CORRELATION BETWEEN SEASONAL CHANGES IN MYOCARDIAL CONTRACTILITY AND SOME PARAMETERS OF LIPID METABOLISM IN THE DAMAGED HEART

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KEY WORDS: correlation; matrix; lipolytic enzymes.

Lipid metabolism plays an exceptionally important role in the energy supply for the intact heart [6]. This accounts for the importance of investigations of lipolytic processes which provide the various tissues of the body, including the heart, with free fatty acids (FFA), highly important energy donors [2, 7], during the development of pathological changes of varied etiology in the myocardium.

Since a clear seasonal pattern of the onset and development of certain cardiovascular diseases has been established [3, 8], it was decided to study seasonal rhythms of some parameters of lipid metabolism in the normal and pathologically changed heart.

EXPERIMENTAL METHOD

Experiments were carried out in winter (December-February) and summer (June-August) on 130 male Chinchilla rabbits weighing 3.0 ± 0.5 kg. Three models of pathological processes in the heart were used: 1) overloading of the hitherto intact myocardium due to coarctation of the ascending aorta by one-third of its initial diameter; 2) focal ischemic damage to heart muscle caused by ligation of the inferior branch of the left coronary artery at the boundary between its lower and middle thirds; 3) diffuse changes in the heart associated with the action of diphtheria toxin, injected intravenously as a single dose of 0.3 MLD/kg body weight. The peak systolic pressure in the left ventricle during occlusion of the ascending aorta for 5 sec was investigated in all the experimental animals 1, 3, and 6 days after the beginning of the process, and the values of η, the coefficient of potential working capacity of the heart [5], and the FFA concentration [4] were then calculated. Activity of lipoprotein lipase (LPL), triacylglycerolipase (TGL), monoacylglycerolipase (MG), and tributyrinase (TB) was determined [1] in pre- and postheparin blood plasma, myocardium, and adipose tissue of the rabbits. The results were processed on the T1-58 computer and subjected to statistical analysis.

EXPERIMENTAL RESULTS

If the time course of the above-mentioned pathological processes in the heart in the winter and summer seasons is compared, a general rule can be observed. In all three cases intensification of lipolysis took place in the body tissues, which differed depending on the three types of damage to the myocardium and on the season of the year. This intensification led to an increase in the blood FFA concentration. Correlation analysis showed strong negative correlation in the summer between the parameter reflecting myocardial contractility (η) and the FFA concentration in the case of hemodynamic overloading of the myocardium, whereas no such correlation was present in winter. In myocardial infarction negative correlation was found in summer and positive in winter, whereas after poisoning with diphtheria toxin positive correlation was found between η and the blood FFA concentration in summer but no correlation in winter.

Analysis of correlations between the activity of the lipolytic enzymes involved in lipid metabolism in the various tissues of the body and myocardial contractility showed that in all three pathological processes in the heart muscle the lipolytic enzymes could be divided into three groups: 1) those with positive correlation with myocardial contractility; 2) those with negative correlation; 3) enzymes with no correlation between their ac-

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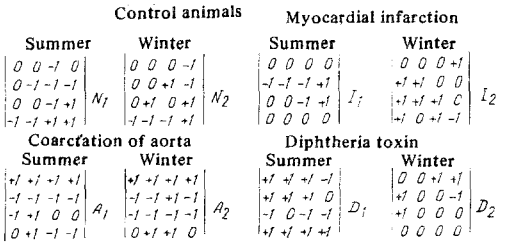

Fig. 1. Seasonal correlations between activity of lipolytic enzymes and myocardial contractility.

tivity and myocardial contactility. These correlations are represented in Fig. 1 in the form of a matrix, the elements a_{ij} of which, at the intersections between the i-th line and the j-th column, assume one of three values: +1, −1, or 0 depending on whether positive, negative, or no correlation exists between the activity of the i-th enzyme located in the j-th tissue and myocardial contractility. Matrices of this type can be called matrices of enzyme involvement in myocardial contractility, or, in short, EM matrices. Four pairs of EM matrices were obtained: control animals (N_1, N_2), hemodynamic overloading of the myocardium (A_1, A_2), myocardial infarction (I_1, I_2), and poisoning with diphtheria toxin (D_1, D_2); in each pair the first matrix was obtained from data relating to summer, the second, from data relating to winter. The enzymes and tissues were numbered as follows:

Preheparin	Postheparin	Myocardial	Adipose tissue
1	2	3	4 and
LPL	TGL	MG	TB
1	2	3	4

It will be clear from Fig. 1 that the number of enzymes whose activity correlated positively with myocardial contractility was greater in the control animals in winter than in summer, and they were located not only in the myocardium and adipose tissue, but also in the blood stream. However, in winter no correlation was present between η and activity of the lipolytic enzymes in the majority of cases.

