FUNCTIONAL STATE OF THE LEFT VENTRICLE IN CARDIOCYTOTOXIC SHOCK

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UDC 616.127-005.8-06:616-001.36-07:616.124.2-008.1-07

Changes in the cardiodynamics and contractile function of the myocardium were studied in experimental shock arising in 20 anesthetized dogs in response to intracoronary injection of anticardiac cytotoxic serum. Besides signs of a disturbance of left ventricular function (a fall in the systolic index, the working stroke index of the left ventricle, the rate of rise of intraventricular pressure, the indices of myocardial contractility, and the ejection fraction) a decrease was observed in the end-diastolic volume and pressure in the left ventricle. These results indicate that disturbances of the cardiodynamics are due to both cytotoxic injury to the heart and a disturbance of the blood flow to the left heart.

KEY WORDS: *heart; cardiocytotoxic shock.*

Injection of anticardiac cytotoxic serum into the coronary circulation was shown previously to give rise to severe disturbances of the hemodynamics, similar in several of their features to the symptom complex of cardiogenic shock, and also to marked morphological changes in the vessels and the contractile apparatus of the left ventricle [1, 2, 5].

This paper described the results of a study of changes in myocardial contractility and the pumping function of the left ventricle in the acute stage of development of cytotoxic degeneration of the myocardium.

EXPERIMENTAL METHOD

Experiments were carried out on 20 mongrel dogs weighing 15-22 kg anesthetized with morphine and chloralose (0.0025 and 0.07 g/kg, respectively). Changes in the cardiodynamics and contractile function of the myocardium of the left ventricle were assessed on the basis of the following indices: the pressure in the left ventricle and its diastolic component, the blood volume in the left ventricle during the various phases of the cardiac cycle, the injection fraction, and indices of myocardial contractility.

To record the pressure in the left ventricle and the rate of changes of this pressure (dp/dt) a hydraulic system was used: the external pressure sensor of the ÉM 1-02 electromanometer (intrinsic frequency of the system up to 70 Hz) or the intraventricular pressure sensor with an intrinsic frequency of 800 Hz [6]. The results were recorded on the Mingograph M-34 apparatus (Elema, Sweden). The rate of change of pressure was measured by means of an electronic differentiator of the authors' own design [4].

From the pressure in the left ventricle and its maximal rate of rise (dp/dt_{max}) the indices of myocardial contractility $\frac{dp/dt_{max}}{Ip}$; $\frac{dp/dt_{max}}{IIT}$ were calculated [12, 13].

Department of Experimental Cardiology, A. A. Bogomolets Institute of Physiology, Academy of Sciences of the Ukrainian SSR, Kiev. (Presented by Academician of the Academy of Medical Sciences of the USSR N. N. Gorev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 11, pp. 1291-1294, November, 1976. Original article submitted April 1, 1976.

