THE USE OF AN EXPERIMENTAL MODEL OF HYPERTONIA FOR ASSESSING THE EFFICIENCY OF SCHIZANDRA CHINENSIS IN ATHEROSCLEROSIS

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The experimental cholesterol model of atherosclerosis has been successfully used in research studying the significance of certain basic pathogenic factors of this disease, as well as to test many recently proposed methods of the prophylaxis and therapy of atherosclerosis [1]. Experimental research has made possible the clinical use of many pharmacological substances, vitamins, hormones, etc. to prevent and treat atherosclerosis [9]. In the case of patients suffering from hypertonic disease along with atherosclerosis, however, many of these agents have proved to be rather ineffective.

These two conditions are known to occur frequently in combination. It has been observed both clinically [8, 10] and experimentally [5, 13] that arterial hypertonia is one of the factors intensifying the development of atherosclerosis. Since many atherosclerosis patients suffer simultaneously from hypertonia, further research is needed to find new agents to prevent and treat atherosclerosis, and such agents should be tested on an experimental model of hypertonia combined with atherosclerosis, instead of on an experimental model of atherosclerosis alone, as has been done up to now.

The purpose of our investigations was to make a comparative study of the efficiency of Schizandra chinensis seeds on both an experimental model of atherosclerosis and a model of hypertonia combined with atherosclerosis.

There are no literary data concerning the influence of Schizardra chinensis on the development of experimental atherosclerosis.

METHODS

The investigations were performed on 28 mole Chinchilla rabbits weighing 2.4-3 kg each, which had been kept under identical conditions and fed the customary diet. The animals were divided into two equal groups of 14 rabbits each.

Before the experiments with experimental atherosclerosis were begun, the common carotid artery in eight of the rabbits was exposed through a skin flap. When the post-operative wound had healed, systematic measurements of the rabbits' blood pressure were made until the normal blood pressure values were established. Then the main trunks of the right and left renal arteries were constricted by ligation with a wire 0.7-0.8 mm in diameter in order to reproduce hypertonia.

In all the rabbits before the experiments began, we determined the total blood cholesterol content according to M. A. Levchenko and the lecithin content according to Samson's method; after the experiments began, the

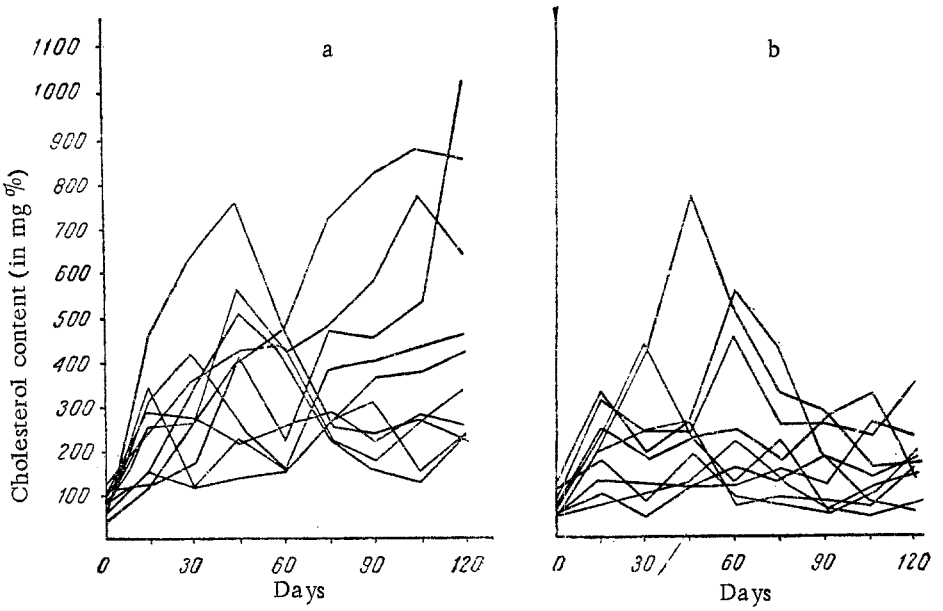

Fig. 1. Effect of Schizandra chinensis on the blood cholesterol content of the control (a) and experimental (b) rabbits with experimental atherosclerosis.

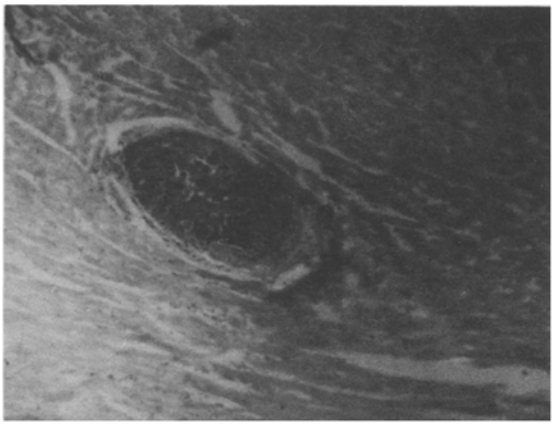

Fig. 2. Acture lipoidosis of an intramuscular artery of the heart in a rabbit given cholesterol. Stained with Sudan III and hematoxylin. Photomicrograph 35x.

