EFFECT OF DIHYDROERGOTOXIN ON CAPACITANCE VESSELS OF THE MYOCARDIUM

V. I. Ovsyannikov

UDC 615.256.54.015.4:612.172.1

Experiments were carried out on isolated cats' hearts with perfusion of the coronary vessels with blood from a donor cat by means of a constant delivery pump. Dihydroergotoxin, injected into the coronary vessels in a dose of 0.5 mg, caused a decrease in their capacity as a result of active constriction of the coronary veins, for it was also observed in experiments on the heart stopped by strophanthin. The decrease in the coronary capacity was not connected with the action of endogenous catecholamines on β-adrenergic receptors of the coronary vessels. Unlike dihydroergotoxin, another α-adrenoblocker (phentolamine) did not cause constriction of the coronary veins. It is concluded that constriction of the coronary veins through the action of dihydroergotoxin is due to its direct action on the smooth muscles of the vessels.

KEY WORDS: veins of the heart; dihydroergotoxin.

Previous investigations [2-4] showed that adrenalin and noradrenalin reduce the lumen of the venous part of the coronary blood stream. No data on responses of the capacitance vessels of the myocardium to other vasoactive substances evidently exist in the literature. Dihydroergotamine, like the catecholamines, evokes a constrictor response of the capacitance vessels of skeletal muscle [8].

The object of this investigation was to study whether the veins of the myocardium respond actively to dihydroergotoxin.

EXPERIMENTAL METHOD

Experiments were carried out on 12 isolated cats' hearts the coronary vessels of which were perfused with blood from a donor cat by means of a constant delivery pump [2]. The isolated heart was left in the animal's thorax. Perfusion was carried out through a cannula inserted via the ascending part of the arch of the aorta toward the aortic valve. A change in the resistance of the coronary vessels was judged from changes in perfusion pressure. Changes in the outflow from the coronary vessels reflected changes in capacity of the blood vessels of the heart. The outflowing blood was led into a measuring system through wide polyethylene catheters, with side openings, introduced in the left and right ventricles. The ends of the catheters were 4-5 cm below the level of the heart, thus avoiding retention of blood in the chambers of the heart and so ruling out the possibility of changes in the outflow of blood into the recording system as a result of changes in cardiac activity. The coronary perfusion pressure was recorded by an ID-2 electromanometer with low-capacitance detector. The total capacity of the perfusion system used varied by 0.08 ml during changes in pressure of 100 mm. The strength and frequency of the cardiac contractions were recorded by an isometric strain gauge [1], sutured to the anterior wall of the left ventricle. Records were produced by the N327-5 automatic lighter.

Dihydroergotoxin (DH-ergotoxin, Spofa, Czechoslovakia) and phentolamine (Regitin, Ciba) were used and were injected in doses of 0.5 mg (0.5 ml) into the main channel of the perfusion pump. Blocking of the β-adrenergic receptors was achieved by intracoronary infusion of propranolol (Obsidan) at the rate of 0.5

Laboratory of Physiology and Pathology of the Circulation, K. M. Bykov Department of Physiology of Visceral Systems, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad.
(Presented by Academician of the Academy of Medical Sciences of the USSR S. V. Anichkov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 80, No. 7, pp. 52-54, July, 1975. Original article submitted October 7, 1974.

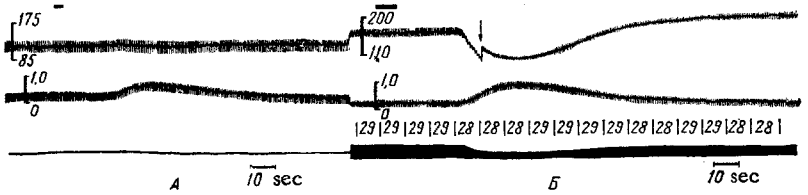

Fig. 1. Changes in resistance and capacity of coronary vessels following injections of 0.5 mg dihydroergotoxin into them in experiments on the arrested heart (A) and on the heart contracting spontaneously (B). From top to bottom: marker of injection of substance, coronary perfusion pressure (in mm), outflow from coronary vessels (in ml), strength of cardiac contractions; numbers represent number of beats in 10 sec. Arrow in B marks displacement of curve during electrical compensation of signal from electromanometer.

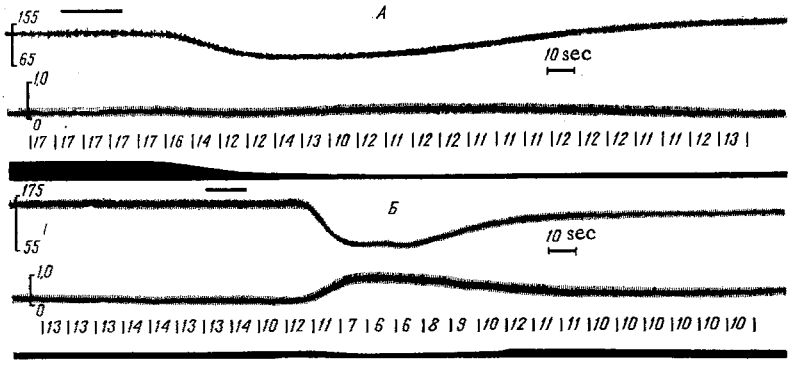

Fig. 2. Changes in resistance and capacity of coronary vessels following injection of 0.5 mg phentolamine (A) and 0.5 mg dihydroergotoxin (B) into them. Legend as in Fig. 1.

ml/min in a total dose of 2-3 mg. The heart was stopped by intracoronary injection of 0.5-1 ml of 0.05% strophanthin K solution.

