LIPOPROTEIN-LIPASE ACTIVITY AND HEPARIN EFFECT ON BLOOD SUGAR LEVEL AND SERUM LIPIDS IN POST-MYOCARDIAL-INFARCTION PATIENTS

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In atherosclerosis and, more particularly, in myocardial infarction serious disorders are established not merely in the lipid, but also in the carbohydrate metabolism. Along with that, the mutual dependence existing between the two processes is noteworthy. In myocardial infarction many authors (3, 7, 10, 12, 14, 16, 17, 20, 24, 25, 28) find elevated values of cholesterol, beta-lipoproteins and total lipids.

The cholesterol/ phospholipids ratio reflects more adequately the susceptibility or resistance of cholesterol to arterial wall infiltration. Many authors emphasize the importance of this indicator which exhibits increased values in atherosclerosis, especially in its active stage (11). Gertler and co-authors (cited by 11) established a high cholesterol /phospholipids coefficient both in atherosclerosis and diabetes mellitus.

Upon single administration, and in the course of prolonged treatment as well, heparin brings about a decrease of cholesterol and increase of phospholipids (1), i. e. it exerts a beneficial effect on the cholesterol/phospholipids indicator. It is a well known fact that phospholipids cause stabilization of the cholesterol molecule and interfere with its infiltration into the vascular wall.

In a study on atherosclerosis, Leopold and Wieland, Schrade and co-authors (cited by 11) found a higher triglyceride content in the serum compared with that of cholesterol. In coronary disease a great number of authors (16, 17, 19, 21, 25) observed disorders equally in the cholesterol, and particularly in the triglycerides' exchange. Thus, according to Hayes and Neill (22), in myocardial infarction even triglyceride metabolism disturbances are more frequent than those of cholesterol.

Glivera and Boyd, Kritzman and co-authors (cited by 11) and many others (3, 12, 14, 16, 24, 25) report an increase of beta-lipoproteins and a substantial increase of bound cholesterol in cases with myocardial infarction. Meyer and Davjidovskii (cited by 11) and Olivera (26) admit that lipoproteins rather than cholesterol underlie the atherosclerotic process, and might play a definite role in atherogenesis.

The level of beta-lipoproteins is more significantly and regularly decreased by therapeutically applied heparin than the cholesterol level (2), and not only in myocardial infarction (3), but also in diabetes (5), myxedema (4) and in healthy subjects (4).

In myocardial infarction the lipoprotein-lipase activity is lowered (12, 27), while its inhibitors are enhanced (15 and Hood, cited by 9). The con-

tent of endogenic heparin is likewise reduced (Nikkila, Antonini, Chazov — cited by 9, and 6, 13, 15). The lowered lipoprotein lipase activity and endogenic heparin content favour the prethrombotic and thrombotic conditions in the organism.

Hyperglycemia and glucosuria in acute infarction of the myocardium are probably due to a forme fruste of diabetes mellitus (28). Along with the well known lipolytic effect of heparin, in the past few years reports have been published on its hypoglycemic action in healthy subjects, as well as in certain diseases.

Proceeding from literature data and from the results of previous studies, we undertook the task to study the activity of lipoprotein lipase using an improved method, as well as the effect of heparin on the level of blood sugar and serum lipids in patients with past history of myocardial infarction.

Material and Method

The heparin test was applied to 15 patients with past myocardial infarction, sustained six months previously, and 17 healthy individuals — controls. The age of the patients ranged from 33—69 years or 54 years average, and of the healthy persons — from 20 to 56, or 36 years in the average.

The test was conducted in the following fashion: in the morning before meal, 150 mg heparin were introduced via intravenous drip infusion of 500 ml physiologic saline over a 4-hour period. Determination of blood sugar, serum lipids, endogenic heparin and lipoprotein lipase activity was performed just prior to and immediately after the infusion. Blood sugar was determined according to Haggedorn-Jensen, cholesterol — according to Ilko, total lipids — Bragdon Bloor, phospholipids — according to Svanberg—Svannerholm, beta-lipoproteins — after Burstein, non-esterified fatty acids — after Dancomb, endogenic heparin — after Pipta and lipoprotein-lipase activity — after Lukasik.