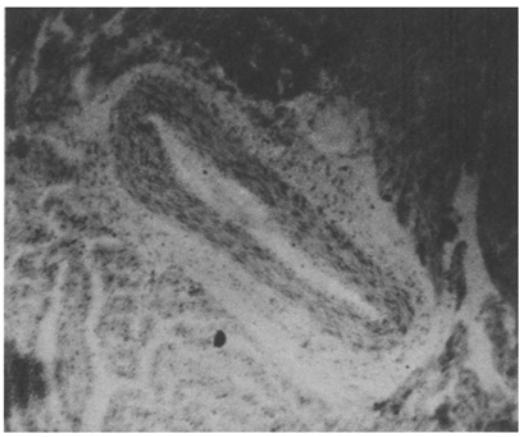

Fig. 3. Absence of lipodosis in myocardial artery of rabbit given cholesterol plus Schizandra chinensis. Stained with Sudan III and hematoxylin after-stain. Photomicrograph 35x.

biochemical examinations of the blood were carried out every 15-17 days.

Experimental atherosclerosis was induced in the control group of rabbits by the daily administration of 0.2 g/kg cholesterol in a 10% sunflower oil solution, introduced into the stomach with the aid of a probe.

The other group of rabbits received the same daily dose of cholesterol plus a 0.2 g/kg dose of ground Schizandra chinensis seeds.

At the end of the experimental period (four months), the rabbits were sacrificed by air embolism; the aorta and heart were extracted and fixed in 20% formalin.

The aorta was stained totally with Sudan III, and the changes observed in it were diagrammed schematically.

TABLE 1

Degree of Atherosclerotic Changes in the Aorta and Coronary Arteries of Normotonic Rabbits Killed after Four Months of Experiments with Experimental Atherosclerosis

Rabbit group	Number of rabbits	Degree of atherosclerosis				No changes
		++++	+++	++	+	
Aorta						
Control (received cholesterol alone)	10	2	3	4	1	–
Experimental (received cholesterol + Schizandra chinensis)	10	–	1	3	2	4
Coronary arteries						
Control (received cholesterol alone)	10	5	1	1	1	2
Experimental (received cholesterol + Schizandra chinensis)	10	2	–	3	1	4

Key: +, slight atherosclerotic changes; ++, moderate changes; +++, acute changes; ++++, very acute changes.

The degree of atherosclerotic changes was also studied mircoscopically on a series of heart sections, stained for fat with Sudan III.

RESULTS

The total blood cholesterol content in all twenty normotonic rabbits, i.e., those without partial constriction of the renal arteries, ranged between 55 and 100 mg% before the experiments began. Two weeks after the start of cholesterol feeding, the blood cholesterol content had increased to 350-450 mg% in the majority of the control rabbits (Fig. 1).

As Fig. 1 shows (left-hand curve), the blood cholesterol level was still higher on the 45th day of the experiments; in six out of ten rabbits, it was as high as 400-778 mg%. Thereafter, the blood cholesterol content remained high in the majority of rabbits until the very end of the experiments. By the end of the fourth month, of cholesterol feeding, for example, it was 638-1025 mg% in three rabbits.

The animals which were given Schizandra chinensis as well as cholesterol showed a relatively low cholesterol level (see Fig. 1b), unlike the control rabbits. In most of the experimental rabbits, the cholesterol level usually fluctuated between 50 and 250 mg%. Relatively high indices (400-770 mg%) were only observed at certain times in four out of ten rabbits. By the 90th-120th day of the experiments, however, the cholesterol level had decreased to 64-225 mg% (in nine out of ten rabbits).

It should be noted that the most acute vascular atherosclerotic changes were observed in the rabbits with a high blood cholesterol content.

Aortic lipoidosis was especially pronounced in the animals of the control group (Table 1).

As Table 1 shows, acute atherosclerotic changes were found in five out of the ten control rabbits; in these animals, the aortic walls were swollen, and the internal surface of the aorta was covered with large atherosclerotic plaques merging into each other. Moderate atherosclerotic changes of the aorta were found in four out of the remaining five rabbits in this group, and slight changes were observed in one rabbit.

