ROLE OF ALIMENTARY HYPERGLYCEMIA IN THE PATHOGENESIS OF SOME DISTURBANCES OF LIPID METABOLISM

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Alimentary hyperglycemia in rabbits is accompanied by elevation of the serum cholesterol and triglyceride level and also by a progressive rise in the serum concentration of pre-β-lipoproteins, carriers of endogenous triglycerides. Feeding hyperglycemic animals with cholesterol for a short time leads to earlier and more marked atherogenic changes in the body than similar feeding of normoglycemic animals.

KEY WORDS: *hyperglycemia; hyperlipidemia; atherosclerosis; triglycerides; cholesterol.*

The role of the alimentary factor in the pathogenesis of atherosclerosis has been known for a long time. Whereas originally cholesterol was regarded as the principal factor in the pathogenesis of this disease [2, 7], in recent years the atherogenic action of an excessive intake of carbohydrates, especially those that are easily assimilated, has been investigated [4, 8, 9, 16, 18]. The role of disturbances of carbohydrate metabolism in atherogenesis has been confirmed by the frequent coexistence of diabetes mellitus and atherosclerosis [11, 18]. The most important index of early disturbances of lipid metabolism is hyperlipidemia, due to hypercholesteremia, triglyceridemia, or a combination of both. These different types of hyperlipidemia correspond to definite changes in the composition of the serum lipoproteins, the transport form of lipids [3, 6, 10, 14, 15].

The object of this investigation was to study disturbances of lipid metabolism in rabbits fed with excessive amounts of glucose.

TABLE 1. Serum Concentrations (in mg %) of Glucose, Cholesterol, and Triglycerides in Rabbits Receiving Glucose for Six Months (M ± m)

Periods of observation	No. of investigations	Glucose	Cholesterol	Triglycerides
Before glucose feeding (control)	20	111,55±2,31	30,33±2,90	46,04±2,64
During glucose feeding:				
after 1 month	20	130,3±2,42	36,93±2,52	59,9±2,18
P		<0,001	>0,05	<0,001
after 2 months	19	151,95±3,57	46,0±2,84	75,74±1,72
P		<0,001	<0,001	<0,001
P_1		<0,001	<0,001	<0,001
after 3 months	19	168,05±2,87	59,84±2,17	89,57±1,82
P		<0,001	<0,001	<0,001
P_1		<0,001	<0,001	<0,001
after 6 months	17	208,18±3,07	77,52±1,89	113,53±3,74
P		<0,001	<0,001	<0,001

Note. Here and in Table 2: P) criterion of significance of differences between experiment and control; P_1) the same between two groups of experiments.

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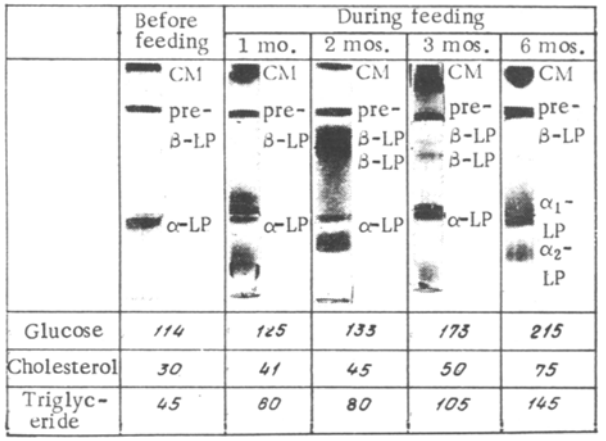

Fig. 1

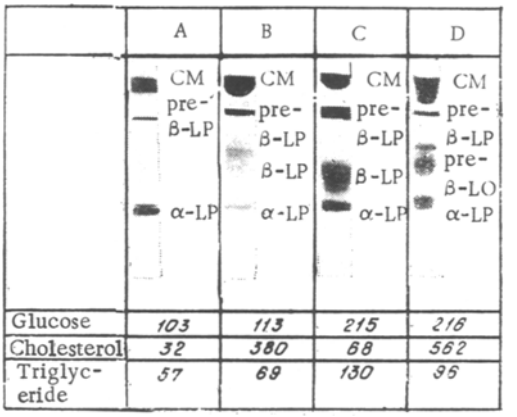

Fig. 2

Fig. 1. Disc electrophoresis of lipoproteins of rabbit receiving glucose for 6 months. CM) chylomicrons; pre-β-LP) pre-β-lipoproteins; β-LP) β-lipoproteins; α-LP) α-lipoproteins. Concentrations of glucose, cholesterol, and triglycerides shown below (in mg %).