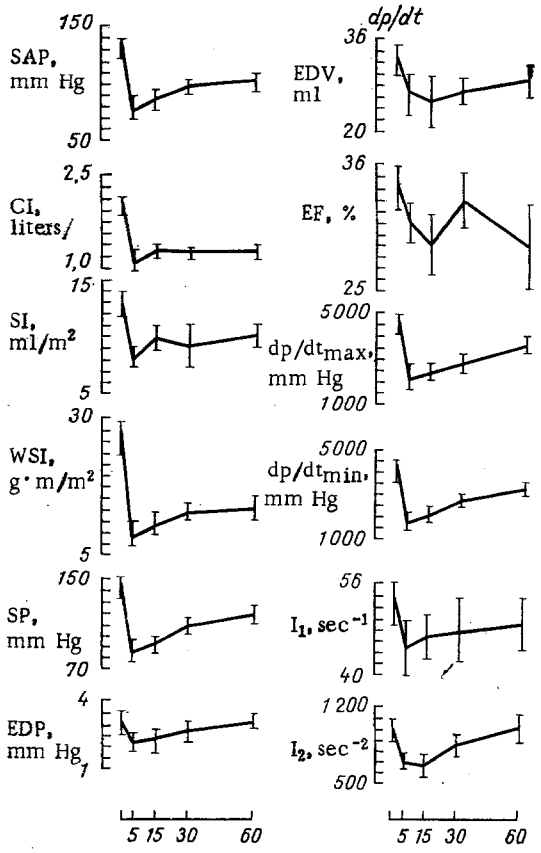

Fig. 1

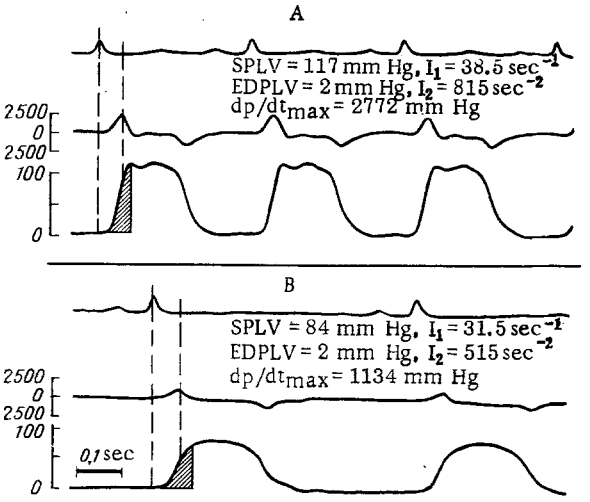

Fig. 2

Fig. 1. Changes in indices (M ± m) of hemodynamics, cardiodynamics, and myocardial contractility during development of cardiocytotoxic shock. SAP) Systemic arterial pressure; CI) cardiac index; SI) systolic index; WSI) working stroke index of left ventricle; SP) systolic pressure in left ventricle; EDP) end-diastolic pressure in left ventricle; EDV) end-diastolic blood volume in left ventricle; EF) ejection fraction of blood from left ventricle; dp/dt_{max}) maximal rate of rise of pressure in left ventricle; dp/dt_{min}) maximal rate of fall of pressure in left ventricle; I_1) myocardial contractility index $\left(\frac{dp/dt_{max}}{IP}\right)$; I_2) myocardial contractility index $\left(\frac{dp/dt_{max}}{IIT}\right)$. Scale below shows time from beginning of reaction (in min). Initial part of each curve corresponds to initial values. Here and in Fig. 2, dp/dt_{max} expressed in mm Hg/sec.

Fig. 2. Effect of intracoronary injection of anticardiac cytotoxic serum on cardiodynamics. A) Control; B) 5 min after injection of 1.5 ml anticardiac serum into circumflex branch of left coronary artery. From top to bottom: ECG (lead I), rate of change of pressure in left ventricle, pressure in left ventricle (in mm Hg), SPLV) systolic pressure in left ventricle, EDPLV) end-diastolic pressure in left ventricle, dp/dt_{max}) maximal rate of rise of pressure in left ventricle, I_1) myocardial contractility index $\frac{dp/dt_{max}}{Ip}$; I_2) myocardial contractility index $\left(\frac{dp/dt_{max}}{IIT}\right)$.

The minute blood volume (20 experiments) and the blood volume in the left ventricle (12 experiments) were determined by the thermodilution method [3, 10, 11]. The mean arterial pressure was recorded through a catheter introduced into the arch of the aorta. The heart rate was determined from the ECG (lead I). These results were used to calculate the cardiac and systolic indices, the working stroke index of the left ventricle, and the ejection fraction of the left ventricle. All experiments were carried out on animals breathing naturally and without thoracotomy.

Anticardiac cytotoxic serum was obtained by immunizing rabbits with tissue homogenate of dog's heart. The serum in a dose of 1-1.5 ml (titer in the complement fixation test

1:320: to 1:1280) was injected into the descending or circumflex branch of the left coronary artery through a catheter inserted into the corresponding coronary vessel through an incision in the external carotid artery. The corresponding branch of the left coronary artery was perfused with the animal's own blood by means of a constant-output pump.

EXPERIMENTAL RESULTS AND DISCUSSION

After intracoronary injection of anticardiac cytotoxic serum and a short latent period of 40-60 sec marked disturbances of the hemodynamics and of cardiac activity were observed. The systemic arterial pressure fell during the first 3-5 min of the reaction on the average from 132 to 76 mm Hg (by 43% of its initial level), the cardiac index fell by 46%, the systolic index by 36%, the working stroke index of the left ventricle by 64%, and the systolic pressure in the left ventricle by 41%. In the subsequent course of the reaction a tendency was observed for the arterial pressure and, to a lesser degree, the cardiac and systolic indices, to be restored although by the 60th minute these parameters were still sharply reduced (Fig. 1).

