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CHANGES IN CONTRACTILE ACTIVITY OF THE RABBIT MYOCARDIUM AS A RESULT OF BURN SHOCK OF VARIED DURATION

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Experiments were carried out on papillary muscles isolated from the rabbit heart 10, 60, or 180 min after thermal injury to the animal. Isometric contractions were recorded during stimulation of the preparation at changing frequencies (within the range from 0.1 to 2 Hz) and during poststimulation potentiation. The degree of disturbance of myocardial contractility as a result of burns was found to increase with an increase in the duration of burn shock: In all the papillary muscles isolated 3 h after burning and in 50% of those isolated 1 h after burning the "biphasic" frequency—strength (f—P) relationship characteristic of the normal myocardium was converted into "monophasic" (the amplitude of the contractions decreased progressively with an increase in frequency) and poststimulation potentiation, normally absent, appeared. After shock lasting 10 min, poststimulation potentiation was observed only in some preparations and no change in f—P was present. The normal inotropic relationships of the myocardial rhythm were restored after a twofold increase in $[Ca^{++}]_o$ or after prolonged (3-4 h) perfusion of the preparation with normal Tyrode solution. Changes in inotropic relationships of the myocardial rhythm in burn shock were similar to the changes in f—P observed after blockade of the calcium channels with compound D-600.

KEY WORDS: burn shock; contractile activity of the myocardium; frequency—strength dependence.

The study of the causes of the decrease in cardiac output in response to thermal injury has recently attracted increasingly wide attention. By studying changes in the contractility of the heart in the intact organism several workers have obtained indirect evidence of the development of insufficiency of the heart muscles during burns [2-5]. Myocardial depressants have been found in some investigations in the blood serum of burned animals and patients [6, 8, 11]. To obtain direct proof of the effect of thermal trauma on the myocardium, the present writers previously studied the contractile activity of isolated fragments of myocardium taken from the heart of rabbits 1 h after burn trauma [1]. These experiments showed that myocardial contractility was disturbed in 50% of the preparations. The disturbance was of the type that the normal "biphasic" dependence of the strength of myocardial contractions on the frequency of stimulation was converted into "monophasic" (within the frequency range 0.1 to 2 Hz).

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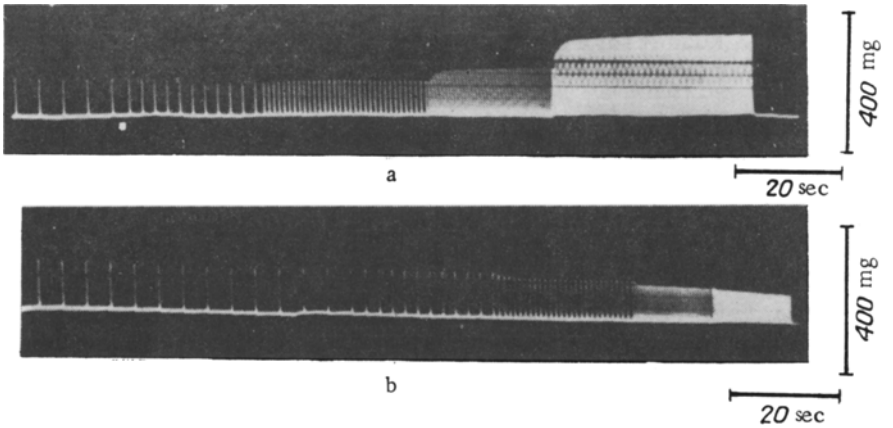

Fig. 1. Changes in isometric contractions of rabbit papillary muscle during repetitive stimulation at frequency varying in the order 0.1 — 0.2 — 0.5 — 1 — 2 Hz. a) Control; b) burns.

The object of the present investigation was to study the contractile properties of isolated fragments of ventricular myocardium taken from the rabbit heart at different times after thermal trauma.

