RATE OF GLUCONEOGENESIS IN THE LIVER OF RATS WITH MYOCARDIAL INFARCTION

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In myocardial infarction a profound imbalance develops in the endocrine system, manifested by a fall in the insulin concentration in the blood and, according to some data, a fall in the thyroxine level accompanied by a sharp rise in levels of glucocorticoids, catecholamines, and somatotropin [3, 6, 7, 9, 16, 17]. One result of this is an increase in the concentration of tissue protein breakdown products in patients with myocardial infarction, mainly of amino acids, but also of glycerol, fatty acids, lactate, and pyruvate [1, 4, 12, 14, 15].

In this disease all the conditions are thus created for more rapid gluconeogenesis — the synthesis of glucose from noncarbohydrate compounds. This conclusion is confirmed by the high blood glucose level (risk factor) in patients with ischemic heart disease, especially in its severest manifestation, namely myocardial infarction [2, 10]. However, the rate of gluconeogenesis, as a possible compensatory mechanism for supplying additional energy for the heart muscle in myocardial infarction, has not previously been studed by the direct method.

The object of this investigation was to study the rate of glucose synthesis de novo in the liver in rats with myocardial infarction.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 200-225 g. The animals were divided into five groups: 1) healthy, 2) undergoing a mock operation, and 3, 4, and 5) rats with myocardial infarction, studied 3, 10, and 20 days respectively after occlusion. Myocardial infarction was produced in the rats by ligating the descending branch of the left coronary artery under endotracheal ether anesthesia [5]. The presence of a myocardial infarct in the experimental animals was confirmed histologically and by means of the ECG [8].

The liver was perfused [13] in rats deprived of food for 24 h. The perfusion fluid consisted of Krebs—Henseleit bicarbonate buffer (95% O_2 + 5% CO_2) at 37°C (pH 7.5 ± 0.15). The liver was perfused for 100 min, and every 20 min the perfusion fluid was tested for glucose concentration (in a glucose oxidase—peroxidase—o-toluidine system) and for ammonia, glutamine, and urea by the diacetyl monooxime method.

EXPERIMENTAL RESULTS

The results showed (Table 1) that the perfused liver of healthy rats, deprived of food for 24 h, and which contained no glycogen at this time, was able to synthesize glucose from endogenous noncarbohydrate compounds. In fact, toward the end of the experiment the concentration of glucose synthesized de novo in the course of 100 min was almost twice that found after 20 min of perfusion, and the ammonia concentration increased at the same time. The increase in the ammonia concentration was particularly considerable if the intensive detoxication of ammonia in the form of urea and glutamine, whose levels were considerably elevated toward the end of the investigation, is taken into account. Similar changes in gluconeogenesis also were observed in the group of rats undergoing the mock operation.

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TABLE 1. Changes in Glucose, Ammonia, Glutamine, and Urea Concentrations in Liver Perfusate of Rats with Myocardial Infarction (M ± m)

Compound tested	Group of animals	Duration of perfusion, min				
		20	40	60	80	100
Glucose	1	28,81±1,51	34,17±2,03	41,16±1,97	43,36±2,30	54,76±2,01
	2	27,22±1,64	31,62±1,64	37,06±1,08	41,77±1,72	53,43±2,48
	3	91,66±7,11*	105,24±8,76*	120,88±7,41*	132,55±8,36*	147,37±6,35
	4	20,66±4,20	28,79±1,17*	39,21±1,57	43,64±1,44	49,39±1,17*
	5	22,15±1,62*	32,77±1,40	40,03±1,40	49,33±1,44*	64,99±3,05*
Ammonia	1	28,81±1,17	42,33±1,29	30,13±0,97	53,77±2,1	32,94±1,13
	2	26,52±0,95	41,41±2,15	28,23±1,98	56,14±0,99	33,94±1,96
	3	41,52±4,02*	60,35±6,20*	81,41±7,98*	97,82±5,42*	121,29±5,14*
	4	24,41±6,00	39,94±4,00	56,17±3,35*	56,52±4,47	69,99±10,36*
	5	40,11±3,22*	58,88±2,49*	44,88±1,26*	65,11±2,06*	54,46±1,71*
Glutamine	1	1,14±0,18	3,19±0,37	6,28±0,46	7,66±0,58	11,85±0,71
	2	1,37±0,12	3,25±0,24	6,76±0,45	7,84±0,48	12,07±0,51
	3	5,11±1,00*	10,11±1,51*	14,60±1,51*	18,45±1,15*	24,87±3,49
	4	3,43±1,22	5,17±1,27	7,40±2,05	9,91±1,33	13,36±1,19
	5	4,85±0,29*	5,07±0,50*	7,33±0,60	9,02±0,71	10,75±0,17
Urea	1	34,17±1,42	40,07±2,15	47,71±1,83	53,65±1,98	62,61±2,32
	2	33,83±2,06	40,83±2,15	51,58±1,99	54,99±1,72	65,41±1,92
	3	77,49±3,06*	125,98±9,31*	169,99±11,67*	191,09±9,30*	218,99±9,45*
	4	49,66±1,67*	61,99±1,99*	75,66±1,27*	81,99±1,56*	95,49±2,20*
	5	38,16±3,44	45,83±3,17	55,86±4,44	68,83±6,90	76,99±4,51

