Besides views on the general physiological hormone-modulating role of the polypeptide circulating in the blood [1], data have also been obtained to show that SP participates in the local regulation of the microcirculation and, in particular, in degranulation of mesenteric mast cells [2], reactions of inflammation and antidromic vasodilatation of the skin vessels [13], etc. In the case when regulation of the microhemodynamics is coupled with local, but well-marked changes in concentration of the mediator, it can be postulated that SP has a regulating effect on the activity of tissue or plasma ACE.

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# EFFECT OF INOTROPIC FACTORS ON POSTEXERCISE CHARACTERISTICS OF THE HEART


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UDC 612.173.4.014.46:[615.217.22 + 615.217.324

KEY WORDS: pumping function; postexercise characteristics; inotropic factors.


The pumping function of the heart, like that of any pump, is largely determined by its ability to overcome the load at the output and, as has been recently shown [2, 3] it can be described by means of postexercise or output characteristics, i.e., the relationship between intraventricular pressure and blood flow in the aorta during constant filling. There have been few investigations into the study of factors influencing postexercise curves. It has been shown that paired stimulation of the isolated cat's heart with a hydraulic model of the aorta [4] causes a rotation shift of the postexercise curve around the extrapolated value of the blood flow at zero pressure, thereby increasing the extrapolated value of the pressure at zero blood flow. Isoproterenol, as has been calculated on a model of the left ventricle (using the method of Fourier analysis of pressure and blood flow curves), increases whereas propanol reduces the extrapolated value of the blood flow at zero load [5].


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(Presented by Academician of the Academy of Medical Sciences of the USSR E. I. Chazov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 93, No. 6, pp 5-7, June, 1982. Original article submitted November 29, 1981.

0007-4888/82/9306-0695$07.50

TABLE 1. Parameters of Intracardiac Hemodynamics and of Exercise Characteristics of the Heart in Control Tests and under Inotropic Influences

| Experimental conditions | $P_M$, mm Hg | $Q_M$, ml/sec | $P_M/Q_M$, mm Hg/ml | $P_S$, mm Hg | $Q_S$, ml/sec | EDP, mm Hg | HR, beats/min | $dP/dt_{max}/P$, $sec^{-1}$ |
|---|---|---|---|---|---|---|---|---|
| Control | 249±13 | 39,0±3,3 | 6,85±0,82 | 126±4 | 19,0±0,9 | 2,9±0,5 | 176±9 | 71±9 |
| Adrenaline ($n$=8) | 285±13 | 55,7±3,7 | 5,33±0,48 | 164±7 | 23,3±0,9 | 3,6±0,9 | 174±8 | 99±12 |
| $P$ | <0,001 | <0,01 | <0,05 | <0,01 | <0,05 | >0,05 | >0,05 | <0,05 |
| Control | 216±9 | 41,8±2,3 | 5,82±0,60 | 115±6 | 19,2±1,6 | 4,3±1,0 | 173±4 | 64±8 |
| $CaCl_2$ ($n$=7) | 257±9 | 46,6±2,4 | 5,60±0,35 | 132±6 | 23,1±2,3 | 4,3±1,1 | 172±4 | 73±9 |
| $P$ | <0,01 | <0,05 | >0,05 | <0,001 | <0,01 | >0,05 | >0,05 | <0,05 |
| Control | 245±19 | 43,2±3,5 | 5,95±0,74 | 122±3 | 21,6±2,3 | 5,1±0,9 | 155±8 | 69±8 |
| Obsidan ($n$=7) | 169±16 | 33,5±3,7 | 5,63±1,03 | 91±2 | 15,4±1,8 | 5,5±1,1 | 120±11 | 40±6 |
| $P$ | <0,001 | <0,01 | >0,05 | <0,001 | <0,01 | >0,05 | <0,01 | <0,05 |

Legend. $P_S$) Systolic pressure with normal load; $Q_S$) maximal velocity with normal load.

