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ELECTROMECHANICAL COUPLING DISTURBANCES IN MYOCARDIAL CELLS IN THE COMPRESSION SYNDROME

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The compression syndrome (CS) is accompanied by a marked decrease in cardiac output [2]. Marked changes have been demonstrated in electrical activity of the heart [5, 6] and a decrease in its contractility in CS [3]. According to one view, insufficiency of the cardiovascular system in CS is due to the toxic properties of the plasma [4, 5]. However, no direct investigations into the action of plasma on myocardial cell function have yet been undertaken.

The aim of this investigation was to study the action of plasma from rabbits with CS on myocardial electrical and contractile activity. The methods used were developed by the writers previously in order to study the action of "burn" plasma, isolated from the blood of animals exposed to burn trauma, on the myocardial cells [1].

EXPERIMENTAL METHOD

Intracellular transmembrane resting (RP) and action (AP) potentials and mechanical contractions in response to electrical stimulation of the capillary muscles of the heart were investigated in 17 rabbits: six preparations were taken from healthy rabbits, 11 from rabbits with CS. CS was induced by compression (90 kg) of the soft tissues of the thigh for 12 h. Blood and hearts from rabbits with CS were taken 1.5 h after decompression under urethane anesthesia (1 g/kg). The papillary muscles were isolated from the right ventricle. Isolation of the muscles, their arrangement in the working chamber, the conditions of stimulation, the method of obtaining blood plasma, details of the apparatus and composition of the Tyrode solution were all described previously. Contractions of the preparations were recorded during the experiments in response to stimulation at frequencies of 0.1, 0.2, 0.5, 1, and 2 Hz successively, and intracellular potentials of single myocardial fibers were recorded in response to stimulation at 1 Hz: 1) in Tyrode solution, 2) after replacement of the Tyrode solution by blood plasma from control (healthy) rabbits, 3) after replacement of normal plasma by blood plasma from animals with CS, and 4) after removal of the CS plasma and reperfusion with plasma from control animals. The plasma was diluted 1 : 1 with Tyrode solution. To prevent frothing of the plasma during oxygenation, "antifoam" was used.

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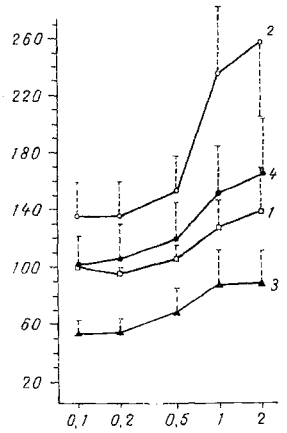

Fig. 1

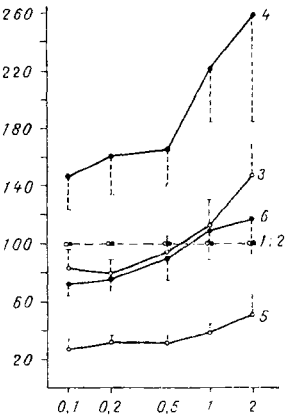

Fig. 2

Fig. 1. Action of plasma from control rabbits and from rabbits with CS on frequency–force relations in papillary muscles of the heart. 1) Tyrode solution, 2) control plasma, 3) after replacement of control plasma by CS plasma, 4) after replacement of CS plasma by control plasma. Abscissa (here and in Fig. 2), frequency of stimulation (in Hz, logarithmic scale); ordinate, amplitude of contractions (in %, amplitude of contractions at a stimulation frequency of 0.1 Hz in Tyrode solution taken as 100%).

Fig. 2. Relative changes in amplitude of contractions of papillary muscles of control rabbits and rabbits with CS under the influence of control and CS plasma. 1, 3, 5) Papillary muscles of control rabbits; 2, 4, 6) papillary muscles of rabbits with CS; 1, 2) Tyrode solution, 3, 4) control plasma, 5, 6) CS plasma. Ordinate, amplitude of contractions (in %, amplitude of contractions at each frequency in Tyrode solution taken as 100%).

