EFFECT OF ANABOLIC STEROIDS AND STROPHANTHIN ON THE COURSE OF EXPERIMENTAL ATHEROSCLEROSIS IN RABBITS WITH CHRONIC LEFT VENTRICULAR HYPERFUNCTION

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Administration of anabolic steroids (nerabol, dihydrotestosterone, and androstanazol) with strophanthin to rabbits with experimental atherosclerosis and chronic left ventricular hyperfunction leads to restoration of normal protein and lipid metabolism and to a uniform increase in weight of all parts of the heart muscle.

Atherosclerosis with chronic circulatory failure is accompanied by disturbance of lipid and protein metabolism [2, 8]. During recent years, in addition to cardiac glycosides, substances stimulating protein synthesis have come to be used [3, 6, 9, 13, 14].

The possibility of correcting the disturbed metabolism by means of anabolic steroids – nerabol, dihydrotestosterone (DHT), and androstanazol (AST) – in conjunction with strophanthin was studied in rabbits with experimental atherosclerosis and chronic left ventricular hyperfunction.

EXPERIMENTAL METHOD

Experiments were carried out on 34 male chinchilla rabbits weighing 2.2-3 kg. Experimental atherosclerosis was produced by Anichkov's method by feeding the animals with cholesterol in a dose of 0.3 g/kg daily with vegetables for 3 months. The abdominal aorta was constricted by 50% of its original diameter by Meerson's method [10] 45 days after the beginning of the experiment (period I), thus throwing an additional chronic load on the left ventricle. This experimental model of a load on the left ventricle of the rabbit's heart corresponds to the load on the myocardium of patients with atherosclerotic cardiosclerosis with chronic circulatory failure. Fifteen days after the operation (stable hyperfunction of the heart – period II) the rabbits were divided into 5 groups each containing 6 or 7 animals. The groups received the following treatment: 1) cholesterol only; 2) cholesterol + 0.01 mg/kg strophanthin intramuscularly; 3) cholesterol + strophanthin + 1 mg/kg nerabol intramuscularly; 4) cholesterol + strophanthin + 1 mg/kg DHT intramuscularly; 5) cholesterol + strophanthin + 1 mg/kg AST by mouth. Strophanthin and the anabolic hormones were given to the animals 6 times a week for 1 month (period III). Before the investigation began and again before coarctation of the aorta and at the end of periods II and III the following blood serum indices were determined in all the animals: cholesterol, lecithin, cholesterol-lecithin ratio, lipoproteins, total protein, protein fractions, and albumin-globulin (A/G) ratio. At the end of the experiment the animals were decapitated and the DNA and RNA content in the myocardium of the left ventricle, the rate of the heart, the thickness of the walls of the left and right ventricles, and the ratio between the weight of the heart and the body weight were determined.

EXPERIMENTAL RESULTS

The results showing the blood biochemical indices of the experimental animals at the different times are given in Table 1.

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TABLE 1. Dynamics of Changes in Biochemical Indices of Atherosclerosis in Blood Serum of Rabbits (M± m)

