FACTORS INFLUENCING THE SERUM CHOLESTEROL AND β-LIPOPROTEIN LEVELS IN FASTING RABBITS

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The effect of starvation under ordinary conditions, in the presence of a deficiency of pyridoxine (administration of 4-deoxypyridoxine) and thiamine (administration of hydroxythiamine), and also during administration of neurotropic drugs (amphetamine, diazepam) was studied in male rabbits. Starvation for 7-10 days led to an increase in the serum cholesterol and β-lipoprotein concentration. Pyridoxine deficiency and administration of amphetamine caused a greater increase in the level of cholesterol and, in particular, of β-lipoproteins. Thiamine deficiency and administration of diazepam, on the other hand, had a restraining effect on the increase in the cholesterol and β-lipoprotein levels in hunger stress. Prophylactic administration of the preparation Aerovit helped to reduce the severity of the metabolic changes. The cholesterol concentration in the liver of the fasting animals was increased by an especially marked degree during amphetamine administration and pyridoxine deficiency; administration of Aerovit prevented the increased accumulation of cholesterol in the liver. Differences in the serum and liver cholesterol concentrations must be attributed to changes in cholesterol biosynthesis in hunger stress.
KEY WORDS: experimental hypercholesteremia; atherosclerosis; antivitamins; starvation; Aerovit.

It has recently been shown that the serum cholesterol and β-lipoprotein concentrations depend more on the intensity of endogenous cholesterol synthesis than on its intake. Cholesterol synthesis rises significantly in states of nervous and emotional stress [1-3, 9, 11]. Meanwhile, it is not yet clear why during exposure to comparable external factors, the degree of the changes in lipid metabolism should differ so substantially. It might be assumed from data in the literature that differences in the response of the body, in the form of increased cholesterol biosynthesis (hypercholesteremia), would depend on the functional state of the nervous system and also on the intake of certain vitamins [1, 3-5, 7, 8, 12-14].

These arguments served as the basis for an experimental study of the effect of a deficiency of thiamine and pyridoxine and also of administration of neurotropic drugs (amphetamine, diazepam) on hypercholesteremia induced by hunger stress in experiments on rabbits. The effect of administration of the vitamin preparation Aerovit on this index also was studied. According to clinical observations [6], Aerovit has a definite hypocholesterogenic action, but its effect on cholesterol biosynthesis induced by nervous and emotional stress has not been studied.

EXPERIMENTAL METHOD

Experiments were carried out on 108 male rabbits weighing 2.1-4 kg which were starved for 7-10 days [10]. During this period they received either water only or water with the addition of the test substances. To modify the functional state of the nervous system, some animals were given diazepam (0.2 mg/kg daily) or amphetamine (15 mg/kg daily) during the course of the experiment. Vitamin insufficiency was induced by administration of antimetabolites. Pyridoxine deficiency was produced by administration of 4-deoxypyridoxine (20 mg/kg daily) and thiamine deficiency by administration of hydroxythiamine (100 mg/kg daily). To reduce the severity of the changes in lipid metabolism the substance Aerovit was given (0.1 tablet per animal per day). This preparation is used to treat the disturbances of lipid metabolism in persons with nervous and emotional

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TABLE 1. Effect of Starvation under Different Conditions on Serum Cholesterol and β-Lipoprotein Concentrations in Rabbits (M ± m)

Conditions	No. of animals	Cholesterol concentration, mg%		β-Lipoprotein concentration, mg %	
		initial	at end of starvation	initial	at end of starvation
Starvation	20	61,2±4,2	121±7,3	94±3,8	178±8,3
Starvation and administration of 4-deoxypyridoxine	8	65±3,4	147±5,2	95±10,2	364±87*
Starvation and administration of hydroxythiamine	6	57±4,6	108±4,3	95±7,9	171±11,2
Starvation and administration of diazepam	8	41±7,4	102±20	83±15	133±13*
Starvation and administration of amphetamine	10	66±2,8	142±11	87±12	305±54*
Control	16	66,7±0,9	66,1±1,0	66,1±1,88	64,0±1,84

*P < 0.05 compared with animals starved but not treated with preparations.