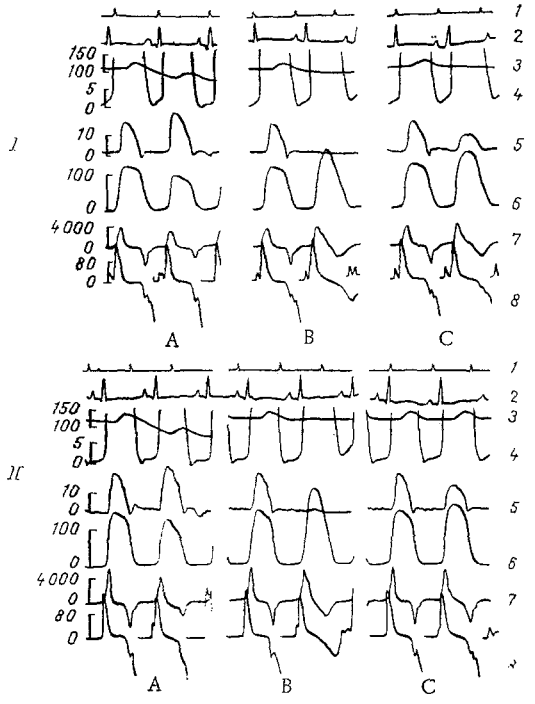


Fig. 1. Changes in hemodynamic parameters during a reduction (A) or an increase (B, C) in the load against which the left vertricle worked. B) Complete, C) partial compression of aorta. I) Control, II) injection of adrenaline. 1) Time marker, 250 msec, 2) ECG in standard lead II, 3) intra-aortic pressure, 4) intraventricular diastolic pressure, 5) velocity of blood flow in aorta, 6) intraventricular systolic pressure, 7) first derivative of intraventricular pressure relative to time, 8) ratio of first derivative to pressure at the same moment.

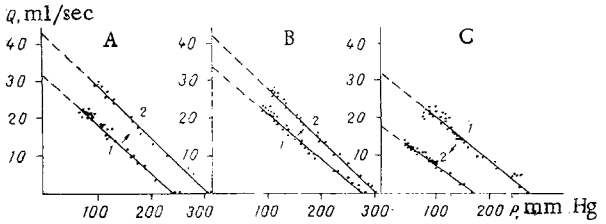


Fig. 2. Relationship between systolic pressure in left ventricle (P) and maximal velocity of blood flow in aorta (Q) in control (1) and under the influence of various factors (II).

The aim of this investigation was to determine the shape and position tion characteristics of the intact heart during exposure to various inotro

## EXPERIMENTAL METHOD

Experiments were carried out on 14 cats anesthetized with urethane (600 mg/kg) and chloralose (40 mg/kg) under open chest conditions with artificial ventilation of the lungs and heparinization. A double catheter was introduced through the apex of the left ventricle: One lumen was used to measure blood pressure (Siemens-Elema 746 pressure transducer, Sweden), the other served for injection of the drugs. In the course of the experiments the following parameters were recorded on the Mingograph-82 instrument (Siemens-Elema), with attachments: intra-aortic pressure (catheterization through the femoral artery), systolic and diastolic pressure in the left ventricle (catheter introduced through the apex of the left ventricle), the first derivative of the intraventricular pressure relative to time (dp/dt), the ratio of the first derivative to the pressure at that same moment (dp/dt/P), and ECG in the equivalent of standard lead II. The velocity of the blood flow in the aorta was recorded by means of externally applied transducers of the MF-5 electromagnetic flow meter (Nihon Kohden, Japan). To construct postexercise curves, i.e., curves of dependence of systolic pressure in the left ventricle and maximal velocity of blood flow in the aorta with constant filling, the load against which the left ventricle worked was altered for a short time [2]. An increase in the load on the left ventricle was produced by partial or complete compression of the aorta during one contraction by means of a ligature passed beneath the aorta distally to the blood flow transducer. The load was reduced by lowering the pressure in the aorta by means of a pneumatic valve device and cardiosynchronizer. For this purpose, a catheter (3-4 cm long, 2-3 mm in diameter) was inserted through the brachiocephalic or subclavian artery into the arch of the aorta. The electromagnetic valve enabled the vessel with lowered pressure to be connected to the catheter for one contraction (0.2-0.3 sec), and this caused a transient fall of pressure in the aorta. The signal was sent to the valve synchronously with the R wave on the ECG by means of the cardiosynchronizer. Output characteristics in the control and during exposure to the various factors were plotted from the results of 20-40 contractions with modified load. To change the inotropic state of the heart adrenaline (3 mg/kg/min) and $CaCl_2$ (10 mg/kg/min) were injected into the heart in the course of 3-5 min. Obsidan (30 mg/kg/min) was injected intravenously. The experimental results were subjected to statistical analysis by polynomial regression methods in order to determine the shape of the postexercise curves [1].