Unquestionable ECG evidence of myocardial infarction sustained in the past was established in all patients.

Results

The results of the study show that in post-myocardial-infarction patients the content of cholesterol, total lipids, phospholipids, triglycerides and beta-lipoproteins is statistically significantly increased as compared to healthy subjects, whereas the content of endogenic heparin and lipoprotein-lipase activity are lowered. No statistically reliable difference is established between blood sugar and non-esterified fatty acids' content. In patients with a past history of myocardial infarction, the cholesterol-phospholipids coefficient is slightly higher (Table 1).

Under the effect of heparin, a statistically reliable reduction of total lipids, phospholipids and beta-lipoproteins, as well as an increase of non-

esterified fatty acids and endogenic heparin take place in the post-infarction patients. The cholesterol-phospholipids coefficient remains practically unchanged. Changes in the blood sugar level are not observed in all the patients; in four of them with obvious carbohydrate metabolism disorders, the blood

Table 1

Correlation between Blood Sugar, Serum Lipids, Lipoprotein-Lipase Activity and Endogenic Heparin in Patients with Past Myocardial Infarction and in Healthy Individuals

	With myocardial infarction n = 15 M ± τ	Healthy individuals n = 17 M ± τ	t	P
Blood sugar in mg %	114±40	105±14	1 3	0.1
Cholesterol in mg %	270±109	223±37	6.4	0.001
Total lipids in mg %	685±143	568±73	7.7	0.001
Phospholipids in mg %	218±31	196±26	3	0.01
Triglycerides in mg %	196±108	153±44	2.87	0.02
Beta-lipoproteins in F. E.	68±18	40±11	1.2	0.001
Non-esterified fatty acids in μM/ml	0.62±0.17	0.52±0.1	1.66	0.1
Lipoprotein-lipase activity in μM/ml	1.73±0.54	2,40±0.42	3.35	0.01
Heparin in U/ml	7.50±2.4	9 ±0.61	7.5	0.001
Cholesterol/phospholipids coefficient	1.23±0	1.14±0	0.1	0.1

sugar shows an increase under the effect of heparin, but the difference proved to be statistically unreliable (Table 2).

Table 2

Effect of Heparin on the Level of Blood Sugar and Serum Lipids in Patients with a Past History of Myocardial Infarction

	n	Pre-heparin value	Post-heparin value	t	P
Blood sugar in mg %	15	114±40	114±34	0.15	0.1
Blood sugar in patients with disturbance in carbohydrate metabolism	4	161±47	148±52	1.46	0.1
Cholesterol in mg %	15	270±109	262±55	0 55	0.1
Total lipids in mg %	15	683±143	628±122	4.5	0.001
Phospholipids in mg %	15	218±34	205±34	3	0.01
Triglycerides in mg %	15	196±108	168±106	2	0.05
Beta-lipoproteins in F. E.	15	68±18	47±25	7	0.001
Non-esterified fatty acids in μM/ml	15	0.62±0.17	0.82±02	6.6	0.001
Lipoprotein-lipase activity in μM/ml	15		1.73±0.54		
Heparin in U/ml	15	7.5 ±2.4	8.6 ±2.2	5	0.001
Cholesterol/phospholipids coefficient	15	1.23±0	1.27±0	0.1	0.1

In the patients with and without hypertension under review, heparin exerts a moderate, regular reduction of the blood pressure.

Discussion

The lipoprotein-lipase activity in atherosclerosis, respectively in patients with myocardial infacrtion in the past history, is reduced (12, 27). This is confirmed by our study too. Some authors relate the fall of lipoprotein-lipase activity to the enhanced activity of its inhibitors (15). Nevertheless, emphasis is being laid on the close correlation between disturbed synthesis, or reduced secretion of endogenic heparin in post-myocardial-infarction patients, and the lowered lipoprotein-lipase activity. The lower lipoprotein-lipase activity and endogenic heparin content observed corroborates, although indirectly, the close relationship existing between them (Table 1).