TABLE 2. Effect of Prophylactic Administration of Aerovit on Some Metabolic Indices in Rabbits Starved for 10 Days (M ± m)

Index studied	Starvation (20 rabbits)		Starvation + Aerovit (20 rabbits)	
	initial level	at end of starvation	initial level	at end of starvation
Cholesterol, mg %	59,3±4,3	200±25	63±4,5	138±18,1*
Lecithin, mg %	176±5,3	212±8,8	170±4,4	196±7,9
Total protein, g%	6,69±0,08	6,38±0,1	6,25±0,11	6,42±0,09*
β-Lipoproteins, %	70,65±1,22	74,8±1,56	71,7±1,1	72,0±1,25*
Protein fractions, %:				
Albumins	56,5±0,66	54,6±0,84	54,5±0,72	52,4±0,69
Globulins:				
α_1	5,5±0,22	5,95±0,22	6,2±0,18	6,15±0,36*
α_2	8,85±0,29	9,1±0,23	9,45±0,24	8,95±0,18
β	11,5±0,18	11,7±0,12	12,0±0,24	12,6±0,30*
γ	17,4±0,39	18,3±0,37	18,3±0,42	19,9±0,53

*P < 0.05 compared with corresponding control.

stress [6]. Before the beginning of starvation, on its fifth day (in the case of starvation for 10 days), and at the end of starvation the concentrations of cholesterol (by the method of Mrskos and Tovarek), lecithin (as lipoid phosphorus), and β-lipoproteins (by the method of Burstein and Samaille and by paper electrophoresis), and the ratio between the serum protein fractions were determined. The content of total lipids and cholesterol in the liver was determined after decapitation of the animals. Animals which were not starved were used for comparison.

EXPERIMENTAL RESULTS

Changes in the cholesterol and β-lipoprotein levels in rabbits after starvation for 7 days, after thiamine and pyridoxine deficiency, or after changes in the functional state of the nervous system are shown in Table 1.

It will be clear from Table 1 that starvation for 7 days was followed by elevation of the serum cholesterol and β-lipoprotein levels, probably because of increased biosynthesis of cholesterol; pyridoxine deficiency and administration of amphetamine led to a higher hypercholesteremia and, in particular, to an increase in the β-lipoprotein concentration. Thiamine deficiency and administration of diazepam, on the other hand, had a restraining effect on the increase in the cholesterol and β-lipoprotein levels in hunger stress. Indices of metabolism such as the ratio between the blood serum protein fractions and the total blood lipid level showed no significant differences from their values in starvation but without administration of the test substances. Administration of Aerovit for a longer period (up to 37 days) likewise was unaccompanied by any changes in lipid metabolism of satiated rabbits.

The effect of starvation for 10 days and the results of prophylactic administration of Aerovit on the development of hypercholesteremia and β-lipoproteinemia are demonstrated in Table 2. Administration of Aerovit led to a reduction in the severity of the metabolic changes and differences were particularly considerable between the cholesterol and β-lipoprotein levels on the fifth day of starvation: The cholesterol concentration in the rabbits receiving Aerovit was 118 ± 12 mg %, whereas in the starved rabbits not receiving Aerovit the concentration was higher, namely 160 ± 15 mg % (P < 0.05).

At the end of the experiment the animals were killed and the cholesterol and total lipid content determined in their livers. In the intact animals the total lipid content was 9.55 ± 0.49 g % and the cholesterol content 294 ± 17 mg %; after starvation these indices rose to 13.6 ± 0.51 g % and 388 ± 21 mg % of the wet weight of the liver, respectively. Under the influence of Aerovit the total lipid level rose rather less and their content was lower than after starvation without administration of Aerovit (12.7 ± 0.49 g %), but the cholesterol level in this case was significantly lower, namely 325 ± 15 mg % (differences compared with starved animals not receiving Aerovit are statistically significant). In hydroxythiamine hypovitaminosis the content both of total lipids and of cholesterol was lowered under the influence of starvation (8.7 ± 0.93 g % and 256 ± 28 mg %, respectively). Conversely, pyridoxine deficiency led to a greater increase in the cholesterol concentration in the livers of the starving animals (up to 463 ± 36 mg % compared with the control; $P < 0.001$).

The lipid content increased only very little in pyridoxine deficiency and, at 9.78 ± 0.7 g %, its level differed only a little from that in intact animals.

Pyridoxine deficiency, it can be postulated, should promote increased synthesis of cholesterol and the formation of β-lipoproteins, whereas thiamine deficiency should block their increased formation. The lower cholesterol content in the liver following administration of Aerovit (325 ± 15 mg %) must be attributed both to its reduced formation and to its increased metabolism. This leads ultimately to a decrease in the serum levels of both cholesterol and β-lipoproteins. These arguments are in agreement with clinical observations on the hypocholesterogenic action of pyridoxine and ascorbic acid through the formation of bile acids from cholesterol. The possible lipotropic effect of certain vitamins included in the formula of Aerovit (cyancobalamine, α-tocopherol, etc.) likewise must be taken into account.

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