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EFFECT OF EXCESSIVE SACCHAROSE ADMINISTRATION ON METABOLIC PROCESSES IN THE LIVER OF RABBITS WITH RESTRICTED MOBILITY

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Translation of "Vliyaniye izbytochnogo vvedeniya sakharozy na obmennyye protsessy v pecheni krolikov, ogranichennykh v podvizhnosti", Kardiologiya, Vol. 20, No. 4, Apr. 1980, pp. 75-80.

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16. Abstract

The administration of saccharose (3 g per 1 kg for 2 months) intensified changes encountered in hypokinesia. There was a more marked increase in the content of cholesterol, pre- and -lipoproteins, phospholipids, and glycosaminoglycans in the blood. At the same time, the administration of saccharose improved the course of metabolic processes in the liver of immobilized rabbits, restored to normal levels the reduced glycogen level, the rate of glycolysis and the conversion of cholesterol to bile acids and their discharge in the cystic bile.

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EFFECT OF EXCESSIVE SACCHAROSE ADMINISTRATION ON METABOLIC PROCESSES IN THE LIVER OF RABBITS WITH RESTRICTED MOBILITY

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It was established that a surplus concentration in the simple carbohydrate ration leads to an increase in obesity and in the number of cases of atherosclerosis [10, 24, 25]. When glucose and saccharose are added to the food of rats and rabbits, an increase in the concentration of fatty acids, cholesterol, triglycerides and lipoproteins [7, 11-14] is noted. Both in atherosclerosis patients and in experiments with animals which are kept on a surplus carbohydrate ration for a long time, the developing chronic hyperglycemia disturbs metabolic processes [1, 3, 12-14]. /75*

A life with restricted mobility is associated with an increase in the cholesterol level in the blood and tissues and predisposes one to atherosclerosis [3, 8, 15, 17, 18]. In economically developed countries, along with an increase in the intake of simple carbohydrates (three-fold since the beginning of the century), there has been a decrease in the number of professions which involve sufficient physical activity [3, 5, 10, 17, 20, 22, 24, 25].

The liver is the organ in which the synthesis of cholesterol, its storage, and its conversion into lipoproteins and cholic acids occur [4, 19, 20]. For this reason it is interesting to study changes in

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* Numbers in the margin indicate pagination in the foreign text.

the carbohydrate lipid exchange in the liver in conjunction with the effect of two risk factors, restricted mobility and excess saccharose intake.

Material and Methods

Experiments were run on 122 rabbits of both sexes of mass 2.5-3 kg. The animals were kept in a single chamber on an ordinary nutritional ration (hay, oats, black bread, vegetables). The experimental rabbits were divided into 2 groups. In the first group, restriction on movement was achieved by placing the animals in narrow cages, in the second group the restriction on movement was combined with the daily administration of saccharose through a probe in the stomach, at a rate of 3 g per k kg of body mass. On days 3, 5, 10, 15, 25, 30, 45 and 60 of the experiment, the (total, free, ether bonded) cholesterol, phospholipid, pre- and -lipoprotein and glycosaminoglycane concentrations in the blood serum were determined. The sugar curve was also determined on days 1, 5, 15, 30, and 60 of the experiment. After 10, 15, 30 and 60 days, 5-9 rabbits from the control and experimental groups were killed and in the liver tissue we determined the glycogen concentration [23], the level of preformed lactic acid and its increase during incubation with glucose in a Krebs Ringer buffer, pH 7.35 at 37° C for 1 hour [21], and oxygen intake in a Varburg apparatus. A part of the organ was dried to a constant mass and the total concentration of lipids and cholesterol was determined in the dry residue. The amount of vesical bile, the levels of cholesterol, cholic acids and dry residue in it were studied. Cholesterol in the blood and the tissues was determined by a Liberman Burkhard color reaction [2], phospholipids were

determined by the Fisk Subbaroi method in the A. Ye. Braunshteyn modification [2], pre-β and β-lipoproteins were determined by the M. Ledvina method [6], glycosaminoglycanes were determined by Remington's method [9] and bile cholesterol, by the Sperry Bredy method in P. Z. Khasigov's modification [19], while cholic acids were determined by the Shire and Kuhn method in the M. P. Skakun modification [16].

