comparative analysis of the content of volatile metabolites of biogenic amines in the exhaled air with daily excretion of catecholamines in the urine revealed that in acute myocardial infarction, there is a significant increase in the output of volatile amines through the exhaled air and increased excretion of catecholamines in the urine.

REFERENCES

1. Mamadiev MM, Khuzhamberdiev MA, Askarov BA, Amanov K. Modeling of living systems: towards medical diagnostics based on physical methods of analysis of volatile metabolites of biogenic amines. FIT of Elmi magazine habarlar. 2001;3-4:187-189.
2. Klimenko VA, United Kryvorotko days. Analysis of exhaled air as a marker of biochemical processes in the body. Theoretical medicine. 2011;1(28): 138-143.
3. Kistenev YUV, Chuikova KI, Gomboeva SS, Karapuzikov AA. To study the relationship between the absorption spectra of gas emissions from patients with acute viral hepatitis obtained by laser optical-acoustic spectroscopy and blood biochemical parameters. 2017; 4:32-37.
4. What diseases smell like. Paramedic. Ambulance information site; http://www.feldsher.ru/news-view-1258.html.
5. Bykova AA, Malinovskaya LC, Chomakhidze PS, Trushina OV, etc. Analysis of exhaled air in the diagnosis of cardiovascular diseases. Cardiology 2019; 59(7):61-67.
6. Lavoisier Antoine Laurent. Section science and technology: Chemistry/ Circumnavigation. Online online; http://www.krugosvet.ru/enc/nauka_i_tehnika / chemistry / LAVOISE_ANTUAN_LORAN. HTML.
7. Korzhov VI, Vidmachenko AV, Korzhov MV. Carbon monoxide / / Journal. Academy of medical Sciences of Ukraine. 2010; T16, 1: 23-37.
8. Khujamberdiev MA, Saidullaev vehicle, Mamadiev MM. Disorders of deamination of nitrogenous compounds in the heart muscle in experimental atherosclerosis. Bulletin of Experimental Biology and Medicine. 1986; 12: 78-80.
9. Phillips M. Analysis of exhaled air in medicine. In the world of science. 1992; 9-10: 42-48.
10. Khujamberdiev MA, BA Askarov. Method of analysis of exhaled air as a possible criterion in the diagnosis of cardiovascular diseases. Journal of Theoretical and Clinical Medicine. 2003; 1:114-117.
11. Ageev BG, Kistenev SE, Nekrasov EV, etc. Evaluation of exhaled air samples by laser optical-acoustic spectroscopy in patients with pulmonary tuberculosis. Bulletin of Siberian Medicine. 2012; 4:117-121.
12. Chuikova KI, Kistenev yuv, Gomboeva SS. Application of gas analysis in the diagnosis of liver diseases. Bulletin of Siberian Medicine. 2012; 6:179-185.
13. Klimanov IA. Mechanisms of formation of exhaled air condensate and markers of oxidative stress in pathologies of the respiratory tract. Pulmonology. 2009;2:113-119.
14. Berezina AV. Creation of technologies and evaluation of the effectiveness of treatment of socially significant diseases using the method of multicomponent microanalysis of exhaled air. Journal of breath research, IOP Publishing. 2013;5:47-51.