system, as well as activity of the renin-synthesizing structures, differs in Wistar and Koletsky rats under conditions of emotional stress.

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EFFECT OF L-DOPA ON THE DEVELOPMENT OF EXPERIMENTAL HYPERLIPIDEMIA AND ATHEROSCLEROSIS

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KEY WORDS: hyperlipidemia; atherosclerosis; L-dopa.

L-dopa, a precursor for catecholamine biosynthesis [2], is used in the combined treatment of Parkinson's disease [3, 7, 9]. There is information in the literature that this disease is often preceded by cerebrovascular atherosclerosis [4, 5].

It was therefore decided to study the effect of L-dopa on lipid metabolism and, in particular, on the development of experimental hyperlipidemia and atherosclerosis, and the investigation described below was undertaken for this purpose.

EXPERIMENTAL METHOD

Male albino rats (weighing 250-300 g), guinea pigs (weighing 250-300 g), and rabbits (weighing 2.5-3 kg) were used. Hyperlipidemia was induced in the rats by intraperitoneal injection of Triton WR-1339 in a dose of 225 mg/kg. L-dopa was injected twice, intraperitoneally, in a dose of 100 mg/kg, 24 h before and at the same time as the injection of Triton. Guinea pigs received cholesterol (CH) in a dose of 0.5 g/kg in sunflower oil by gastric tube daily for 25 days; L-dopa was given by the same method in a dose of 100 mg/kg. Atherosclerosis was induced in the rabbits by daily administration of 0.3 g/kg of CH in sunflower oil for 3 months. L-dopa was given perorally in a dose of 100 mg/kg. The acute toxicity of L-dopa was determined in experiments on mice. Peroral administration of L-dopa in a dose of 4 g/kg had no toxic action; LD_{50} by intraperitoneal injection was 2750 mg/kg body weight. Concentrations of total CH [11] and triglycerides (TG) [13] were determined in the blood and liver. The rabbits were killed by injection of air into the auricular vein; the aorta was isolated along its whole length and subjected to planimetry [1], after which its total CH content was determined.

EXPERIMENTAL RESULTS

The experiments on rats showed that during hyperlipidemia induced by Triton administration L-dopa reduced the increase in the CH level and, to a lesser degree, in the TG level in the blood (Fig. 1). After administration of CH to guinea pigs for 25 days, an increase in the serum CH and TG levels was observed. Combined administration of L-dopa and CH caused a marked hypolipidemic effect. In addition, under the influence of L-dopa a marked decrease in the TG concentration in the liver was noted, from 12.7 ± 1.1 to 6.25 ± 0.49 mg/g

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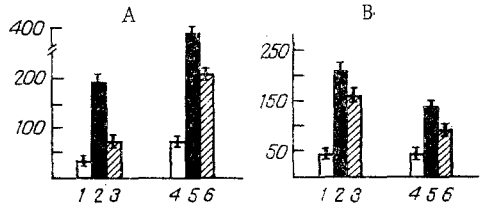

Fig. 1. Serum CH (1-3) and TG (4-6) concentrations in rats (A) and guinea pigs (B) during induced hyperlipidemia and administration of L-dopa. Ordinate, CH and TG concentration (in mg%). A: 1, 4) control, 2, 5) administration of Triton WR-1339, 3, 6) administration of Triton WR-1339 and L-dopa; B: 1, 4) control, 2, 5) administration of CH, 3, 6) administration of CH and L-dopa.

TABLE 1. Effect of L-dopa on Lipid Indices in Rabbits with Experimental Atherosclerosis

Experimental conditions	CH			TG		Index of atherosclerotic change in aorta, %
	serum, mg%	liver, mg/g	aorta, mg/g	serum, mg%	liver, mg/g	
1. Control (n = 5)	46,4±11,3	2,74±0,25	2,84±0,2	43,5±5,2	7.06±0,9	—
2. Administration of CH (n = 7)	1030,0±108,0	15,5±2,61	25,5±1,4	554,6±117,0	30,2±0,9	35,8±7,5
3. Administration of CH and L-dopa (n = 9)	628,0±184,8	16,0±0,84	19,7±1,2	181,0±91,9	13,9±2,7	16,4±4,3*
P_{2-3}	<0,01			<0,05	<0,001	<0,05

*Mean data for six rabbits with lesions.