Indices characterizing the contractile power of the myocardium of the left ventricle showed substantial changes (Figs. 1 and 2). The maximal rate of rise of pressure in the left ventricle (dp/dt_{max}) fell from 4621 ± 302 to 2190 ± 532 mm Hg/sec, and during the period of greatest fall of systemic arterial pressure it was 53% lower than initially, although by the end of the first hour of the reaction it was only 16.5% lower. In some cases changes in the first derivative of the pressure in the left ventricle preceded the other hemodynamic changes. This applied in particular to changes in the rate of fall of pressure in the left ventricle (dp/dt_{min}), which could be substantially reduced as early as 5-10 sec after intracoronary injection of the anticardiac cytotoxic serum. The myocardial contractility indices also fell, especially clearly in the initial phase of the reaction (Figs. 1 and 2). However, the degree of fall of these indices of contractility was significantly less than dp/dt_{max} (on the average 13 and 25% of the initial level, respectively).

On the basis of changes discovered in the indices of myocardial contractility a decrease in the contractile power of the myocardium of the left ventricle could thus be diagnosed in response to intracoronary injection of anticardiac cytotoxic serum. The tendency toward recovery of the myocardial contractility indices evidently indicated the activation of compensatory mechanisms in the course of development of the reaction. Since the electrocardiographic and morphological findings indicated progressive injury to the heart muscle in the area of direct action of the anticardiac cytotoxic serum, it must be concluded that recovery of contractile power was due to strengthening of the function of the unaffected areas of the left ventricular myocardium. The possibility of responses of this type during local ischemic injury to the left ventricular myocardium has been demonstrated in several investigations [7, 9].

The development of shock during cytotoxic injury to the heart in most (10 of 12) experiments was accompanied by a decrease in the end diastolic blood volume in the left ventricle, which was statistically significantly lower than the initial values after 5, 15, and 30 min of the response (the mean decrease after 5 min was 4.7 ± 2.17 ml; $P < 0.05$).

The end systolic (residual) blood volume in the left ventricle changed variously: In seven experiments it fell (on the average by 6 ml) and in five it rose (on the average by 3.5 ml).

The ejection fraction was reduced after 15 and 60 min of the reaction, further evidence of a disturbance of the contractile power of the left ventricular myocardium and of the pumping function of the heart. The end diastolic pressure in the left ventricle remained unchanged or fell. The mean reduction in the end diastolic pressure at the beginning of the response was 1.05 ± 0.35 mm Hg ($P < 0.02$). The clearest decrease in indices of blood filling of the left ventricle during diastole was observed in the initial stage of the response (the first 5-15 min).

The structure of disturbances of the cardiodynamics during cytotoxic injury to the myocardium thus indicates that, despite weakening of the contractile power of the myocardium, no signs of congestive heart failure developed. The most probable cause of this unique character of development of cardiovascular failure is a decrease in the venous return to the heart. The possibility of retention of blood in the depots and a decrease in the venous return to the heart during the development of postinfarctive shock in man is based on clinical

observations [8, 14]. One of the important physiological consequences of a fall in the diastolic blood filling of the left ventricle is the fact that under these circumstances the basic mechanism of compensation of cardiac activity (the Frank–Starling mechanism) is impeded. This may aggravate the disturbances of the hemodynamics and blood supply to the heart and may lead to progression of the myocardial lesions caused by cytotoxic damage to the heart.

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ATHEROSCLEROSIS INDUCED IN RABBITS BY PROLONGED ELECTRICAL STIMULATION OF THE HYPOTHALAMUS

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UDC 616.13-004.6-092.9-02:616.831.41-001.2

The effect of prolonged electrical stimulation of emotiogenic zones of the hypothalamus in rabbits on their blood lipid level and the development of atherosclerosis was studied with the aid of a specially designed autonomous system. A negative emotional state observed during stimulation was accompanied by hyperlipemia and by the development of atherosclerosis in one third of uncastrated and two thirds of castrated animals.

KEY WORDS: *Electrical stimulation of the hypothalamus; emotions; lipids; atherosclerosis.*

During prolonged emotional stress induced by frequent interchange of a stereotype of higher nervous activity animals develop atherosclerosis without the addition of cholesterol to the diet [7]. The writers have previously studied the basic mechanisms of its development [8-10].

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(Presented by Academician of the Academy of Medical Sciences of the USSR P. N. Beselkin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 11, pp. 1294-1296, November, 1976. Original article submitted December 29, 1975.