EFFECT OF PREDNISOLONE ON METABOLISM OF THE ISOLATED HOMOLOGOUS HEART WHEN PERFUSED FROM A LIVING DONOR

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Under the influence of prednisolone the incorporation of methionine-S^{35} into sarcoplasmic proteins of all parts of the isolated heart perfused from a living donor is considerably inhibited. Prednisolone has no such effect on the donor's heart.

With the steady increase in the use of hormones in recent years during organ transplantations [3, 5, 6], and especially in heart transplanation, it has become necessary to investigate the effect of hormones on metabolism of the isolated heart, because the character of biochemical processes in the myocardium largely determines the viability of the transplanted heart.

In the investigation described below the effect of prednisolone on protein synthesis in the myocardium and the state of enzyme systems in the blood plasma and myocardium of the homologous heart were studied during perfusion from a living donor. The results were compared with data for the effect of prednisolone on analogous indices in the donor's heart.

EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 2.5-3 kg. The animal's heart was removed and connected to the circulatory system of a donor animal via the carotid artery and jugular vein. The temperature of the isolated heart was maintained automatically at 38°C; the rate of perfusion was 8-10 ml/min. A solution of prednisolone was injected every 5 min for 1 h in three experiments in a dose of 10 mg/kg body weight. Methionine-S^{35}, in a dose of 20,000 pulses/min/g was injected into the blood stream 30 min after the beginning of addition of prednisolone. In three control experiments similar perfusion of the homologous heart was carried out but without the addition of prednisolone. The experimental and control animals were sacrificed 1 h after administration of the radioactive isotope, and total [2], contractile, and sarcoplasmic [1, 4] proteins were isolated from the tissue of the ventricles. Only total proteins were isolated from the atria and interventricular septum. Radioactivity of the isolated proteins was determined by means of an end-window counter. Activity of lactate dehydrogenase (LDH and LDH-1) [7, 8], glutamate-oxaloacetate transaminase (GOT), and glutamate-pyruvate transaminase (GPT) [9] in the heart tissue and blood plasma was determined at the beginning of perfusion and 60 and 90 min later. In the control experiments blood plasma was investigated at the beginning of perfusion and 1 h later.

EXPERIMENTAL RESULTS

Prednisolone considerably inhibited protein synthesis in all parts of the isolated heart (by 40-60%) compared with the control; synthesis of sarcoplasmic proteins in both ventricles was inhibited by 64.5 and 58% respectively, while no appreciable change took place in the synthesis of contractile proteins (Table 1). Meanwhile, prednisolone had practically no effect on protein synthesis in the donor's heart.

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TABLE 1. Incorporation of Methanionines-S^{35} (pulses/min/5 mg protein) into Mycardial Proteins during Perfusion of Isolated Heart from a Living Donor

	Part of heart	Isolated heart	Donor's heart	Degree of of changes (in %)	P
		M ± m			
Prednisolone	Left atrium	300 ± 31.7	497 ± 52.9	− 29.6	< 0.05
	Right atrium	294 ± 29.2	550 ± 24.9	− 46.6	< 0.01
	Left ventricle				
	Total protein	300 ± 56.6	687 ± 55.5	− 57.4	< 0.02
	Sarcoplasmic proteins	262 ± 85.9	568 ± 51.3	− 53.9	< 0.05
	Contractile	297 ± 119.4	400 ± 17.0	− 25.8	> 0.5
	Right ventricle				
	Total protein	354 ± 8.3	721 ± 47.5	− 51.0	< 0.01
	Sarcoplasmic proteins	272 ± 57.7	430 ± 52.5	− 45.6	< 0.05
	Contractile	266 ± 123.8	359 ± 97.1	− 26.0	< 0.5
	Interventricular septum	363 ± 53.7	610 ± 42.0	− 40.5	> 0.05
Control	Left atrium	572 ± 17	550 ± 42.5	+ 40	< 0.5
	Right atrium	473 ± 57	540 ± 76.3	− 12.5	> 0.5
	Left ventricle				
	Total protein	734 ± 43	677 ± 39.9	+ 9.8	> 0.5
	Sarcoplasmic proteins	737 ± 64.3	603 ± 76.6	+ 4.0	> 0.5
	Contractile	250 ± 15	220 ± 56.8	+ 13.6	> 0.5
	Right ventricle				
	Total protein	638 ± 29	705 ± 94.5	+ 13.0	> 0.5
	Sarcoplasmic proteins	580 ± 60.8	523 ± 53	+ 10.0	> 0.5
	Contractile	248 ± 18	265 ± 63	− 7.0	> 0.5
	Interventricular septum	745 ± 115	601 ± 104.4	+ 24.0	> 0.5