EXPERIMENTAL RESULTS

The action of plasma from the control rabbits and the rabbits with CS on contractions of the papillary muscles of the heart (17 experiments) is compared in Fig. 1. At all frequencies of stimulation (from 0.1 to 2 Hz) the control plasma increased the amplitude of contractions of the myocardial preparations compared with their amplitudes in Tyrode solution (Fig. 1, curves 1 and 2). The positive inotropic effect of the control plasma was particularly marked at frequencies of stimulation of 1 and 2 Hz. Replacement of the control plasma by plasma from rabbits with CS (CS plasma) caused a marked reduction in amplitude of contractions at all frequencies of stimulation. Nevertheless, the shape of the frequency–force curve (curve 3) was unchanged: Dependence of the amplitude of contraction on stimulation frequency was ascending in character. After the CS plasma had been replaced by control plasma, the amplitude of the contractions increased at all frequencies of stimulation (curve 4).

Of the 17 muscles tested six were taken from normal rabbits and 11 from rabbits with CS. There was no difference in the character of response of the two sets of preparations to control and CS plasma: Control plasma strengthened but CS plasma weakened contractions. However, complicated differences were found in the action of the control plasma: Contractions of preparations from animals with CS were strengthened by control plasma by a greater degree than contractions of preparations from normal animals. Changes in the amplitude of contractions of both types of myocardial preparations in response to the action of control and CS plasma are shown as percentages in Fig. 2. The amplitude of contractions at each frequency in Tyrode solution was taken as 100%. It will be clear from Fig. 2 that the amplitude of contractions of preparations from animals with CS under the influence of control plasma was far greater at all frequencies of stimulation (curve 4) than the amplitude of contractions of normal preparations (curve 3). The increase in amplitude of contractions of preparations from animals with CS at frequencies of stimulation of 1 and 2 Hz under the influence of control plasma was approximately twice that of the control preparations. Replacement of control plasma by CS plasma led to marked depression of the amplitude of contractions both of the

TABLE 1. Action of Plasma from Control Rabbits and Rabbits with CS on Intracellular RP and AP of Papillary Muscles

Solution	Changes of first type					Changes of second type				
	RP, mV	AP, mV	duration of AP, msec at undermentioned level of repolarization			RP, mV	AP, mV	duration of AP, msec at undermentioned level of repolarization		
			20 %	50 %	80 %			20 %	50 %	80 %
Tyrode	79±6,9	119±8,9	67±14,9	143±26,4	221±39,9	78±6,6	105±6,4	41±12,7	94±12,1	147±4,0
Tyrode + control plasma	79±5,8	109±5,8	59±6,9	106±13,5	161±27,1	78±4,8	97±1,4	54±5,9	97±14,7	144±6,5
Tyrode + CS plasma	79±2,6	112±4,3	91±15,4	154±27,2	197±37,3	72±7,2	75±7,3	29±10,7	46±13,4	68±15,5

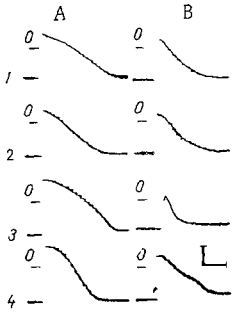

Fig. 3. Changes in intracellular potentials of cardiomyocytes under the influence of control and CS plasma. A) Changes of first type, B) of second type. 1) Tyrode solution, 2) control plasma, 3) CS plasma, 4) replacement of CS plasma by control plasma. Horizontal line on left of each frame is potential zero line (isoelectric line). Calibration: 50 mV, 100 msec.

normal preparations and of those from animals with CS. However, the ratio of the amplitude of contractions of preparations from animals with CS to that of contractions in Tyrode solution remained higher than the corresponding ratio for the amplitude of contractions of normal muscles (curves 5 and 6).