## EXPERIMENTAL RESULTS

Examples of hemodynamic parameters recorded during a change in load against which the left ventricle worked, under normal conditions and after injection of adrenaline, are shown in Fig. 1. In all the columns of Fig. 1 the first contraction is the control, the second the one with a modified load. The action of adrenaline in this experiment was characterized by elevation of the systolic pressure from 131 to 164 mm Hg, an increase in the maximal velocity of the blood flow in systole from 18.0 to 20.6 ml/sec, and also by an increase in the first derivative of pressure with respect to time and of Veragut's index (dp/dt/P) from 3670 and 37 to 67,000 mm Hg/sec and 45 $sec^{-1}$, respectively. The end-diastolic pressure (EDP) and the heart rate (HR) were unchanged (1.8 mm Hg, 200 beats/min). The dose of adrenaline used thus had a marked positive inotropic effect, but virtually no effect on filling of the heart.

Against the background of the action of adrenaline, just as under normal conditions, the load on the left ventricle was changed. Postexercise curves of the left ventricle plotted from the data of analogous experiments under normal conditions and after injection of adrenaline, $CaCl_2$, and obsidan are shown in Fig. 2. The broken line is obtained by extrapolating the experimentally obtained postexercise curve (continuous line). On average the systolic pressure was reduced to 60-75% of the normal values or to 20-35% of the maximal pressure developed after complete compression of the aorta, i.e., the characteristic curve could be plotted over a fairly wide range. Mathematical analysis of the results of these and other experiments showed that in most cases (36 of 44) the highest guaranteed accuracy (the lowest guaranteed risk value) for an adopted level of reliability of 0.95 was obtained by a linear function, and only in 8 cases in a quadratic function (4 cases under normal conditions, 3 with injection of calcium, 1 with injection of adrenaline). Deviations of the extrapolated values of pressure and blood flow by the quadratic function from corresponding values of the linear approximation did not exceed 10% on average. Incidentally, in [3, 4] it was concluded that the output characteristic curve recorded in terms of the average intraventricular pressure for the cycle and the mean velocity of the intra-aortic blood flow for the cycle are convex in shape. This difference from our own data can perhaps be explained by the choice of coordinates of output characteristics.

Under the influence of positive inotropic factors (adrenaline, $CaCl_2$) the postexercise curves were shifted upward and to the right. The mean values of parameters of the output characteristics and some parameters of the hemodynamics under normal conditions and during exposure to the factors are given in Table 1. Under the influence of adrenaline $Q_M$ (the extrapolated value of the velocity of the blood flow to zero pressure, or the velocity component) increased on average by 48%, whereas $P_M$ (maximal pressure at zero blood flow, or the force component) increased by only 15%. Since $Q_M$ increased much more than $P_M$, the angle of slope of the postexercise characteristic curve relative to the blood flow axis changed: the tangent of this angle, equal to the ratio $P_M/Q_M$, decreased significantly (Table 1).

Calcium increased $P_M$ and $Q_M$ practically equally (on average by 20 and 12%, respectively). The angle of slope of the postexercise characteristic curve to the blood flow axis showed no significant change. The action of $CaCl_2$, like that of adrenaline, was not accompanied by significant changes in the heart rate or EDP. That is why the decrease in the angle of slope of the output characteristic curve relative to the blood flow axis during administration of adrenaline was probably due to the specific character of action of catecholamines on the myocardium.

Obsidan shifted the postexercise curve downward and to the left, reducing $P_M$ and $Q_M$ on average by 26 and 16%. Obsidan caused a significant reduction in HR. To differentiate between the effects of obsidan and a low heart rate on the exercise curves, in three experiments in which obsidan was injected HR was maintained constant by electrical stimulation of the right auricle with square pulses 4-6 V in amplitude and 1-2 msec in duration. While the heart rate was kept constant the postexercise curves, just as in the absence of stimulation, were shifted downward and to the left, and $P_M$ and $Q_M$ were reduced by 28.6 and 20.6%, respectively. Consequently, the action of obsidan on postexercise curves was not associated with any change in rhythm.

The existence of a falling postexercise curve of the left ventricle thus confirms the conceptual model which represents the ventricle as a hydraulic source with finite internal resistance. The postexercise characteristic curve, which can be expressed in terms of maximal values of intraventricular pressure and blood flow velocity under normal conditions and during exposure of the heart to inotropic influences, is close to linear.

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