POTENTIATION OF HUMAN MYOCARDIAL CONTRACTILITY BY BLOOD SERUM

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Since the classical investigations of Ringer [13] it has been known that if normal salt solution is replaced by frog blood serum, contractions of the frog heart, if depressed during a long experiment, are potentiated [14, 15]. Similar effects are observed in experiments on isolated fragments of myocardium from warm-blooded animals, if the perfusing salt solution is replaced by blood serum from animals of the same species [4, 11, 12]. This positive inotropic effect of blood serum and plasma has been shown not to be connected with the presence of catecholamines in them [4, 11, 12]. The myocardium of patients with rheumatic heart disease undergoes functional changes in the course of a long illness and it differs from the normal myocardium of warm-blooded animals in its reaction to a change in the ionic composition of the medium [1, 5] and its reaction to certain cardiotropic drugs [2, 3, 5]. The study of the direct action of blood serum from healthy donors is thus important both to reveal the cellular mechanisms of its action and also to determine whether the disturbed myocardial contractility of patients with heart defects can be restored.

The aim of this investigation was to study the inotropic effect of blood serum from healthy donors on contractility of isolated myocardial fragments from patients with congenital and acquired heart defects.

EXPERIMENTAL METHOD

The investigation was conducted on trabeculae from the auricle of the right atrium, taken during open heart operations before connection to the assisted circulation apparatus (ACA). As a rule, during such operations the venous blood is returned to the ACA through a cannula introduced in the right atrium through the auricle (in this case part of the auricle is removed). The removed part of the auricle was immersed in nutrient medium No. 199, oxygenated with carbogen (95% O_2 + 5% CO_2) and sent to the Laboratory in a container. The method of isolation of the myocardial trabeculae and of recording isometric contractions was described previously [1, 2]. Serum (10 ml) was oxygenated for 10 min with carbogen and the pH and PCA were measured by means of ion-selective electrodes (from Radiometer, Denmark). Tyrode solution (composition in mM: NaCl — 131, KCl — 4.5, $NaHCO_3$ — 11.0, NaH_2PO_4 — 0.6, $MgCl_2$ — 0.5, $CaCl_2$ — 2.0, glucose — 11.0, pH 7.2-7.3) was added to the serum in a dilution of 1:1. The scheme of the experiment was as follows: the myocardial preparations were stimulated for 60-90 min with above-threshold square pulses with a frequency of 0.5 Hz and perfused with Tyrode solution at 30-32°C. During this time the amplitude of contractions of the myocardial trabeculae reached a certain value, after which it did not change with time. During successive changes of the frequency of stimulation 0.1-0.2-0.3-0.5-1.0-1.25-1.5-2.0 Hz contractions were recorded (control). The amplitude of contractions at each frequency of stimulation flattened out at a stable level. The Tyrode solution in the perfusion system was then replaced by serum. The oxygenation temperature and tension of the myocardial preparation were the same as in Tyrode solution. The preparation was perfused with serum for 20 min with a frequency of 0.5 Hz, after which the amplitude of contractions was measured during stimulation at the same frequencies as were used in the control. At the end of the experiment the myocardial preparation was rinsed for 30 min with Tyrode solution.

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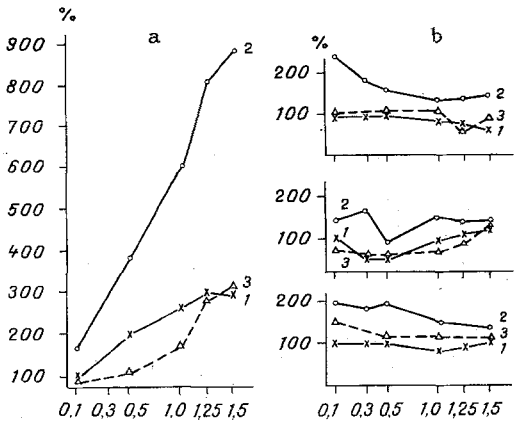

Fig. 1. Frequency–strength curves for atrial trabeculae of patients with congenital (a) and acquired (b) heart defects. 1) Tyrode solution; 2) human blood serum (dilution 1:1); 3) rinsing with Tyrode solution. Abscissa, frequency of stimulation (in Hz); ordinate, amplitude of contractions (in percent); amplitude of contractions at 0.1 Hz taken as 100%.

TABLE 1. Changes in Amplitude of Evoked Contractions of Myocardial Fragment from Patients with Congenital and Acquired Heart Defects under the Influence of Healthy Human Blood Serum (ΔM ± m)

Heart defect	Frequency of stimulation, Hz				
	0,1	0,5	1,0	1,25	1,5
Congenital	86,7±38,9	111,1±54,05	80,5±40,12	52,88±29,5	44,42±36,9
(7)	(7)	(6)	(7)	(6)	(6)
P	<0,05	<0,05	<0,05	<0,05	>0,05
Acquired	133,64±53,2	136,4±32,72	123,12±32,72	74,9±26,22	41,2±29,32
(8)	(8)	(8)	(8)	(4)	(7)
P	<0,01	<0,05	<0,01	<0,01	>0,05

Legend. ΔM) Increase in amplitude of contraction under the influence of serum compared with contraction in Tyrode solution at same frequency of stimulation (100%). Number of measurements shown in parentheses.