Results and Discussion

Restricted mobility caused the most rapid and significant changes in the level of pre-β and β-lipoproteins and sugar in the blood. Even 30 minutes after the beginning of the experiment, their concentration had increased by 48 and 15%, respectively. After 60 minutes the increase in glycemia was 20%, and after this we observed a gradual decrease (after 90 minutes, 14%), after the second hour the increase became unreliable. Another increase in the level of pre-β and β-lipoproteins on the first day was noted from the 120th to the 180th minute (on average, by 50%).

An investigation of the sugar concentration in the blood by the type of sugar curve (every 30 minutes for 6 hours) on the 10th and 30th day of hypokinesia, did not cause substantial differences from the initial level. The increase in the concentration of pre-β and β-lipoproteins in comparison to the initial concentration over the same period of time was 95%.

The combined effect of hypokinesia and the administration of saccharose was accompanied by a 3 1/2 hour hyperglycemic state with

maximum increase in the blood sugar level after 30 minutes (by 66%). Administering this quantity of saccharose to healthy rabbits was associated with less pronounced hyperglycemia (after 30, 60 and 90 minutes, by 40, 21 and 13%, respectively). On the last days the hyperglycemia peak was somewhat reduced, and we simultaneously observed a change in the character of the sugar curve. From the fifth day of the combined experiment the sugar curve became pathological, at first double peaked and at the end of the experiment triple peaked: after 30-60 minutes, by 43 and 38%, after 150 minutes, by 16% and after 210-270 minutes, by 17, 15 and 9%.

Under conditions of restricted mobility we observed an almost total disappearance of glycogen in the liver (Table 1). During the first 2 weeks of the combined effect, the glycogen level in the liver was also reduced; however, to a considerably smaller degree than in rabbits in the first group; and by the 30th day they did not differ from the control group.

During the first 2 weeks of restricted mobility, judging by the reduced level of preformed lactate and its increase during incubation, the rate of the glycolytic assimilation of carbohydrates in the liver was reduced. The introduction of saccharose to a motionless animal led to restoration of both of these indices to normal.

A part of the glucose formed after saccharose hydrolysis evidently consisted in glycosaminoglycanes (mucopolysaccharides), the concentration of which in blood serum during the combined experiment increased progressively after 3, 5, 10, 15, 30 and 60 days of the ex-

TABLE 1

THE EFFECT OF THE DURATION OF SACCHAROSE ADMINISTRATION ON CHANGES IN THE GLYCOGEN LEVEL, THE RATE OF GLYCOLYSIS AND OXYGEN INTAKE IN THE LIVER OF RABBITS WITH RESTRICTED MOBILITY

Duration of experiment	Group of animals	Statistical index	Glycogen, mg%	Lactic acid, micromols per 100 mg		Oxygen intake, microliter/hr
				preformed lactate	increase to glucose	
Control						

periment by 32, 45, 61, 53, 65 and 72%. During hypokinesia the concentration of mucopolysaccharides was reliably greater than the initial index, but only after 15 and 30 days of the experiment (by 60 and 54%). In addition, some part of the saccharose administered was evidently transformed into lipid, while the cholesterol concentration in the blood serum in rabbits in the second group from the fifth day was on average 10% greater than in the first group. Even more significant changes were noted in the concentration of pre- and -lipoproteins. Only after three days of the combined experiment was their concentration lower (by 21%) than during hypokinesia, and over the other periods (5, 10, 15, 30 and 60) days it was higher by 66, 59, 130, 156 and 65%, respectively. The concentration of phospholipids in the blood serum was increased on the third and fifth days of hypokinesia, and with the addition of saccharose, from the tenth day of the experiment; however, in both cases, especially in the first group, to a smaller degree than cholesterol. Thus, 3, 5, 10, 15, 25, 30, 45 and 60 days after the beginning of the experiment the cholesterol concentration in the combined experiment differed from the indices obtained during hypokinesia by -0.8, + 22, -39, +26, +9, +17, +10, 8%, and the phospholipid concentration over the same period differed by -22, -13, +25, +19, +33, +15, +5, +29%. Since the stability of cholesterol in a dissolved state depends on the phospholipid level, an insufficient increase of it in the blood and reduction in the tissues during hypokinesia [12, 14] was perhaps one of the reasons for the increased accumulation of cholesterol in the tissues (Table 2). We should note that administering saccharose in the combined experiment was associated with a smoother rise in cholesterinemia; the gap between the level of cholesterol and phospholipids did not attain such values as during hypokinesia.

