World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-23, June 2023
ISSN: 2749-3644

MODERN METHOD OF DETECTING VOLATILE METABOLITES OF BIOGENIC AMINES IN MYOCARDIAL INFARCTION

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Article history:

Received: April 11th 2023
Accepted: May 11th 2023
Published: June 20th 2023

Abstract:

The volatile metabolits of biogenical amins of exhaled air were studied for the first time, the functional activity of sympatic-adrenal system on the excretion of combined and free fractions of catecholamins and DOFA in daily urine was studied simultaneously. It is shown the results of the investigation on the new methods of noninvasing diagnosing of Ischemic Heart disease in this paper. This method is based on analyzes of expirating air. The results of investigation showed the possibility of the surface ionizating detector in diagnosis of Ischemic Heart disease. It was revealed the statisticly importance of difference in containing the amines in expirating air of patients ill with Ischemic Heart disease and healthy people. The advantage of this method concludes whole harmless, expressive ness and canceling the operative intervention and possibilities of mass testing, and cheap price of observation. The difference in eliminating the amines with expirating air can be stable marker for early diagnosing of the preinfarctive state.

Keywords: cardiovascular disease, coronary heart disease, sympathetic-adrenal system, catecholamine, exhaled air.

DOING. The massive damage to human health from cardiovascular disease (CVD) poses serious challenges for both clinicians and public health workers. In many countries of the world, diseases of the heart and arteries 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 has been shown that coronary heart disease (CHD) has recently been one of the main causes of early disability, disability and mortality among CVDs [2].

As is known, 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; extremely rarely, a clinician has the opportunity to examine a patient before his cardiovascular system is seriously affected [1, 3]. It follows from this that therapeutic measures alone cannot solve the problem of death from CVD [4].

Arterial spasm acts as the main mechanism for the occurrence of coronary insufficiency in morphologically unchanged vessels. Violations of neurohumoral regulatory mechanisms, which are currently relatively insufficiently studied, lead to spasm. The development of coronary insufficiency is promoted by nervous and (or) physical stress, which causes an increase in the activity of the sympathetic-adrenal system (SAS). Due to 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 work of the heart, in turn, increases the demand for oxygen in the myocardium. The activation of the blood coagulation system, as well as the inhibition of its fibrinolytic activity and changes in platelet function, observed under the influence of increased SAS activity, 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 research methods, which are more or less pronounced inconvenience, and in some cases even 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 coronary heart disease 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 (EA) [10, 11].

As you know, between the body and the environment there is a constant gas exchange, the supply of oxygen and the removal of carbon dioxide and many organic compounds. Carbon dioxide is easy to detect, since its content in exhaled air (BB) reaches 5%. Other volatile components of explosives, unfortunately, have much lower concentrations - about 10-6 and even lower. To detect such tiny compounds,

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Volume-23, June 2023
ISSN: 2749-3644

very sensitive equipment is needed. 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 the analysis of explosives [12, 13].

Breath analysis has developed into a promising branch of medical technology in recent years. Doctors have begun to use this test to diagnose an ever-expanding range of diseases without the negative effects of invasive procedures. The problem of detecting volatile organic substances in explosives has a long history. Since the time of Hippocrates, physicians have known that the smell of explosives can serve as a clue in the diagnosis of diseases. In many IV assays, the patient is expected to receive an appropriate dose of the analyte precursor. The presence of abnormal amounts of degradation products in explosives 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.

VV analysis is an expressive method with high specificity, low cost of research, which does not require surgical intervention (implemented on an outpatient basis), and mass testing is also possible. When examining patients, the transfer of infection from the patient to the attendants is excluded. Atraumatic and harmless research allows for dynamic monitoring.

In the literature available to us, there are single works devoted to the analysis of EVs [7, 15], and there are no works on the study of volatile metabolites of biogenic amines in EVs in patients with IHD, as well as in parallel with the simultaneous study and qualitative assessment of the functional state of the SAS. Often, the state of the SAS 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 IHD. The study of the functional state of the SAS in terms of the level of excretion of all CA fractions with their parallel study in the composition of explosives has not been previously carried out. As is known, the most adequate method for assessing the state of the SAS is the study of CA in the urine.

THE PURPOSE OF THE STUDY: to study the content of volatile metabolites of biogenic amines in EVs in patients with MI and the relationship of their impairment with the functional activity of the CAS and to develop a new gas analytical method for diagnosing this pathology.

MATERIALS AND RESEARCH METHODS. Under our supervision there were 45 male patients aged 31 to 68 suffering from ischemic 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 Emergency Center.