EXPERIMENTAL RESULTS AND DISCUSSION

The lumen of the coronary veins in the working heart may be influenced by changes in the rhythmic activity modifying the degree of extravascular compression of the coronary vessels [2]. To study whether the myocardial vessels can respond actively to the action of dihydroergotoxin, experiments were carried out on hearts stopped by strophanthin.

Dihydroergotoxin, if injected into the coronary vessels, increased the outflow of blood from the coronary system in all eight experiments, i.e., it reduced the capacity of the system (Fig. 1A) on the average by 0.4 ± 0.04 ml. The resistance of the coronary vessels under these circumstances was reduced in all experiments by $5.8 \pm 1.1\%$ (7.5 ± 1.5 mm Hg) from the original perfusion pressure in the coronary vessels of 127 ± 6 mm Hg.

Dihydroergotoxin thus causes a change in the lumen of the venous heart of the coronary vascular system independently of the action of extravascular factors and responses of resistive vessels (for the capacity of the vascular system of an organ is determined mainly by its venous portion) [6, 7]. Consequently, in this case an active response of the veins took place.

The writer showed previously [2-4] that adrenalin and noradrenalin evoke an active response in the myocardial veins through their effect on β-adrenergic receptors. Since dihydroergotoxin blocks α-adrenergic receptors, it might be supposed that the α-adrenergic effect of endogenous catecholamines circulating in the donor's blood would thereby be increased, with a consequent decrease in the coronary capacity. To study this problem experiments were carried out on hearts contracting spontaneously, in which dihydroergotoxin was injected into the coronary vessels after blocking of their β-adrenergic receptors. Against this

background also, dihydroergotoxin reduced the coronary capacity (Fig. 1B) in all eight experiments, on the average by 0.6 ± 0.1 ml. The resistance of the coronary vessels in all cases fell on the average by 41 ± 2.3% (49 ± 7 mm Hg) when the original perfusion pressure was 117 ± 13.6 mm Hg. Besides a decrease in the capacity of the coronary vascular system and a decrease in its resistance, in all cases dihydroergotoxin produced a decrease in the strength of the myocardial contractions (by 56 ± 6%) and, in six of eight experiments, it slowed the heart beat (by 10 ± 2.7%). These experiments show that the action of dihydroergotoxin on the capacity of the coronary system is based on a mechanism unconnected with blocking of α-adrenergic receptors and differing from the mechanism of the β-adrenergic action of the catecholamines.

This independence of the effect of dihydroergotoxin on the myocardial veins of blocking of the α-adrenergic receptors also was confirmed by experiments in which the action of dihydroergotoxin was compared on the same preparation with the action of phentolamine, another agent blocking α-adrenergic receptors. These substances also were injected after blocking of the β-adrenergic receptors. Dihydroergotoxin (Fig. 2B), as in the previous experiments, constantly increased the outflow of the blood from the coronary vessels on the average by 0.6 ± 0.08 ml. By contrast, phentolamine (Fig. 2A) did not reduce their capacity in a single case. Meanwhile phenotolamine, like dihydroergotoxin, lowered the resistance of the coronary vessels and reduced the strength and frequency of the cardiac contractions. It can accordingly be concluded that the constrictor effect of dihydroergotoxin on the coronary veins was not the result of its properties as an α-adrenoblocker, but was due to the direct action of this substance on the smooth muscle of the coronary veins. Since it is mainly the large coronary veins that possess a well-developed muscle coat and ability to change their lumen activity [5], it is possible that their constriction determined the decrease in the coronary capacity during the action of dihydroergotoxin.

LITERATURE CITED

1. V. I. Ovsyannikov, Fiziol. Zh. SSSR, No. 12, 1415 (1968).
2. V. I. Ovsyannikov, Fiziol. Zh. SSSR, No. 10, 1481 (1971).
3. V. I. Ovsyannikov, Vestn. Akad. Med. Nauk SSSR, No. 12, 10 (1973).
4. V. I. Ovsyannikov and B. I. Tkachenko, Fiziol. Zh. SSSR, No. 6, 902 (1972).
5. O. Bucher and M. V. Koebling, Acta Anat. (Basel), 17, 369 (1953).
6. B. Folkow, Circulation, 21, 760 (1960).
7. S. Mellander and B. Johansson, Pharmacol. Rev., 20, 117 (1968).
8. S. Mellander and I. Nordenfelt, Clin. Sci., 39, 183 (1970).