Time of investigation	Group of animals	Cholesterol (in mg %)	Lecithin (in mg %)	β-lipoproteins (in %)	Total protein (in g %)	Albumins (in %)	A/G
Before taking cholesterol	1	68±5,1	148±6,8	63,6±1,1	6,56±0,34	62,11±1,11	1,63±0,09
	2	84±6,2	161±8,3	65,2±1,31	6,25±1,16	61,2±0,72	1,57±0,08
	3	85±6,9	160±9,3	66,1±1,39	6,21±0,31	59,52±1,1	1,47±0,08
	4	81±6,8	138±6,6	64,8±1,25	6,14±0,3	60,66±1,12	1,54±0,09
	5	65±4,9	136±6,2	65,7±1,23	6,36±0,38	60,06±1,08	1,5±0,09
End of period I	1	396±44,4	362±42,1	82,1±2,36	7,25±0,4	58,79±0,93	1,42±0,08
	2	374±41,2	325±39,8	81,4±2,18	7,36±0,44	57,77±0,91	1,36±0,07
	3	426±48,3	354±41,2	84,1±2,41	7,12±0,39	58,03±1,2	1,38±0,07
	4	388±43,1	321±38,9	81,6±2,17	7,3±0,42	56,84±1,14	1,31±0,07
	5	415±47,2	386±43,1	83,6±2,43	7,18±0,41	59,1±1,12	1,44±0,08
End of period II	1	358±38,2	318±35,2	80,1±1,91	6,92±0,4	52,31±0,8	1,09±0,05
	2	347±39,3	306±34,7	79,3±1,84	7,02±0,41	53,41±0,9	1,14±0,06
	3	409±42,3	347±37,1	80,6±1,95	6,81±0,38	53,13±0,76	1,13±0,06
	4	360±41,4	316±34,9	79,8±1,88	7,01±0,41	52,17±0,82	1,09±0,05
	5	386±43,1	327±36,1	81,2±2,1	6,84±0,39	51,8±0,71	1,07±0.04
End of period III	1	856±59,3	561±56,3	86,2±2,42	6,06±0,3	51,19±1,1	1,04±0,03
	2	586±51,4	380±49,8	85,8±2,4	6,13±0,3	53,17±1,15	1,10±0,06
	3	155±7,1	212±7,6	73,6±1,8	7,52±0,42	58,15±1,26	1,38±0,07
	4	108±6,5	251±8,2	71,3±1,74	7,88±0,46	59,57±1,21	1,47±0,07
	5	160±7,4	280±9,4	72,6±1,76	7,74±0,45	58,28±1,3	1,39±0,08

TABLE 2. Pathological and Biochemical Indices of Myocardial Hypertrophy (M±m)

Index	Group of animals				
	1	2	3	4	5
Weight of heart in g and ratio of weight of heart to body weight	5,88±0,43 0,0021±0,0001	7,54±0,46 0,0023±0,0001	7,84±0,5 0,0028±0,0002	8,14±0,5 0,00278±0,0002	8,48±1,51 0,00278±0,0002
Total DNA content (in μg)	31,75±1,42 (100%)	33,17±1,46 (104%)	34,49±1,48 (108%)	39,88±1,52 (125%)	38,16±1,5 (121%)
Total RNA content (in μg)	47,24±1,56 (100%)	50,51±1,54 (106%)	56,44±1,56 (119%)	75,7±1,82 (160%)	68,26±1,77 (144%)
RNA/DNA ratio	1,48±0,05	1,52±0,05	1,63±0,06	1,9±0,07	1,8±0,07

During period I the changes in the indices studied were characteristic of the initial period of experimental atherosclerosis [5, 11].

At the end of period II (after coarctation of the aorta) a decrease was found in the concentrations of cholesterol, lecithin, β-lipoproteins, and total protein in the blood serum, but it was not significant. Only the fraction of albumins and the albumin-globulin ratio showed a statistically significant decrease. These changes could be attributed to the operation, the postoperative period, and the development of compensatory hyperfunction of the heart [4, 7]. Toward the end of period III the concentrations of cholesterol, lecithin, β-lipoproteins, and globulins continued to rise in the rabbits of group 1 (control), but the total protein and albumin levels fell, a characteristic finding in the late stages of experimental atherosclerosis in rabbits with a raised arterial pressure [1, 5].

In the rabbits of group 2, receiving strophanthin without the anabolic steroids, the indices of lipid and protein metabolism were approximately the same as in the rabbits of group 1.

In the animals of the remaining three groups the serum levels of cholesterol, lecithin, β-lipoproteins, and globulins and the cholesterol-licithin ratio all showed a statistically significant decrease, the total protein level was back to normal, while the albumin fraction and the A/G ratio had risen almost to their initial level. These positive changes in the indices were statistically significant, especially in the animals receiving DHT and AST.

The absolute and relative weights of the heart and the thickness of the walls of the left and right ventricles in the rabbits receiving anabolic steroids were 1.3-1.4 times greater than in the control animals (Table 2), indicating uniform hypertrophy of the two ventricles [12, 13]. The total content of nucleic acids in the myocardium of the animals receiving anabolic steroids was considerably higher than in the control.

Administration of anabolic steroids together with strophanthin thus has a decidedly positive effect on protein and lipid metabolism in rabbits with experimental atherosclerosis and chronic hyperfunction of the heart. The action of strophanthin alone, on the other hand, was slight. In their effectiveness in the correction of protein and lipid metabolism the anabolic agents were arranged in the following order: DHT > AST ≥ nerabol.

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