EXPERIMENTAL RESULTS

Typical frequency–strength curves, recorded in separate experiments on isolated myocardial preparations taken from the heart of patients with congenital (Fig. 1a) and acquired (Fig. 1b) heart defects, are illustrated in Fig. 1. As the frequency of stimulation was increased from 0.1 to 1.5 Hz the amplitude of contractions of the myocardial preparation from a patient with congenital heart disease rose steadily. By contrast, the amplitude of contractions of the myocardial preparations from patients with acquired heart defects, during stimulation with a frequency of 1.5 Hz, either did not exceed the amplitude of contractions during stimulation with a frequency of 0.1 Hz, and sometimes it was actually even lower, or despite the apparent increase between the frequencies of 0.5 and 1.5 Hz, during stimulation with a frequency of 1.5 Hz it was only a little greater than the amplitude corresponding to a frequency of stimulation of 0.1 Hz (100%). Thus in experiment 2, illustrated in Fig. 1b, the amplitude of contraction of the preparation in Tyrode solution during stimulation with a frequency of 1.5 Hz was 15% higher than initially.

Blood serum from healthy donors (dilution 1:1) increased the amplitude of contractions of myocardial preparations from patients with both congenital and acquired heart defects. The character of the frequency–strength curves, moreover, was unchanged by serum. The increase in amplitude of contractions of myocardial preparations due to serum for both types of defect is illustrated in Table 1. The increase clearly occurred at all frequencies of stimulation. It reached a maximum at a frequency of 0.5 Hz. At higher frequencies of stimulation the positive inotropic action of the serum was reduced.

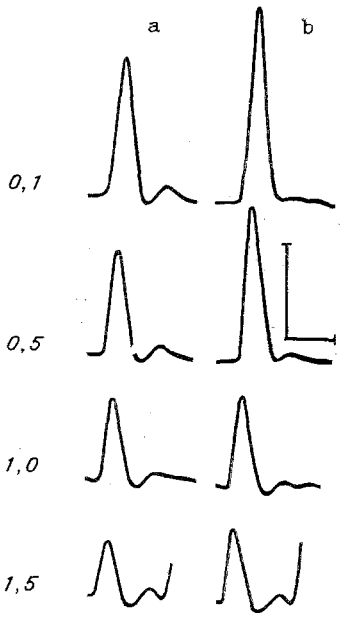

Fig. 2. Increase of contractions and depression of after-contractions of myocardial preparation from a patient with acquired heart defect under the influence of blood serum from a healthy donor (dilution 1:1). a) Tyrode solution; b) healthy human blood serum diluted with Tyrode solution. Numbers give frequency of stimulation of trabeculae.

Besides the different character of the frequency-strength curves, the myocardium of patients with congenital and acquired heart defects also differed in that, besides the basic contractions, additional after-contractions also developed in myocardial preparations of patients with acquired defects during repetitive stimulation, and their tone increased. As was shown previously [3], this is evidence of a disturbance of calcium homeostasis in the myocardial cells during the contraction-relaxation cycle. The distinguishing features of the action of serum on the myocardium of patients with acquired heart defects were that the increase in amplitude of the principal contractions, induced by serum, was accompanied by a decrease in amplitude of the after-contractions (Fig. 2). The decrease in amplitude of the after-contractions under the influence of serum was particularly marked at frequencies of 0.1 and 0.5 Hz. Serum also lowered the muscle tone (not shown in Fig. 2).

Healthy human blood serum thus causes the development of a positive inotropic effect in the myocardium of patients with congenital and acquired heart defects. The action of serum is exhibited in 100% of cases. Remembering that the myocardium of patients with acquired heart defects in some cases has reduced sensitivity to catecholamines and cardiac glycosides [3, 5], and that the sensitivity of the contractile proteins of the myocardium of patients of this group is an order of magnitude less than that of patients with acquired heart defects [6], the results confirm that blood and its components may be used with advantage as the basis of cardioplegic solutions [7] for open heart operations.

The descending type of frequency—strength curves, the after-contractions, and tone recorded in the myocardium of patients with acquired heart defects, are evidence that in rheumatic heart disease the transport systems of cardiac cells, responsible for the maintenance of calcium homeostatis during the contraction—relaxation cycle, are disturbed. Reduction of the after-contractions and tone, induced by blood serum, indicates that serum normalizes calcium homeostasis in the cells of the pathologically changed patients' myocardium.

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EFFECT OF AN ASSISTED CIRCULATION ON THE STATE OF THE ERYTHROCYTES AND MICROCIRCULATION

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An important cause of hypoxia arising during an assisted circulation (AC) is a disturbance of the microcirculation (MC) [2]. Meanwhile the damaging action of AC on erythrocytes is well known [1, 3].

The aim of the investigation described below was to study the character of the blood flow in the mesentery of the small intestine, morphology of the erythrocytes, and their ability to aggregate in arterial and venous blood during the course of an assisted circulation in order to establish the role of the changes in the state of the erythrocytes in the disturbance of MC.

EXPERIMENTAL METHOD

Experiments were carried out on 12 mongrel dogs weighing 14-42 kg. After premedication with trimeperidine intravenous pentobarbital (30 mg/kg) and endotracheal ether-oxygen anesthesia were used, supplemented by neuroleptanalgesia during perfusion. Hypothermic perfusion was carried out by means of the AIK-5M apparatus, with a countercurrent foam-film oxygenator for 3 h. The apparatus was filled with fresh donors' blood. The hemodilution was 25-30%. The volume velocity of perfusion was maintained at 2.4-2.6 liters/m^2/min. The MC in the mesentric vessels was examined intravitally by means of an apparatus mounted on the MBR-1 microscope and MFN-12 photographic attachment. Blood for investigation was taken from the femoral artery and vein. Morphological changes in the erythrocytes and their ability to aggregate were assessed by means of the phase-contrast system of the MBI-15 microscope. The usual method was used for electron-microscopic study of the erythrocytes. Ultrathin sections were ex-

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