Legend. Total number of rats 50; 10 animals in each version of the experiments. *$P < 0.05$ compared with group 2.

After high occlusion of the descending branch of the left coronary artery of the rats the rate of glucose synthesis from endogenous noncarbohydrate compounds rose sharply in the liver. These changes were particularly marked by the 3rd day of myocardial infarction, when the concentration of newly synthesized glucose was increased by 200% and the concentrations of ammonia, glutamine and urea were increased by 3.57, 2.06, and 3.34 times respectively (perfusion for 100 min).

The liver of rats with myocardial infarction present for 10 days synthesized glucose de novo at the same rate as the control animals although the ammonia concentration toward the end of perfusion was 2.06 times higher than normal in these animals. However, their glutamine and urea levels did not differ significantly from normal.

By the 20th day of the experiment the parameters studied in the control and experimental animals were very close, and only the ammonia level in the perfusate still remained 1.6 times higher in rats with myocardial infarction.

Hence, although the original perfusate contained no glucose, substrates for its synthesis, or gluconeogenic precursors, nevertheless by the 20th minute of perfusion glucose began to appear in the test fluid in sufficient quantity for determination by the enzymic method. It can be concluded from this fact that glucose synthesis de novo in the liver can take place on account of endogenous compounds of the interstitial fluid and hepatocytes (water-soluble proteins, free amino acids, etc.), as was confirmed by the rise of the ammonia, glutamine, and urea concentrations in the perfusate. Together with the increase in the glucose concentration, all these findings reflect the intensity of gluconeogenesis as a process in the liver. The results agree with data in the literature [13].

The rate of glucose synthesis de novo in the rat liver rose sharply 3 days after occlusion of the coronary artery. On average for the whole period of investigation it was twice as high as in animals undergoing the mock operation. Meanwhile, in perfusate of rats with infarction the concentrations of ammonia, glutamine, and urea increased by 2.16, 2.33, and 3.17 times respectively. Correlation found between the levels of these compounds indicates that detoxication of ammonia to urea is undisturbed in rats with myocardial infarction, whereas detoxication to glutamine is substantially weakened. This phenomenon was described previously by one of us (V.A.B.) in patients with myocardial infarction [11].

It was also shown that the increase in the rate of gluconeogenesis in the liver by the 3rd day correlated with profound changes of ischemic character in the ECG. Later the rate of glucose synthesis from noncarbohydrate compounds fell and normalization of the ECG took place reciprocally.

In our opinion the increase in the rate of glucose synthesis from noncarbohydrate compounds in myocardial infarction is due to stress, as a result of which the concentration of hormones with powerful gluconeogenic properties (adrenalin, glucocorticoids, glucagon, somatotropin, and so on) rises. The marked stimulation of gluconeogenesis in myocardial infarction can be regarded as a compensatory-adaptive mechanism, aimed at supplying the additional quantity of glucose in order to maintain homeostasis of the affected organ and of the body as a whole.

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CHEMILUMINESCENCE OF INDIVIDUAL HUMAN BLOOD SERUM FRACTIONS ACTIVATED BY FERROUS IONS

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Measurement of the parameters of chemiluminescence (CL) of the blood serum is used as an additional diagnostic test in several diseases [4, 12]. For instance, the state of patients with various surgical diseases can be assessed from changes in Fe^{++}-activated CL of whole serum [3, 9]. However, the causes of these changes in CL have not yet been finally explained [3]. This accounts for the special importance of the study of the contribution to total serum CL made by its individual fractions [2, 7, 11].

The investigation described below showed that when changes in CL of whole blood serum are interpreted not only the quantity of apoB-containing lipoproteins (LP), but also changes in the levels of individual proteins and of high-density LP must be taken into consideration.

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