ON THE ISSUE OF DIAGNOSTICS OF CORONARY HEART DISEASE: MODELING OF BIOGENIC AMINE EXCHANGE KINETICS AND DEVELOPMENT OF CARDIOSCLEROSIS

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Abstract

Currently, the issue of early diagnosis of coronary heart disease (CHD) remains the most urgent task of cardiology. Gas analysis method for analysis of exhaled air (BB) is a new approach to solving this problem [5].

Keywords: kinetic parameters, cardiosclerosis, semi-empirical model, statistically significant difference.

Introduction

Our theoretical and clinical studies of this method, conducted with the aim of developing a non-invasive method for the diagnosis of CHD, led to the following main results:: CHD is accompanied by a violation of the exchange of biogenic amines [6], in the composition of Volatile amines are detected in IHD patients [1, 2], and the diethylamine content in IHD is most significantly increased in patients with post-infarction cardiosclerosis (PICC) [7], secondary amines (BA) can be formed in the process of schiff base reduction (SHO) under acidosis conditions in саркосомахcardiac sarcosomes [8].

However, the nature of the dependence of the kinetic parameters of VA formation on the degree and scale of ischemic zones of the myocardium remains unclear.

THE aim of this work is to construct a semi-empirical model for studying the development of cardiosclerosis and to obtain the dependence of the kinetic constants of VA exchange rates on some geometric characteristics of ischemic zones on the myocardial surface.

Material and Methods

We previously [7] found a statistically significant difference in the content of volatile amines inIV in patients with CHD. PIX in comparison with healthypeople. For VA research inIV in patients with CHD during treatment, we used a gas-analytical method. To get samplesIV in a hospital setting, 16 men with a diagnosis of CHD. PIX at the age of 39-64 years were examined and IV tests were performed daily 4 times a day for 10 days. All patients were diagnosed based on clinical observation, laboratory analysis, and functional diagnostics. For 3-15 years, patients underwent inpatient and outpatient treatment. SamplesExplosives were obtained using traps using bidistilled water in a volume of 200 ml as an absorber.

Research Results

Based on statistical analysis of the results of measurements of the BA content inBBThe following values of gas-analytical parameters were obtained: M_1; M_2; m_1; m_2.

M_1 – the average value of the amine content in the first half of the observation period of patients (320 observations).

M_{M_2} – the same, only in the second half of the observation period (320 observations).

m_{m_1} and m_{m_2} – dispersions of the gas-analytical indicator in the first and second halves of the observation period of patients. Respectively:$M_1=600$;$M_2=250$ $m_{m_1}=120$; $m_{m_2}=80$. These values are given in units of $10-9^{-9}g$ / l.

According to the Student's criterion, t=2.3.

The obtained results show that in the course of treatment of patients inThe BB content of amines is statistically significantly reduced (t>2).

Statistically significant difference in the BA content inIV in patients with PIX, which we found in this study, shows that the metabolism of biogenic amines significantly changes during treatment. Volatile components of biogenic amines can be formed during the reduction of schiff bases, which are the main products of LPO [3]. As is known, SHO can be formed by the interaction of aldehydes with primary amines. Such a mechanism proposed byMannich, found in plants and called the reactionMannikha. In the human body, under the conditions of LPO initiation, a qualitative change in the activity of monoamine oxidase (MAO) occurs. A decrease in the activity of MAO in relation to deamination of primary amines, and vice versa, an increase in its activity to diamines leads to the accumulation of primary amines and various aldehydes. Therefore, under LPO conditions, SHO accumulates. Reduction of SHO leads to the formation of volatile metabolites of biogenic amines in the form of secondary amines. Thus, we propose a new mechanism for the formation of secondary amines in the human body under LPO conditions. Previously, it was shown that SHO can be restored in the process of their interaction with epinephrine and clinical observations of the content of volatile metabolites of biogenic amines inIVs in patients prove the possibility of such a mechanism. Therefore, activation of the sympathoadrenal system should stimulate the process of SHO recovery. This is precisely the case in the initial stage of NQMI developmentNQMI, which was also revealed by us on the basis of clinical studies. Since the treatment of CHD is performed in combination with antioxidant and standard therapy, we can conclude that the suppression of LPO led to the restoration of biogenic amine metabolism disorders. This is evidenced by the dynamics of the decrease in the volatile metabolites of biogenic amines inIV in patients with PIX during treatment with antioxidants. To study the kinetics of VA formation at the intact tissue-ischemic tissue interface, we propose a new model for studying the development of cardiosclerosis [3,5,7,10,5,7,10].

