# INTENSITY OF LIPOLYSIS AND CONTRACTILE FUNCTION OF THE HEART IN SOME EXPERIMENTAL PATHOLOGICAL STATES

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Free fatty acids (FFA) are known to play an important role in the energy metabolism for the contractile function of the heart [2, 9, 10]. Data in the literature on the effect of FFA on damaged heart muscle are extremely contradictory [6-9].

It was therefore decided to make a parallel study of lipolytic enzyme activity and changes in the contractile activity of the myocardium in certain pathological states.

## EXPERIMENTAL METHOD

Experiments were carried out on 100 male chinchilla rabbits weighing 3.0 ± 0.4 kg. Ten animals formed the control group. The following pathological processes were modeled in the reamining rabbits (30 animals in each group): hemodynamic overloading of the heart — by coarctation of the ascending aorta by half its diameter; acute focal myocardial ischemia, by ligation of the descending branch of the left coronary artery at the junection between its middle and lower thirds; after a single intravenous injection of diphtheria toxin (0.3 MLD/kg body weight). In acute experiments 1, 3, and 6 days later, the peak systolic pressure in the left ventricle was determined electromanometrically during occlusion of the ascending aorta for 5 sec, and, using equations suggested by the writers, a coefficient ($\eta$) characterizing the potential working capacity of heart muscle was calculated [3], and the energy deficit (ED) in the myocardium was determined. The FFA concentration in the blood of the experimental animals was determined by a micromethod, and activity of lipoprotein lipase (LPL, AC 3.1.1.34), triacylglycerolipase (TGL, EC 3.1.1.3), and monoacylglycerolipase (MG, EC 3.1.1.23) was determined in the blood plasma and myocardial tissue. All numerical data were subjected to statistical analysis on the TI-58 computer (from Texas Instruments).

## EXPERIMENTAL RESULTS

The experimental results are given in Fig. 1 and Table 1. Correlation analysis showed the following significant relationships between the value of $\eta$ and the FFA concentration: in coarctation of the aorta $4 = -0.999$, in acute focal myocardial ischemia $r = -0.96$, and after injection of diphtheria toxin $r = +0.999$. No correlation was found between the FFA concentration and the value of ED in coarctation of the aorta and diphtheria. In acute focal ischemia $r = +0.99$.

The data in Table 1 indicate that in all the three pathological states studied lipolytic enzymes in the blood were activated. No general rules could be found to account for the changes in activity of lipolytic enzymes in the myocardium.

The study of myocardial contractility thus showed that it is reduced as early as on the first day of the pathological process, and that marked ED develops in the heart muscle and lipolysis is intensified, as shown by a sharp increase in lipolytic enzyme activity and an increase in the FFA concentration.

The smallest deviations from normal in the state of myocardial contractility, found in association with coarctation of the aorta, can be explained on the grounds that in this case the increased load falls on the initially intact myocardium, which has preserved all its pow-

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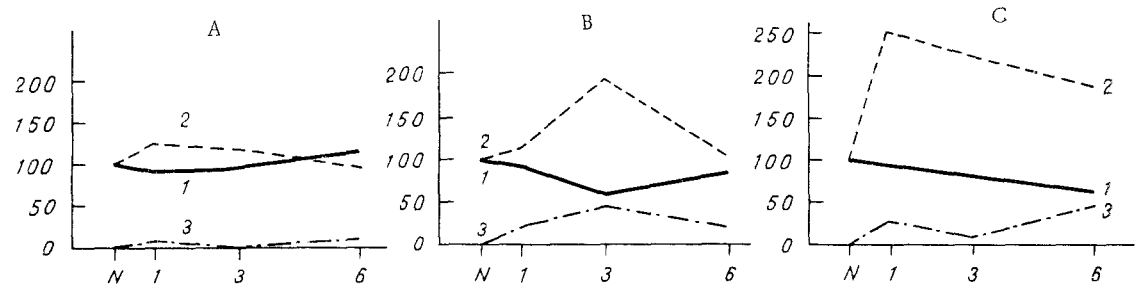


Fig. 1. Dynamics of changes in contractile function of left ventricle (1), FFA concentration (2), and ED of myocardium (3) in coarctation of aorta (A), acute focal myocardial ischemia (B), and after injection of diphtheria toxin (C). All values are percentages of normal, taken as 100. Abscissa, time (in days).