($P < 0.01$). Experiments on rabbits with experimental atherosclerosis revealed the protective action of L-dopa: The index of atherosclerotic changes in the aorta fell significantly (Table 1); in the group of rabbits receiving L-dopa together with CH, no visible atherosclerotic changes were present in three of the nine animals. Under the influence of L-dopa a fall in the serum CH and TG levels and in the TG concentration in the liver also was observed, together with a marked tendency for the CH content in the aorta to decrease. The CH constant in the adrenals of rabbits receiving the atherogenic diet was significantly higher than in intact animals: 218.8 ± 13.8 mg/g compared with 128.8 ± 8.55 mg/g ($P < 0.001$), but L-dopa reduced this effect — the CH content in the adrenals of rabbits receiving L-dopa together with CH was 179.8 ± 10.1 compared with 218.8 ± 13.8 mg/g ($P < 0.05$). The same pattern also was observed with respect to the weight of the adrenals expressed as a ratio of the body weight (0.176 in intact animals, 0.486 in those receiving CH, and 0.391 in animals receiving CH and L-dopa).

During hyperlipidemia induced in rats, guinea pigs, and rabbits, administration of L-dopa thus had a hypolipidemic action. Under the influence of L-dopa the degree of experimental atherosclerotic change in the aorta of the rabbits also was reduced. These results indicate significant differences in the action of dopamine, formed *in vivo* from its immediate precursor (L-dopa), and the action of adrenalin and noradrenalin on lipid metabolism and the development of atherosclerosis. For instance, it is known that under the influence of adrenalin and noradrenalin not only are the blood levels of lipids and atherogenic lipoproteins raised [6, 12], but experimental atherosclerotic and degenerative lesions also develop in the aorta [8, 10].

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PATHOGENETIC ROLES OF ACTIVATION OF LIPID PEROXIDATION AND PROTECTIVE EFFECT OF SODIUM SELENITE DURING ISCHEMIA AND REPERFUSION OF THE MYOCARDIUM

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A temporary reduction of the coronary blood flow is accompanied by a disturbance of the contractile function and rhythm of the heart not only in the period of myocardial ischemia (MI), but also when perfusion of the coronary arteries is resumed [4-7]. The development of arrhythmias and depression of the contractile process are the dominant factors of the disturbance of the systemic hemodynamics in the initial stage of postischemic restoration of the coronary blood flow and they essentially form the cardiac reperfusion syndrome [9]. The mechanism of development of this syndrome is evidently based on summation of metabolic-functional and structural changes in the heart arising during its ischemia and subsequent reperfusion (RP). Among the metabolic disorders in the RP stage, accompanied by myocardial hyperoxia, particular attention should be paid to the process of free-radical lipid peroxidation (FRLP). This is because of data showing, first, the intensification of FRLP during myocardial hyperoxia [13], second, the protective effect of an antioxidant – α-tocopherol – during reoxygenation of the previously ischemized myocardium *in vitro* [13], and third, as the writers' previous investigations revealed, biphasic activation of FRLP during reversible MI: in the period of ischemia and on resumption of the blood flow in the coronary arteries of the heart [9]. With the above facts in mind, the writers postulated the important pathogenetic role of activation of FRLP in the development of both the ischemic and the reperfusion syndromes during reversible disturbance of the coronary blood flow [9]. To obtain proof of this hypothesis, an attempt was made to compare the dynamics of FRLP and cardiac function during transient myocardial ischemia (TMI) for different durations and also to study the effect of sodium selenite, an active inhibitor of FRLP, on cardiac activity during TMI.

EXPERIMENTAL METHOD

Experiments were carried out on 89 noninbred male albino rats weighing 190-210 g. TMI was produced by the method described previously [4, 6] under urethane (1200 mg/kg) anesthesia with artificial ventilation of the lungs with atmospheric air. The duration of the period of MI before myocardial RP was 10, 20, 40, or 120 min. Lipids were extracted from the damaged area of the myocardium by the method in [11]. The intensity of FRLP was determined by a chemiluminescence method using a quantum measuring device for recording weak light fluxes [1]. The cardiac frequency was recorded on the ECG and the peak actual (P_{act}) and maximal (during isometric contraction of the heart, P_{max}) pressure within the left ventricle

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