

THE EFFECT OF PITUITRIN ON THE DEVELOPMENT OF EXPERIMENTAL ATHEROSCLEROSIS

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When studying the effect of intravenous injection of pituitrin in dogs and monkeys [2], we noticed that besides the development of a persistent hypertension by these animals, changes in the activity of the heart were observed, of the coronary insufficiency type. These disturbances of hemodynamics after administration of pituitrin suggested to us the possible effect of an extract of the posterior lobe of the pituitary on the development of atherosclerosis and on cholesterol metabolism.

Experiments were carried out on rabbits in order to discover the effect of pituitrin on the course of experimental atherosclerosis. The experimental atherosclerosis was induced in these animals by the method of Academician N. N. Anichkov [1] (oral administration of cholesterol in oily solution).

EXPERIMENTAL METHOD

For the experiment 25 rabbits of the same species (chinchilla) were used, divided into 3 groups. All the animals were kept on an ordinary diet.

The first group of animals (7 rabbits) received cholesterol only by mouth in a dose of 0.5 g in oily solution daily.

The second group of animals (12 rabbits) received the same dose of cholesterol daily and, in addition, 0.5-0.6 ml of pituitrin P was injected intravenously.

The third series of animals (6 rabbits) received every day pituitrin alone by intravenous injection of a dose of 0.5-0.6 ml.

Blood was taken from all the experimental animals before administration of cholesterol concentration was determined. Before the beginning of the experiment 3 separate serum cholesterol estimations were carried out on each rabbit at intervals of one week. In addition the cholesterol concentration was determined in 2 control rabbits which received neither preparation. These rabbits acted as controls for the third group of animals which received pituitrin alone.

Throughout the whole experimental period, the serum cholesterol level was systematically determined every 2-3 weeks in all the rabbits simultaneously.

According to data in the literature, a severe disturbance of cholesterol metabolism and development of atherosclerosis were observed after feeding rabbits for 4 months on cholesterol. In our experiments, as a rule, rabbits which survived for 4 months were killed for examination of the lungs, liver, kidneys and adrenals. The aorta was next isolated throughout the extent of its thoracic and abdominal portions and removed together with the heart. The aorta was incised along its whole length, treated histologically and stained with Sudan III.

TABLE 1

Blood Cholesterol Concentration in Rabbits Receiving Cholesterol Alone (in mg%)

Rabbit No.	Normal	Experimental				Death of animals
		time from starting cholesterol feeding (in months)				
		1	2	3	4	
1	130	550	950	1175	1000	Killed after 4 months
2	130	1000	1250	1400	1250	The same
4	100	800	750	970	1250	" "
6	80	800	800	1050	980	" "
7	120	800	1200	1800	1400	" "
8	105	780	1100	—	—	Killed after 2 months 8 days
Mean		770	1000	1280	1180	

TABLE 2

Blood Cholesterol Concentration in Rabbits Receiving Cholesterol and Pituitrin Concurrently (in mg%)

Rabbit No.	Normal	Time from beginning of experiment (in months)				Death of animals
		1	2	3	4	
3	130	310	830	—	—	Died after 1 month 21 days
5	70	200	400	490	—	Died after 3 months 4 days
9	190	710	1100	1100	1000	Killed after 4 months
11	115	1100	650	500	500	" " 4 "
12	100	900	1350	—	—	Died after 2 months 7 days
13	120	800	960	—	—	" " 2 " 25 "
23	80	760	1000	—	—	" " 2 " 10 "
24	105	880	880	—	—	" " 2 " 10 "
25	50	680	330	—	—	" " 2 " 10 "
Mean		590	830	—	—	

All rabbits dying or killed before this period were also examined post mortem and the aorta was examined macroscopically.

EXPERIMENTAL RESULTS

The results of our investigations were as follows: From the determination of the blood cholesterol concentration in the group of animals receiving cholesterol alone, we observed a considerable increase in the cholesterol in the first month from the beginning of cholesterol feeding. With continuing cholesterol feeding, the blood cholesterol reached its maximum level at the end of the third month. The monthly values for some of the rabbits are shown in Table 1.

In the group of rabbits receiving cholesterol and pituitrin concurrently we observed a more variegated picture. The results of these investigations are shown in Table 2. As may be seen from Table 2, in rabbits Nos. 3, 5 and 25 a small increase in the blood cholesterol was observed in the first month from the start of administration of pituitrin and cholesterol. In rabbit No. 11, on the other hand, a considerable increase in the cholesterol was observed in the first month (to 1100 mg %), but this began to fall in the second month, and at

the end of the third month it had fallen to 500 mg %. A fall in the cholesterol level in the second month also took place in rabbit No. 25. In rabbit No. 5 cholesteremia developed slowly, and at the end of the third month it had reached 490 mg %.

