EFFECT OF L-DOPA ON CYCLIC AMP CONTENT OF HEART MUSCLE AFTER NEUROGENIC INJURY

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Application of an extraordinary stimulus, such as electrical stimulation of the arch of the aorta, leads to a sharp decline in the catecholamine (CA) concentration in the heart muscle, the basis for the development of dystrophic changes in the muscle [1]. A definite parallel also has been observed between exhaustion of exogenous CA in the myocardium and the decrease in the concentration of cyclic AMP, a secondary messenger in the realization of most metabolic effects of CA [2]. Injection of L-dopa, a precursor of noradrenalin, reduced the severity of the metabolic disturbances in the myocardium and contributed to recovery of its normal function [3].

It was decided to investigate the cyclic AMP concentration in the heart muscle and blood plasma after administration of L-dopa.

EXPERIMENTAL METHODS

In experiments on 36 male rabbits weighing 3.0-3.3 kg dystrophic lesions in the myocardium were induced by electrical stimulation (5-10 V, 50 Hz, 10 msec) of the arch of the aorta for 3 h as described in [1]. L-dopa was injected as a 2% solution intraperitoneally in a dose of 10 mg/kg body weight four times in the course of 48 h after the end of stimulation.

Blood samples were taken in test tubes with the addition of 0.5 M EDTA, pH 7.5; the samples were quickly centrifuged at 8,000 g for 10 min; the plasma was kept in flasks at −20°C.

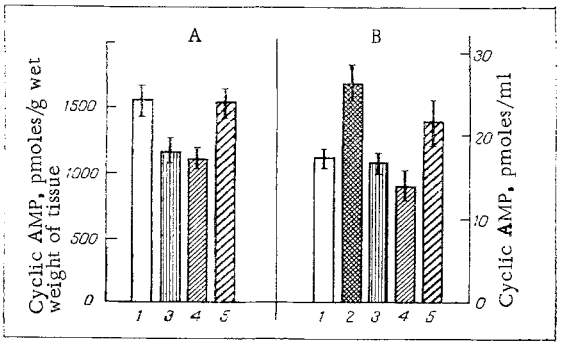

Fig. 1. Cyclic AMP concentration in heart muscle (A) and blood plasma (B) of rabbits following electrical stimulation of arch of aorta (M ± m). 1) Intact rabbits (control); 2) after electrical stimulation for 15 min; 3) after electrical stimulation for 3 h; 4) 48 h after end of electrical stimulation; 5) 48 h after end of electrical stimulation with injection of L-dopa.

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The rabbits were killed by injection of air into the auricular vein. The heart was removed and quickly frozen in liquid nitrogen (in all the experiments the apex and part of the left ventricle were used). Cyclic AMP was extracted with 0.6 N perchloric acid; after centrifugation of the homogenate at 8,000g for 20 min, some of the supernatant was neutralized with crystalline K_2CO_3.

The cyclic AMP concentration was determined in the neutralized supernatant and blood plasma by competitive binding with protein, using kits of reagents ("Amersham") [4].

EXPERIMENTAL RESULTS

The cyclic AMP level in the blood plasma and heart muscle in the control group was 18.0 ± 0.8 pmoles/ml and 1570 ± 120 pmoles/g respectively.

It will be clear from Fig. 1 that the cyclic AMP concentration in the dystrophic myocardium was considerably reduced compared with the control immediately after electrical stimulation, and by an even greater degree 48 h after the end of stimulation ($P < 0.05$). In the rabbits receiving L-dopa, no decrease in the cyclic AMP level was found. The plasma cyclic AMP concentration was increased by 50% after electrical stimulation for 15 min ($P < 0.05$); by the end of stimulation the initial level was practically restored, and after 48 h it was significantly reduced. Injection of L-dopa prevented the decrease in the plasma cyclic AMP concentration. In response to extraordinary stimulation of the aortic reflexogenic zone, injection of L-dopa thus contributed toward normalization of the cyclic AMP concentration both in the heart muscle and in the blood plasma. It can be tentatively suggested that this was due to the ability of L-dopa to become involved in CA biosynthesis and, by acting on adenylate cyclase, to stimulate cyclic AMP synthesis.

The positive effect of L-dopa in neurogenic injury to the myocardium caused by application of an extraordinary stimulus to the reflexogenic zone of the arch of the aorta opens up fresh prospects for the use of this substance in the pharmacotherapy of cardiovascular pathology of neurogenic origin.

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