The intense lipolysis caused by heparin, introduced from outside (see Table 2), is no doubt due to the enhanced lipoprotein-lipase activity under the influence of heparin. This gives us sufficient reason to accept the lowering of lipoprotein-lipase activity as more probable than the enhancement of its inhibitors' activity.

In compliance with the data submitted by Lobova and co-authors (10) and Falsetti (cited by 10), it was established that in patients with past myocardial infarction, the content of cholesterol is augmented most frequently and to the highest degree (see Table 1). Despite conflicting literature reports on the issue, we support the views of the authors accepting that hypercholesterolemia has an essential bearing on atherogenesis.

Parallel to hypercholesterolemia, the content of total lipids, beta-lipoproteins in particular, is also increased. Their elevated level in post-myocardial-infarction patients is recognized practically by all the authors, and some of them attribute to lipoproteins a primary role in the pathogenesis of atherosclerosis.

Phospholipids, although to a lesser degree, similarly display an increase of their content in patients with past myocardial infarction, as compared with healthy individuals. Moreover, the cholesterol/phospholipids coefficient is also elevated in patients with a past history of myocardial infarction (3), diabetes mellitus (5) and myxedema (4), whereas in thyrotoxicosis this indicator shows a slight decrease. The elevated values of the cholesterol/phospholipids coefficient corroborate the idea already postulated above about the unquestionable role played by hypercholesterolemia in atherogenesis.

The data concerning the significance of triglycerides in the pathogenesis of atherosclerosis are contradictory. According to the opinion of some authors (22), in myocardial infarction the disorders in triglyceride metabolism are more frequent, while according to Leopold and Wieland, Schrade and co-authors (cited by 11), the serum triglyceride content is higher than that of cholesterol. We found a rather insignificant rise of triglycerides as compared to cholesterol, and are therefore inclined to accept a constella-

tion between hypercholesterolemia and hyperlipemia in the pathogenesis of atherosclerosis. Many authors (25, 29) point out the important role played by idiopathic hyperlipemia in the pathogenesis of myocardial infarction, similar to that played by idiopathic hypercholesterolemia.

Recently a number of reports have been published in the literature dealing with the hypoglycemic effect of heparin in healthy persons (Wenke et al, cited by 8), in diabetic patients (5), and in patients with myocardial infarction in the past history and unsuspected even by them carbohydrate metabolism disorders (3). We too observed a reduction of blood sugar, although statistically unreliable, under the effect of heparin in patients with myocardial infarction history, with manifest disorders in carbohydrate metabolism. The mechanism through which heparin exerts its hypoglycemic effect remains unknown for the time being. The possibility of a direct hypoglycemic action is by no means ruled out, but anyway, the insulin route seems more probable.

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ЛИПОПРОТЕИНЛИПАЗНАЯ АКТИВНОСТЬ И ЭФФЕКТ ГЕПАРИНА НА УРОВЕНЬ САХАРА В КРОВИ И СЫВОРОТОЧНЫЕ ЛИПИДЫ У БОЛЬНЫХ, ПЕРЕНЕСШИХ ИНФАРКТ МИОКАРДА

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РЕЗЮМЕ

Липопротеинлипазная активность и эффект гепарина на уровень сахара в крови и липиды сыворотки крови исследованы у 15 больных, перенесших инфаркт миокарда, и у 17 клинически здоровых лиц.

У больных, перенесших инфаркт миокарда, в сравнении со здоровыми лицами статистически достоверно повышены содержание холестерина, количества общих липидов, фосфолипидов, триглицеридов и бета-липопротеинов и понижено содержание эндогенного гепарина и липопротеинлипазной активности. Повышен также коэффициент холестерин/фосфолипидов.

Под влиянием гепарина у больных, перенесших инфаркт миокарда наступает статистически достоверное снижение количества общих липидов, фосфолипидов и бета-липопротеинов и повышение количества эндогенного гепарина и неэстерифицированных жировых кислот в крови.

Уровень сахара в крови практически не изменяется в общем у всех больных, перенесших инфаркт миокарда, а лишь у 4 из них, у которых существовало явное нарушение обмена углеводов, под влиянием гепарина уровень сахара в крови снизился.