To study the nature of changes in myocardial contractility under the influence of the control and CS plasma, along with contractions of the preparations, intracellular potentials of single heart fibers were recorded in seven experiments. RP and AP were measured in 22 cells in Tyrode solution, in 22 cells in control plasma, in 62 cells during perfusion with plasma from animals with CS, and in 19 cells during reperfusion with control plasma. At a stimulation frequency of 1 Hz the mean amplitude of RP in Tyrode solution was 78 ± 3.6 mV. Replacement of the Tyrode solution by control plasma caused no significant change in RP, which was 78 ± 3.4 mV. The very small decrease in the amplitude of AP and shortening of its duration were recorded at 50% and 80% levels of repolarization (Table 1). After the change from perfusion with control plasma to perfusion with CS plasma two types of changes in the intracellular AP were discovered. Examples of these changes are given in Fig. 3. In the first case (four experiments) a marked increase was observed in the duration of AP (Fig. 3A). The duration of AP, measured at 20, 50, and 80% repolarization levels was significantly greater than in control plasma (Table 1). An increase in the duration of AP under the influence of CS plasma was not accompanied by any significant changes in their amplitude, nor was there any change in the amplitude of the RP in this case. Replacement of plasma from animals with CS by control plasma again led to shortening of AP (Fig. 3A). Changes of the second type in AP under the influence of CS plasma are illustrated in Fig. 3B. In this case there was a marked decrease in their amplitude and duration. RP under these circumstances fell from 78 ± 4.8 mV in control plasma to 72 ± 7.2 mV in CS plasma. Replacing the CS plasma by control restored the amplitude of AP and increased its duration, whereas RP returned to its initial values under these conditions (Fig. 3B). No differences were found in the action of control and CS plasma on intracellular potentials of normal preparations and of preparations from animals with CS: In most cases control plasma shortened the duration of AP without changing their amplitude and had no effect on RP, whereas CS plasma increased the duration of AP without changing their amplitude or it reduced the amplitude of AP and shortened their duration in both types of preparations.

The investigation thus showed that blood plasma from rabbits with CS in 100% of cases inhibits contractility of the papillary muscles of the heart both in normal animals and in animals subjected to a compression syndrome for 12 h. A reduction in the amplitude of con-

tractions occurred at all tested frequencies of myocardial stimulation. In some cases the negative inotropic action of the CS plasma was associated with a lowered RP, but AP were more like gradual responses: Their amplitude was significantly lowered and their duration shortened. Very probably this was due to a change in the ionic composition of the plasma, for the sodium ion concentration in CS plasma (three experiments) was 10-20 mM lower than in control plasma and the potassium ion concentration in these experiments was 1.5-2 times higher. In other preparations depression of the contractions was not accompanied by any substantial changes in the value of RP or in the amplitude of AP but, on the other hand, the duration of AP was increased in these experiments.

No direct correlation could thus be found between the fall in amplitude of contractions of the myocardial preparations under the influence of CS plasma and changes in the size of RP and the amplitude and duration of AP. The negative inotropic action of CS plasma developed even in cases when there was no change in the size of RP or the amplitude of AP. It can accordingly be concluded that inhibition of contractions of the myocardial preparations was not the direct result of changes in electrical activity. CS plasma evidently disturbs the normal coupling of excitation with contraction in the papillary muscles of the heart. A similar situation was observed previously in a study of the action of "burn" plasma on electrical and contractile activity of the papillary muscles of the rabbit heart [1]. Similar changes in electrical and contractile activity of the papillary muscles of the cat heart in the late stages of hemorrhagic shock were observed by other workers [9]. It can be postulated that inhibition of myocardial contractile function by CS plasma is one cause of the disturbance of the cardiac output in CS.

Like burns, CS is one kind of shock state. In some shock states (burn, cardiogenic, and hemorrhagic shock) special myocardial depressor factors (MDF) appear in the blood [8-10]. Changes in electrical and contractile activity in the myocardial cells under the influence of CS plasma, observed in the present experiments, may perhaps also be caused by MDF. However, the question of the nature of this factor and whether or not it is identical with the toxic factor found, for example, in burn shock [6, 8], requires further study.

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