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

The diagnosis in all examined patients was made on the basis of clinical observation, laboratory analysis and functional diagnostics. For many years - from 3 to 20, patients underwent inpatient and outpatient treatment for coronary artery disease. The patients with acute myocardial infarction observed by us received traditional treatment.

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

Samples of explosives for analysis in patients with myocardial infarction were taken on the first day of the patient's admission to the hospital, on the 7-8th day and on the 12-14th day of the disease.

When choosing patients for the analysis of VV, the pathology of the respiratory organs was excluded.

Determination of adrenaline, noradrenaline, dopamine and DOPA in daily urine was carried out by the trioxyindole fluorimetric method modified by E.Sh. Matlina, Z.M. Kiseleva, I.E. Sofieva [8, 9].

The results of clinical studies were processed using the Excel statistical processing software, as well as the Fisher variance statistics method using Student's t-tests. Arithmetic mean values (M) and mean errors of the arithmetic mean (m) are indicated. Differences between the arithmetic mean values were considered statistically significant at $p<0.05$ (G.G. Avtandilov, 1990). Correlation analysis was used to determine the strength of the relationship between the indicators using Excel statistical processing programs.

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

Examination of patients with NQMI was carried out at admission, then on the 7th-8th day of stay and on the 12th-14th day. On the first day, there was a significant increase to 379· 41 10-9 g/l of volatile

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Volume-23, June 2023
ISSN: 2749-3644

metabolites of biogenic amines in explosives, which is 5.1 times higher than the control value (P<0.001). On the 7th-8th day of the disease, there is a slight decrease in metabolites of biogenic amines to 301· 49 10-9 g/l, which is 4 times higher than in the healthy group (P<0.001). And on days 12-14, the level of diethylamine drops to 207· 47 10-9 g/l, which is 2.7 times higher than the control level (P<0.001) .

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

There was a statistically significant increase in the excretion of free adrenaline (A) compared with healthy 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 2.6 (P<0.001) (P<0.001).

Excretion of all fractions of norepinephrine (NA) was also statistically significantly higher than the control level. An almost 2-fold increase in free NA compared with the control was noted (P<0.001). The increase in conjugated HA in daily urine exceeded the control level by 2.4 times (P<0.001). Accordingly, the increase in the excretion of total NA was 2.2 (P<0.001) in relation to the control.

Excretion of free, conjugated and total dopamine (DA) in patients remained relatively lower than in healthy subjects and was not statistically significant. Excretion of free, conjugated and total dopamine in healthy people was 141.4-7.6 μg/day, respectively; 141.4 7.6 mcg/day; 282.8 10 mcg/day (see Table 3.9). The level of DOPA excretion in patients with QMI on the 1st-2nd day of illness was significantly lower (P<0.001) than in healthy people and amounted to 23.9 1.9 μg/day, while in healthy people DOPA excretion was 47.9 2 μg/day.

The correlation coefficient between volatile amines and total A at QMI was -0.13, indicating a weak inverse relationship. When determining the correlation between diethylamine and total NA, a direct relationship was found (coefficient = +0.03), with DA - feedback (-0.44), with DOPA - also feedback (coefficient = -0.05).

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

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).

Excretion in the daily urine of NA in patients with NQMI is statistically significantly higher than the control level. The excretion of free HA 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 daily excretion of all DA fractions compared with healthy ones, free by 17.9% (P<0.05), conjugated by 3.3% was not statistically significant.

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 CA, in particular HA and A, and a decrease in DOPA in the daily urine of patients with NQMI.

When determining the correlation between the content of volatile metabolites of biogenic amines in explosives and the excretion of A, a weak direct relationship was determined (the correlation coefficient is +0.12). With a correlation with the total excretion of NA, a weak direct relationship was found (coefficient +0.21), with the total excretion of DA - a strong inverse correlation (-0.77), with DOPA - feedback (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 excretion of catecholamines in the urine compared to healthy people.

The 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 EVs were detected by the gas-analytical method, and the daily excretion of CA in the urine in patients with MI and clinically healthy people was simultaneously studied.

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 life of the patient and is quick to perform. For the first time, volatile metabolites of biogenic amines in EVs in patients with coronary artery disease have been studied. 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. Based on clinical studies, new pathways for the formation of amines in EVs in patients with acute myocardial infarction have been identified.