1. A model for studying the process of cardiosclerosis

To study the features of cardiosclerosis development, the following modeling algorithm based on the Monte Carlo method was developed.

1. Selection of an intact heart tissue surface with an area of S..

2. On an intact surface S, a random selection of the origin coordinate of a localized ischemic zone (LIS) with an area of S_0 is made.

3. Determination of the number of LYS-ng that appeared at the interface between intact and ischemic tissue.

4. Calculation of p=ng/n, where n is the total number of LIS.

5. Calculation $B=S_0/Sxn$.

6. Plotting the dependency p=F(B).

Based on this algorithm, a program for IBM PC was compiled in the Q – BASIC algorithmic language and the universal dependence p=F(B) was obtained (see Fig.)
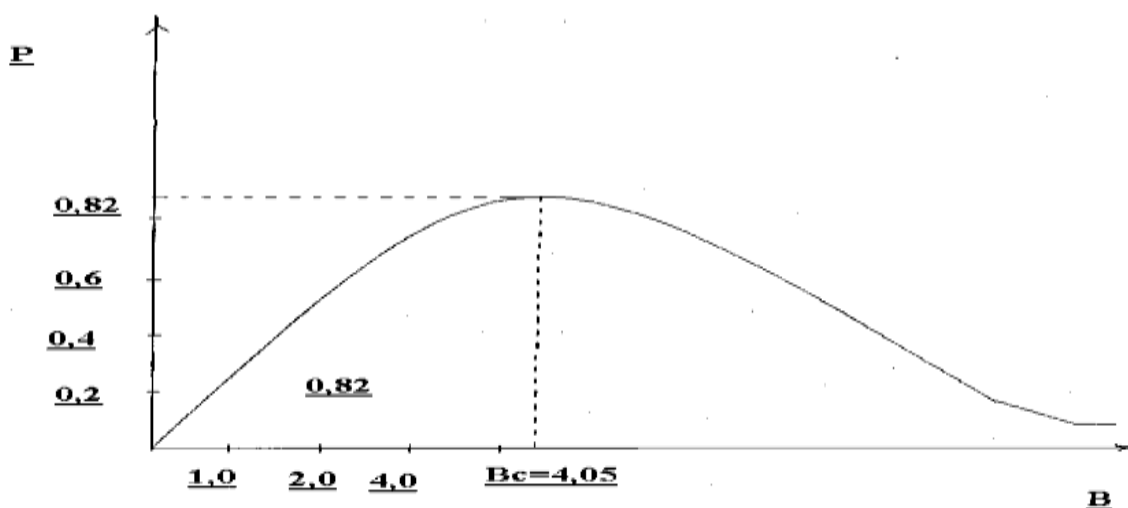
As can be seen from the figure, with growth in p increases and reaches the maximum. The number B characterizes the degree of ischemia of myocardial tissue, and p is the probability of LIS formation at the ischemic-normal tissue interface. Thus, in the case of random generation of LIZ on the surface of intact heart tissue, there is a critical Value-B=Bc at which LIZ, overlapping, form the most developed surface of the interface between the intact and ischemic zones of heart tissue. This universal dependence allows us to divide the process of development of cardiosclerosis into several stages.

1. In<Sun is a reversible stage of acute dystrophic changes.

2. In=Sun is a critical stage in the transition from reversible to irreversible changes.

3. In>>Sun is an irreversible stage of acute dystrophic changes.

Thus, the favorable outcome of CHD treatment depends largely on the possibility of diagnosing it at the first stage, when in<Sun.