Acute changes were observed in the myocardial vessels of all calibers in five of the ten control rabbits. Plaques constricting the arterila lumen were found in the intramuscular arteries and main subepicardial trunks of the coronary vessels. Cholesterol crystals were apparent among the lipoid deposits. The lumen of many of the intramuscular arteries was closed (Fig. 2).

Figure 2 shows acute lipoidosis of an intramuscular artery of the heart with closure of its lumen. In the control group, the coronary arteries of only two rabbits showed no change.

In the rabbits which were given Schizandra chinensis, the aorta showed a completely different picture.

TABLE 2. Cholesterol and Lecithin Content in the Blood and Degree of Atherosclerosis of the Aorta and Coronary Arteries in Hypertonic Rabbits on the 120th Day of Systematic Administration of Cholesterol and Cholesterol Plus Schizandra Chinensis

Rabbit group	Rabbit No.	Total blood cholesterol (in mg %)	Blood lecithin (in mg %)	Lecithin cholesterol coefficient	Degree of atherosclerosis	
					of aorta	of coronary vessels
Control (given cholesterol)	21	1 157	825	0,7	++++	+++
	22	1 182	816	0,72	++++	+++
	23	1 401	824	0,58	+++	++
	24	550	382	0,69	+++	++++
Experimental (given cholesterol + Schizandra chinensis)	25	416	378	0,9	++++	+++
	26	750	535	0,7	++++	++
	27	1 120	459	0,4	++	+++
	28	551	361	0,65	++	++++

Key the same as in Table 1.

No atherosclerotic changes were found at all in the aorta of four out of ten rabbits, in two rabbits, only tiny lipoid spots were seen, moderate changes were observed in three animals, and acute lipoidosis was discovered in the last rabbit.

In the coronary arteries of only two out of ten rabbits could we observe expressed lipoidosis of the intramuscular arteries. Moderate atherosclerotic changes of the coronary arteries were found in three rabbits and slight changes, in one. Both the main trunks of the coronary arteries and the intramuscular vessels of the other four rabbits were completely unaffected. As an example, we include a photomicrograph of a heart section taken from rabbit No. 18, showing one of the intramuscular arteries, free of lipoidosis (Fig. 3).

Since the administration of Schizandra chinensis inhibited or prevented the development of atherosclerosis in the normotonic rabbits, it was interesting to study the effect of this agent on the development of experimental atherosclerosis in the hypertonic rabbits. For this purpose, we conducted experiments on the eight hypertonic rabbits (four in each group) at the same time as the experiments on the normotonic rabbits.

In the hypertonic rabbits, the maximal arterila pressure was 80-120 mm of mercury before the operation, increasing after the operation to 175 mm. A gradual decrease of the arterial pressure to 130 mm of mercury was observed at the beginning of the fourth month of the experiments; the curve of arterial pressure decrease was steeper in the rabbits given Schizandra chinensis.

In the hypertonic rabbits, unlike the normotonic animals, the total blood cholesterol content was high from the very first weeks of the experiment, reaching even higher figures towards the end of the fourth month (Table 2).

Table 2 shows a high cholesterol content and sharply reduced lecithin/cholesterol coefficient in both groups of hypertonic rabbits.

The atherosclerotic changes found in the aorta and coronary arteries of both the control hypertonic rabbits and those which were given Schizandra chinensis were more pronounced than the changes found in the normotonic group of rabbits.

Therefore, the data obtained show that cholesterol feeding caused the same serious atherosclerotic changes in the hypertonic rabbits given Schizandra chinensis as it did in the hypertonic rabbits which received only cholesterol.

The inhibition or complete prevention of the development of atherosclerosis observed in the normotonic rabbits which received Schizandra chinensis was evidently due primarily to the stimulating and tonicizing action of the drug on the central nervous system [4, 7], secondly to an increase in the activity of certain enzymes,

intensification of the carbohydrate [2] and phosphorus [3], metabolisms and stimulation of internal respiration [6] and thirdly, to the fact that the introduction into the organism of Schizandra chinensis causes an increase in the systolic volume of the heart [11], while an infusion of the leaves intensifies the minute volume of a weakened, hypodynamic heart [12].

The positive influence of Schizandra chinensis is not manifested, however, under conditions of hypertonia, a powerful pathologic factor.

SUMMARY

Experiments with 28 rabbits have shown that seeds of Schizandra chinensis administered in a dose of 0.2 g/kg for experimentally induced atherosclerosis will reduce the cholesterol level in the blood and decrease or totally prevent atherosclerosis of the aorta and of the coronaries in the normotonic rabbits. The same doses of S. chinensis administered to hypertensive rabbits fail to exert any effect. In the search for effective agents for prophylaxis and treatment of atherosclerosis it is necessary to test them not only on models of experimental atherosclerosis, but likewise on models of atherosclerosis associated with hypertension.

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