Comparison of the EM matrices A_1 and A_2 with matrices N_1 and N_2 showed that the second line in A_1 and N_1 was the same, i.e., that during the development of hemodynamic overloading of the myocardium in summer the postheparin lipolytic enzymes investigated are not involved in maintenance of myocardial contractility. Comparison of EM matrices I_1 and I_2 with matrices N_1 and N_2 revealed coincidence between the third line and second column in summer, and also between three of the four elements of the primary and secondary diagonals. This indicates that lipolytic enzymes of myocardial tissue and TGL in all the tissues studied play no part in the supplying of energy for contraction of the infarcted myocardium in summer.

The following picture was observed: during hemodynamic overloading of the myocardium in winter and summer the action of the same enzymes in different tissues remains about the same. In acute focal myocardial ischemia associated with direct damage to the heart muscle, groups 1, 2, 3, and 4 in matrices I_1 and I_2 were completely transposed, i.e., all the lipolytic enzymes changed their functions. In diphtheria poisoning, with the change from summer to winter a very small fraction of the lipolytic enzymes still retained its correlation with cardiac activity.

Analysis of the EM matrices thus compiled showed that during the development of pathological processes in the heart energy for myocardial contraction was supplied by intensification of the activity of different lipolytic enzymes specific for each disease; the location of these enzymes, whose activity increased in the initial period of the pathological process in the heart, also changed. These two factors were largely dependent on the time of year when the pathological condition appeared.

The character of correlation between activity of lipolytic enzymes in different tissues of the body and myocardial contractility thus varies depending on the time of year, i.e., the correlation has a seasonal structure.

By presenting correlations between lipolytic enzyme activity and myocardial contractility in matrix form it is possible to assess the differential roles of the individual components of lipolysis in maintaining the contractile function of heart muscle during the development of pathological processes damaging the myocardium.

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MORPHOLOGICAL AND FUNCTIONAL CHANGES IN THE DESYMPATHIZED HEART OF RATS WITH ACUTE MYOCARDIAL ISCHEMIA

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Activation of the sympathicoadrenal system during occlusion of the coronary artery leads to a sharp rise in the blood catecholamine level [6] and to complex changes in metabolism in the heart muscle, which cause disturbances of the contractile function and rhythm of the heart [1, 6, 8]. It is not yet clear to what extent the catecholamines released by the sympathetic nerve endings of the heart contribute to determining the character of functional and structural disturbances in the myocardium in acute ischemia. The investigation described below was carried out to study this problem.

EXPERIMENTAL METHOD

Experiments were carried out on 79 chemically desympathized and 63 control male Wistar rats weighing 140-175 g. Guanethidine (Isobarin, from Pliva, Yugoslavia) was used to produce desympathization [5]. The method of imposing an increasing frequency of contraction on the heart [4] and creation of maximal loading by occlusion of the aorta for 10 sec were used as function tests. Parameters of the contractile function of the heart were recorded after 2, 5, and 10 sec. Systolic pressure in the left ventricle and its maximal rate of rise and fall (dP/dt), and the end-diastolic pressure (EDP) were measured. The intensity of contractile function (ICF) [3] and the contractility index (CI) [9] were calculated. Acute experiments were carried out under urethane anesthesia (160 mg/100 g) under open chest conditions with artificial ventilation. The pressure in the left ventricle was recorded by means of a catheter inserted through the apex of the heart and connected to the transducer of a Mingograph-34 electromanometer (Elema, Sweden). The ECG and the first derivative of pressure were recorded simultaneously by the DÉ-1 instrument. The results were analyzed by Student's t test. The hearts of the experimental and control rats were stained with hematoxylin and eosin, Scharlach R, Sudan black, and Nile blue sulfate to detect neutral fat and acid lipids, by Selye's method for fuchsinophilic granules, and by Shabadash's method for glycogen. Acute myocardial ischemia was induced by high ligation of the anterior descending branch of the left coronary artery.

EXPERIMENTAL RESULTS

Disturbances of the cardiac rhythm appeared during the first minutes after occlusion of the coronary artery. They were more severe in the control animals and took the form of the appearance of polytopic ventricular extrasystoles (single and grouped); ventricular fibrillation developed frequently. The arrhythmias in the ex-

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