2. Kinetics of secondary amine formation

In the ischemic zones, SHO is formed [3, 8, 9,8,9]. Violation of microcirculation in these zones leads to a deterioration of their outflow from the ischemic zone and their further excretion from the body. Therefore, it can be assumed that SHO accumulates at the border between normal and ischemic tissue. Their further recovery and outflow into the microcirculation channel of intact tissue leads to the

appearance ofBB VA. To study the kinetics of these processes, we consider the following system of kinetic equations.

$dn_1/dt = -k_1 n_1$

$dn_2/dt = k_1 n_1 - k_2 n_2$

$dn_3/dt = k_2 n_3$

n_1 – SHO concentration in LIZ

n_2 – concentration of VA in the blood

n_3 – concentration of VA in BB

The time for which the maximum concentration of VA in the blood is established is determined by the following formula:

$t = \ln(k_1/k_2) / (k_1 - k_2)$ (1)

where ln is the$_n$ sign of the natural logarithm, and$_{k1}$ is the rate constant of VA recovery. $_{k2}$ is the rate constant of VA withdrawal from микроциркуляционногоthe microcirculatory bed of heart tissue.

The critical value of the degree of B$_{ischemia\ in\ c}$ can be expressed in V$_c$terms of Vc - the frequency of LIS initiation using the following formula:

$B_c = S_0 V_c \ln(x) / [S k_2 (x-1)]$

Here $x = k_1 / k_2$ characterizes the ratio of inflow to outflow of VA in the microcirculation channel of the heart tissue. As can be seen from this formula V_c increases with x. Therefore, for MI to develop, the LPO intensity must cross V=the V=$_{vc\ boundary}$. This bound depends on x, and as x increases, the threshold value$_{vc}$ increases. Based on the results of this theoretical analysis, X can be called the kinetic coefficient of resistance of a living organism to POL factors.

Discussion of the Results

Theoretical analysis shows that LIS combine to собойform larger islets of myocardial ischemia. There is a critical value for the parameter B, in which there is a qualitative change in the course of coronary heart disease, characterized by the transition of reversible dystrophic changes in the myocardium to irreversible ones. The ischemic-normal tissue interface increases and is well described by parameter B.
 If the frequency of V nucleation is associated with the intensity of LPO, then the relationship between VA and the geometry of the LIS location on the myocardial surface is obtained. Clinical observation of amines in the composition ofIV in patients with CHD shows that this indicator is quite sensitive to the condition of patients with CHD. Relative change not only in the mean value, but also in the variance of the amine content in theBB indicates that the geometry of the interface between normal intact tissue and ischemic tissue plays a significant role in the mechanism of VA formationинтактной ткани от ишемизированной.

Thus, the number of LIS increases with increasing LPO intensity and decreasing x, i.e., decreasing k$_{-1}$ or increasing k$_{-2}$.However, there is a critical value of n that is constant for any variations in the parameters S, S$_0$So, V, k$_{k1}$, and$_{k2}$. therefore, at a critical degree of ischemia and at the given values S$_0$ и of So and S, an increase in V is also accompanied by an increase in x, i.e. k$_1$. Since$_{K1}$ depends on the process of SHO recovery, it can be assumed that all processes that stimulate recovery processes

contribute to the transition to the irreversible stage of acute dystrophic changes in the myocardium. This conclusion is consistent with the development of cardiosclerosis in conditions of activation of the sympathetic-adrenal system.

Conclusions

1. A model for studying cardiosclerosis is constructed.
2. A universal parameter characterizing the degree of cardiosclerosis was found.
3. A universal parameter was used to differentiate post-infarction cardiosclerosis by its geometric characteristics.
4. A relationship was established between the parameter characterizing the degree of myocardial ischemia and the kinetic constants of secondary amine formation.
5. A clinical observation of CHD patients in the dynamics of cardiosclerosis development was carried out and gas-analytical parameters characterizing the state of cardiosclerosis were found.

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