TABLE 2

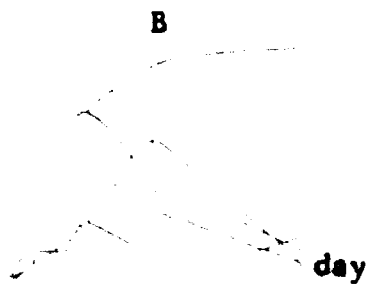
THE EFFECT OF THE PROLONGED ADMINISTRATION OF SACCHAROSE ON CHANGES IN THE LEVEL OF WATER AND LIPIDS IN THE LIVER OF RABBITS WHOSE MOBILITY IS RESTRICTED

Duration of experiment	Group of animals	Statistical index	Ratio of mass of liver/mass of body	Dry tissue residue, mg	Total lipids	Cholesterol
					% of mass of dry tissue	
Control						

Normalization of the glycogen level in the liver under the effect of saccharose loading is evidently one of the factors leading to an improvement in metabolic processes in the liver. Glycolysis activity was restored to normal and the protective secretory function of the liver was increased. While in animals whose mobility is restricted cholesterol is basically secreted from the vesical bile, in the combined experiment, cholic acids were secreted primarily (see Figure, A and B). During the entire course of restricted mobility the concentration of cholic acids in the vesical bile was greater than in the control group by a factor of 2, and in the combined experiment, by a factor of 3-3 1/2. Evidently, the less pronounced reduction in the colloidal stability of cholesterol in dissolved state and its more pronounced transformation into cholic acids partially inhibits the deposit of cholesterol in the livers of rabbits which have received additional saccharose. From the second week of the combined experiment the concentration of cholic acids in the vesical bile increased, while the cholesterol level in the liver after the maximum increased had been attained began to drop gradually (see Figure, B).

It is clear from the figure, A, that in rabbits whose mobility is restricted while the cholesterol concentration in the blood and liver is increased, that the secretion of cholesterol from the bile and its conversion to cholic acids is increased; this evidently leads to a reduction in the cholesterol level in the blood (on the 15th-25th days) and in the liver (on the 30th day). A decrease in the concentration of cholic acids and cholesterol in the vesical bile was associated with another increase in its concentration in the blood and the liver.

Change in the cholesterol level in the blood (1), the liver (2), the bile (3), cholic acids in the bladder bile (4) and in the amount of bile (5) during hypokinesia (A) and hypokinesia combined with saccharose administration (B).



Thus, both during hypokinesia and when it is combined with the administration of saccharose, an attempt is made to normalize hypercholesterinemia by increasing the secretion of cholesterol and cholic acids from the bile. For this reason, in animals in both groups, the increase in the cholesterol level in the blood was undulating. At the same time, despite the fact that more atherogenic agents (cholesterol, pre- and -lipoproteins, glycosaminoglycanes) circulate in the blood during the combined experiment, this did not lead to an increase in the cholesterol deposits in the liver. By normalizing the level of glycogen and glycolysis which had decreased during hypokinesia, the saccharose administered was able to restore the reduced protective secretory functions of the liver, which in turn inhibited the increase of lipid infiltration. However, the hyperprebeta, hyperbetalipoproteinemia and hypercholesterinemia were maintained at a base higher than normal, the cholesterol concentration in the organ did not preclude further weakening of the protective secretory functions of the liver.

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