VV analysis is a non-invasive diagnostic method and will provide important new approaches to elucidate the biochemical functions of the body. Also, a clinical trial of an amine gas analyzer was carried out at the Department of Faculty Therapy of the Andrey State Medical Institute for the examination of patients

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Available Online at: https://www.scholarexpress.net
Volume-23, June 2023
ISSN: 2749-3644

with coronary artery disease. In recent years, a rise in interest in research on explosives 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 improved methods of gas analysis have shown that the presence of biogenic amine metabolites in explosives will help early diagnosis of coronary artery disease and the choice of treatment tactics, as well as prevent the development of complications. This diagnostic method, without the negative consequences of invasive procedures, has become a promising branch of medical technology.

The results of clinical studies of the analysis of VV reveal previously unknown mechanisms underlying the metabolism of biogenic amines in patients with coronary artery disease. As is known, IHD is accompanied by a pronounced impairment of CA biosynthesis and an increase in the activity of the sympathetic-adrenal system in MI, especially in QMI. As already noted in patients with acute coronary artery disease, 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 daily urine. The low content of catecholamine precursors in the daily urine in the first days of observation is apparently due to their accelerated conversion into HA and A, as well as reflex inhibition of their formation due to the excess content of A and HA. According to literary sources, it should be noted that subsequently, for a long time from the onset of the disease, the level of DA and DOPA excretion remains significantly below the norm. 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 capacity of the SAS in patients with MI. This is most clearly seen in patients with Q-wave MI.

As already mentioned, in pathological conditions that cause the accumulation of primary amines, a channel is possible, leading to the formation of diethylamine according to the above mechanism. As already mentioned, the system under consideration has two outputs, the first output is associated with the urea cycle, and the second with explosives. Thus, this system is open, to the input of which oxaloacetic 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 research Askarov B. et al. (2013) show that the steady-state concentration of diethylamine increases with an increase in ACAT activity, and vice versa, an increase in MAO activity leads to a decrease in the steady-state concentration of diethylamine in explosives.

The possibility of determining the degree of cellular myocardial hypoxia by the content of diethylamine in explosives is supposed. Since, as a result of deamination of KA, secondary alkylamines are formed, in particular diethylamine, and a stressful situation aggravates myocardial hypoxia.

BB analysis also provides interesting clues to the biochemical underpinnings of many diseases whose causes are as yet unknown. The value of information that can be obtained from 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 air to blood, or vice versa (M. Phillips).

The non-invasive breath test is beginning to be introduced into the practical work of individual clinical departments. They carry unique information about the ongoing changes in various organs, and at the molecular level. Their significance for practical health care is great.

It can be considered reasonable that the introduction of non-invasive diagnostics will bring significant benefits in recognizing a number of difficult-to-diagnose diseases, as well as significantly protect and make the process of examining patients 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, for example, 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 literary sources, indicate the need to monitor the state of the SAS in patients with MI. This has not only theoretical, but also important practical significance for the diagnosis, prognosis, and determination of tactics for rational therapy of MI and prevention of complications.

CONCLUSIONS: 1. A new additional method for diagnosing coronary heart disease using an amine gas analyzer has been developed. Due to its high sensitivity, the amine gas analyzer allows solving the problem of diagnosing myocardial infarction. The obtained data on volatile metabolites of biogenic amines in exhaled air can be used as additional diagnostic criteria.

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Available Online at: https://www.scholarexpress.net
Volume-23, June 2023
ISSN: 2749-3644

2. This diagnostic method, due to its complete harmlessness, expressiveness, lack of need for surgical intervention, can be implemented on an outpatient basis, as well as for mass testing, the impossibility of transferring infection from the patient to the attendants, and the low cost of the study, allows it to be introduced into practical healthcare.

3. A significant increase in the release of volatile metabolites of biogenic amines with exhaled air was found in patients with myocardial infarction, especially in Q-wave myocardial infarction, which is of great interest in identifying the mechanism of myocardial infarction.

4. A comprehensive study of the sympathetic-adrenal system and the metabolism of biogenic amines in patients with coronary heart disease showed that in acute myocardial infarction there is a pronounced violation of the biosynthesis of catecholamines, which is manifested by an increase in urinary excretion of free and conjugated forms of adrenaline and norepinephrine.

5. In a comparative analysis of the content of volatile metabolites of biogenic amines in the exhaled air with the daily excretion of catecholamines in the urine, it was found that in acute myocardial infarction there is a significant increase in the release of volatile amines through the exhaled air and increased urinary excretion of catecholamines.

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Volume-23, June 2023
ISSN: 2749-3644

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