TABLE 2. Effect of Prednisolone on Enzyme Activity in Blood Plasma and Myocardium during Perfusion of Isolated Homologous Heart from a Living Donor

Enzyme studied	Exptl. conditions	Blood plasma					
		beginning of perfusion (M ± m)	after perfusion for 60 min		after perfusion for 90 min		
			(M ± m)	P	(M ± m)	P
LDH (in Wroblewsky's units/ml)	Prenisolone	427 ± 36.8	457 ± 41	< 0.5	597 ± 24.6	< 0.01
	Control	508 ± 59.6	448 ± 54.7	< 0.5		
LDH-1 (in percent)	Prednisolone	15.3 ± 4.6	15.1 ± 3.1	> 0.5	29.6 ± 3.9	> 0.05
	Control	11.9 ± 4.3	31.5 ± 5.5	< 0.05		
GOT (in i.u./ml)	Prednisolone	20.6 ± 5.5	41.4 ± 8.8	< 0.1	49.3 ± 9.3	< 0.05
	Control	35.3 ± 4.2	26.8 ± 6.06	< 0.5		
GPT (in i.u./ml)	Prednisolone	12.6 ± 1.3	13.0 ± 1.4	> 0.5	13.5 ± 1.4	< 0.05
	Control	17.1 ± 3.5	10.7 ± 4.5	< 0.5		

No changes in these processes likewise were found in the myocardium of intact animals receiving corresponding doses of prednisolone. Whereas during perfusion without prednisolone, the incorporation of labeled amino acid into proteins of the isolated heart was indistinguishable from its incorporation into proteins of the donor's heart, addition of prednisolone caused definite changes in the state of the isolated heart and donor's heart.

As Table 2 shows, for a period of 1 h after injection of prednisolone into the blood stream no changes in LDH, GOT, and GPT activity were observed in the plasma; activity of LDH-1 in the plasma was sharply increased (Table 2). The activity of the other investigated enzymes, with the exception of GTP, was also increased 90 min after the beginning of the experiment. Enzyme activity in the myocardium of the isolated heart was indistinguishable from that in the donor's heart, and prednisolone did not change it substantially.

LITERATURE CITED

1. V. V. Kadykov, Vopr. Med. Khimii, No. 3, 311 (1963).
2. A. S. Konikova, M. G. Kritsman, and O. P. Samarina, Biokhimiya, No. 4, 440 (1954).
3. N. A. Lopatkin, Yu. M. Lopukhin, and I. N. Kuchinskii, in: Current Problems in Transplantation of Organs [in Russian], Moscow (1969), p. 185.
4. V. V. Oppel' and T. P. Serebrenkova, Biokhimiya, No. 4, 648 (1959).
5. C. N. Barnard, Am. J. Cardiol., 22, 811 (1968).
6. D. A. Cooley, J. Cardiovasc. Surg., 9, 403 (1968).
7. B. Hess and S. J. Walter, Klin. Wschr., 39, 213 (1961).
8. F. Wroblewsky and J. S. LaDue, Proc. Soc. Exp. Biol. (New York), 90, 210 (1955).
9. F. Wroblewsky and J. S. LaDue, Ann. Intern. Med., 43, 345 (1955).