TABLE 1. Changes in Lipolytic Enzyme Activity in Blood and Myocardium in Certain Pathological States

| Pathology | Tissue | Enzyme | Time of investigation, days | | | |
|---|---|---|---|---|---|---|
| | | | control | 1 | 3 | 6 |
| Coarctation of aorta | Blood | LPL | 0,27±0,07 | 1,31±0,07 | 2,05±0,07 | 4,07±0,07 |
| | | TGL | 0,23±0,07 | 0,46±0,07 | 1,31±0,07 | 3,69±0,11 |
| | | MG | 2,95±0,11 | 3,37±0,14 | 3,76±0,11 | 5,05±0,11 |
| | Myocardium | LPL | 13,06±0,56 | 27,53±0,67 | 20,87±1,0 | 15,89±0,99 |
| | | TGL | 10,03±0,44 | 10,73±0,67* | 9,21±0,56* | 6,70±0,42 |
| | | MG | 16,33±0,45 | 17,80±0,9* | 24,61±0,89 | 19,83±0,84 |
| Acute focal myocardial ischemia | Blood | LPL | 0,46±0,07 | 1,40±0,14 | 1,75±0,07 | 3,53±0,14 |
| | | TGL | 0,22±0,03 | 1,08±0,14 | 1,08±0,15 | 2,87±0,11 |
| | | MG | 2,64±0,07 | 3,42±0,14 | 3,57±0,15 | 2,56±0,07* |
| | Myocardium | LPL | 17,26±0,67 | 12,39±0,7 | 12,01±0,89 | 24,19±0,58 |
| | | TGL | 9,09±0,34 | 4,08±0,28 | 5,82±0,33 | 11,43±0,55 |
| | | MG | 17,84±0,67 | 10,49±0,84 | 16,68±0,78* | 11,19±1,0 |
| Diphtheria toxin | Blood | LPL | 0,38±0,12 | 4,73±0,22 | 2,79±0,18 | 1,67±0,19 |
| | | TGL | 0,38±0,12 | 2,64±0,05 | 2,09±0,18 | 0,84±0,14 |
| | | MG | 2,79±0,18 | 2,01±0,19 | 1,63±0,07 | 1,66±0,22* |
| | Myocardium | LPL | 17,50±0,44 | 11,31±0,6 | 21,93±0,89 | 24,84±0,78 |
| | | TGL | 9,09±0,34 | 5,36±0,22 | 5,83±0,33 | 5,24±0,44 |
| | | MG | 17,84±0,67 | 9,65±0,67 | 11,43±0,56 | 18,13±1,4 |

Legend. Enzyme activity in blood plasma expressed in micromoles fatty acids/h/ml; in myocardial tissue in micromoles fatty acids/h/g wet weight.* Difference from control not statistically significant; LPL) lipoprotein lipase; TGL) triacylglycerolipase; MG) monoacylglycerolipase.

ers of adaptation in full. The small increase in FFA concentration observed during hemodynamic overloading of the heart did not correspond to any sharp increase in lipolytic enzyme activity. In addition, the minimal values of ED and the presence of strong significant positive correlation between the FFA level and the value of ED suggests that the FFA thus formed are utilized, and that the potentiation of lipolysis can be interpreted as a mechanism of adaptation of the heart to the increased load which is activated in emergency.

In acute focal myocardial ischemia lipolysis also was intensified, but this compensatory mechanism was put into effect only toward the 6th day, as a result of injury to the mitochondrial apparatus in the earlier stages of the disease and the consequent inability for FFA to be utilized. The dynamics of changes in the FFA content in $\eta$ and ED clearly shows the critical moment in the formation of the adaptive powers of the infarcted myocardium, i.e., ability to utilize FFA brought by the blood (at a time when myocardial lipolysis is inhibited). This critical moment (the 3rd day) is characterized by a peak FFA concentration, by the highest value of ED, and by the greatest fall in the value of $\eta$. The subsequently observed fall in FFA concentration was accompanied by an increase in the value of $\eta$, and the decrease in ED is evidence of utilization of extracardial energy substrates. Indirect evidence in support of FFA utilization in acute focal ischemia (just as in coarctation of the aorta) is given by the increase in lipolytic enzyme activity toward the 6th day.

A sharp increase in the intensity of lipolysis was observed as early as on the first day after injection of diphtheria toxin, and despite the onset of a definite ED, myocardial contractility was able to be maintained at close to the normal level. However, by inducing

competitive inhibition of cytochrome B, diphtheria toxin prevents the myocardium from utilizing FFA fully. The decrease in ED during this same period may be linked with activation of glycolysis, which is usual under hypoxic conditions. This is confirmed also by the absence of correlation between the FFA concentration and the value of ED. Inability to utilize FFA was confirmed by persistence of a high concentration throughout this period, by the fall in lipolytic enzyme activity toward the 6th day, possibly in connection with their inhibition by the end-product of the reaction, and also by an increase in the value of ED, leading to a decrease in $\eta$. Comparison of the FFA concentration and the degree of the decrease in $\eta$ in acute focal myocardial ischemia (3rd day) and after injection of diphtheria toxin (1st day) makes it impossible to accept the view that FFA have a toxic action on heart muscle.

In all three pathological processes studied intensification of lipolysis was thus observed; this intensification may be interpreted as a nonspecific restorative mechanisms arising in response to the stress situation (the onset of the disease), in which ACTH, secreted in excess, leads to liberation of heparin, activating heparin-dependent lipolytic enzymes, from mast cells.

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