Fig. 2. Disk electrophoresis of lipoproteins of rabbits receiving cholesterol and glucose separately and together. A) control rabbit, B) rabbit receiving cholesterol, C) rabbit receiving glucose, D) rabbit receiving glucose and cholesterol together. Remainder of legend as in Fig. 1.

EXPERIMENTAL METHOD

Sexually mature male chinchilla rabbits weighing 2.5-3 kg were used; daily for 6 months the animals received glucose in a dose of 6 g/kh body weight with the diet. In the course of the experiment the lipoprotein spectrum, total cholesterol concentration (by the Lieberman-Burchard color test), and triglycerides [12] in the blood serum were investigated. The blood glucose concentration was determined simultaneously by means of the Bio-Lab-Test outfit. Serum lipoprotein fractions were determined by disc electrophoresis in polyacrylamide gel [13].

EXPERIMENTAL RESULTS AND DISCUSSION

As Table 1 shows, prolonged feeding of the animals with glucose led to an increase in the blood sugar and in the serum cholesterol and triglycerides. Parallel with these changes, disc electrophoresis showed an increase in the fraction of pre-β-lipoproteins, carriers of endogenous triglycerides (Fig. 1).

The changes detected in lipid metabolism were consistent with type IV of hyperlipoproteinemia (according to the classification approved by WHO experts [10]), which is characteristic of a combination of disturbances of carbohydrate and lipid metabolism.

Some workers [1, 4] explain the hyperglycemia which develops during prolonged glucose feeding in animals by overstraining and subsequent insufficiency of the pancreatic insular system, whereas others [5] deny any development of such insufficiency in these cases, because the concentration of immunoreactive insulin in the blood remains normal or increases. This problem requires further investigation.

Special attention (Table 2) was paid to the study of the possible provocative effect of alimentary hyperglycemia on the atherogenic changes induced by feeding the animals with cholesterol. For this purpose, during the 7th month of the experiment the rabbits continued to be fed with glucose by the same scheme, but in addition they were given 1 g cholesterol with the diet on alternate days. For comparison, a group of rabbits receiving only cholesterol (1 g daily) for 1 month was used. Clearly, despite the smaller quantity of cholesterol administered, the atherogenic changes in the animals receiving glucose was well developed sooner and were more severe than those in rabbits receiving cholesterol only. This conclusion is also supported by qualitative analysis of the serum lipoprotein spectrum (Fig. 2).

TABLE 2. Serum Concentrations (in mg %) of Glucose, Cholesterol, and Triglycerides in Rabbits Receiving Glucose and Cholesterol Separately or Together (M ± m)

Group of animals	No. of investigations	Glucose	Cholesterol	Triglycerides
Control	116	105,43±1,16	37,21±1,22	49,65±1,32
Receiving cholesterol (1 month)	20	107,14±2,96	425,05±14,3	58,45±3,51
P		>0,5	<0,001	<0,01
Receiving glucose (6 months)	17	208,18±3,27	77,52±1,89	115,53±3,73
P		<0,001	<0,001	<0,001
P_1		<0,001	<0,001	<0,001
Receiving glucose (6 months) and cholesterol (1 month)	10	229,8±3,85	580,0±11,39	105,85±4,21
P		<0,001	<0,001	<0,001
P_1		<0,001	<0,001	<0,001

Preliminary and concomitant hyperglycemia thus lead to changes in lipid metabolism and promote atherogenic changes developing in animals fed with cholesterol.

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