In the third group of rabbits, receiving pituitrin alone daily for 4 months, we observed no increase in the blood cholesterol: the normal values were not exceeded. In rabbit No. 19 only did we find a threefold rise in the cholesterol content, i.e. to 300 mg %.

In the experiments in which both pituitrin and cholesterol were given (second group of animals) the mortality among the animals was high. Of the 12 rabbits included in the experiment only 2 survived for the test period of 4 months. These were killed at the end of the experiment. The remaining rabbits died at various times.

Anatomical examinations showed that the death of the rabbits was the result of an inflammatory process in the lungs, and also that in the rabbits receiving both pituitrin and cholesterol the inflammation of the lungs was suppurative in character, with necrotic destruction of the lung tissues. In the group of animals receiving cholesterol alone, only one rabbit (No. 20) died, and the picture of inflammation of the lungs differed sharply from that observed in the rabbits of the second group receiving pituitrin and cholesterol concurrently: no foci of suppuration were found. In the third group of rabbits, receiving pituitrin alone, only one rabbit (No. 19) died. In this rabbit the inflammation of the lungs resembled the picture of lobar pneumonia: hepatization of the right lung was present.

Macroscopic examination of the aortas of the rabbits killed after feeding for 4 months on cholesterol alone showed that in all the animals the walls of the aorta were grossly thickened, and almost the entire internal surface as far as halfway along the abdominal portion of the aorta, was covered with a continuous layer of atherosclerotic plaques. Particularly large plaques were observed at the orifice and in the thoracic portion of the aorta. In the abdominal aorta, large collections of cholesterol plaques were disseminated, and in its lower portion only isolated plaques were found.

The results of the macroscopic examination of the aortas from rabbits receiving cholesterol and pituitrin concurrently showed a somewhat different pattern of formation of cholesterol plaques. In rabbits Nos. 9 and 11, killed after 4 months, the atherosclerotic changes in the aorta were less pronounced than in the rabbits receiving cholesterol alone and killed at the same times.

In these rabbits (Nos. 9 and 11) the aorta was covered with a continuous layer of cholesterol plaques only in the upper third of its thoracic part, and more distally – to half way along the abdominal aorta – individual groups of plaques were scattered, whereas in the lower third of the abdominal aorta either no cholesterol plaques were observed or occasional isolated ones. Under these circumstances it must be pointed out that the wall of the thoracic aorta, covered with a continuous layer of plaques, was less severely thickened than in rabbits receiving cholesterol alone.

In rabbits dying at various times after receiving both cholesterol and pituitrin, the following macroscopic picture was observed: the aorta of rabbit No. 5, dying after 3 months 4 days, was covered with individual groups of plaques only in the upper third of its thoracic part, and the wall of the aorta was not thickened. In rabbit No. 13, dying after 2 months 25 days, only at its orifice was the aorta covered with a continuous layer of cholesterol plaques, in the thoracic and upper third of the abdominal parts of the aorta there were isolated groups of cholesterol plaques, and in the remaining portion of the aorta no plaques were to be found. In rabbits dying after 2 months 7 days (No. 12) and 1 month 21 days (No. 3), no cholesterol plaques could be found in the aorta. In rabbits killed after 2 months 10 days (Nos. 23 and 24), the walls of the aorta from the orifice to halfway along the abdominal portion were covered with a continuous, thin, translucent layer of cholesterol plaques, but in the lower half of the abdominal aorta no plaques were found. The wall of the aorta was not thickened anywhere in its extent. In rabbit No. 25, killed at the same period (2 months 10 days), cholesterol plaques were observed in isolated groups as far as one third of the way along the abdominal aorta.

In the third group of animals, receiving pituitrin alone, on macroscopic examination of the aorta no cholesterol plaques were observed.

From a comparison of our results it can be seen that not only does pituitrin not enhance experimental cholesteremia and experimental cholesterol atherosclerosis but, on the contrary, it tends to inhibit these processes.

SUMMARY

Experimental atherosclerosis was induced in rabbits by Academician N. N. Anichikov's methods. It was established that pituitrin not only does not intensify the experimental cholesteremia, but on the contrary, reduces it in comparison with its value in control experiments.

LITERATURE CITED

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- [2] A. A. Belous and G. O. Magakyan, Byull. Eksptl. Biol. i Med. Supplement to No. 1, 17-21 (1957).*

*Original Russian pagination. See C. B. Translation.