EXPERIMENTAL METHOD

In all the experiments, preparations of the ventricle (papillary muscles) of the rabbit heart were used as the test object. At various intervals (10, 60, or 180 min) after burning, thoracotomy was performed on the rabbits and the heart was removed and placed in oxygenated Tyrode solution [1, 3]. A papillary muscle (diameter 1-2 mm, length 3-4 mm) was then quickly isolated from the right ventricle and placed in a perfusion chamber through which flowed Tyrode solution of the following composition (in mM: NaCl 136.9, KCl 2.68, $NaHCO_3$ 11.95, $NaH_2PO_4 \cdot 2H_2O$ 0.42, $CaCl_2 \cdot 2H_2O$ 1.8, glucose 5.6), saturated with carbogen (95% O_2, 5% CO_2), at 34-35°C. For 30 min before the beginning of the investigation the preparation was stimulated with supraliminal pulses with a duration of 5-10 msec.

To investigate the frequency—strength (f—P) dependence the strength of isometric contractions of the preparation in response to repetitive stimulation was recorded. The frequency of stimulation was varied stepwise in the order: 0.1 — 0.2 — 0.5 — 1 — 2 Hz; the number of pulses in the volley for each frequency was chosen so that the amplitude of contractions reached the steady-state level. Strict maintenance of the interval between stimulating pulses during the switch from one frequency to another was ensured by the use of programmed stimulation.

To investigate the phenomenon of poststimulation potentiation (PSP) the amplitude of the contraction arising in response to a testing pulse, applied at a definite prime interval after the end of a series of 30 to 40 conditioning stimuli with a frequency of 1 Hz, was studied. The delay time of the testing pulse varied from 0.5 to 180 sec. All contractions of the preparations were recorded isometrically by means of the 6MKhIS mechanotron.

EXPERIMENTAL RESULTS

In the experiments (25) of the control group the relationship between the frequency of stimulation of the preparations and the strength of their isometric contractions at the steady-state level was biphasic in character (Fig. 1a). The first phase of the curve, as Fig. 2a shows, corresponds to a very small decrease in amplitude of the contractions accompanying an increase in the frequency of stimulation from 0.1 to 0.2 Hz; the second phase consists of an increase in amplitude of the contractions in response to an increase in the frequency of stimulation from 0.2 to 2 Hz. This type of dependence of the strength of contraction on the frequency of stimulation is characteristic of the normal myocardium of warm-blooded animals and man [7, 9, 10].

Preparations from burned animals (30 experiments) were investigated in groups of 8-15 experiments in which the duration of burn shock was 10, 60, or 180 min. In papillary muscles isolated 10 min after thermal trauma to the animal, the dependence of the amplitude of the contractile response on frequency of repetitive stimulation remained biphasic, as in the control (Fig. 2b). After burn shock for a period of about 1 h, the frequency—strength depend-

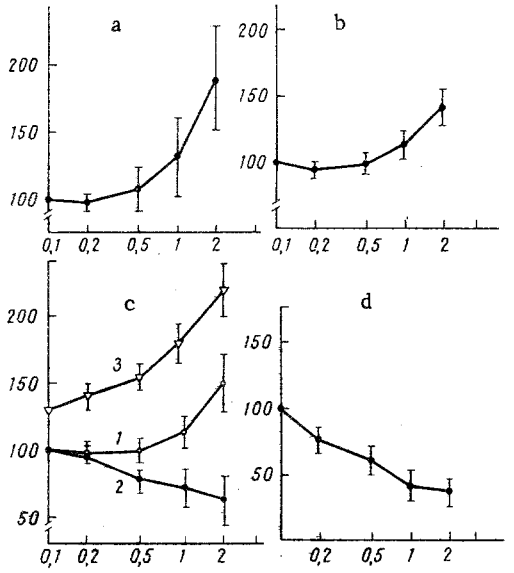

Fig. 2. Dependence of strength of isometric contractions of papillary muscle isolated from rabbit heart on frequency of stimulation. Abscissa: frequency of stimulation (in Hz); ordinate: strength of isometric contraction (in percent of initial level at 0.1 Hz). a) Control (n = 25); b) 10 min after burning (n = 7); c) 1 h after burning: 1) n = 7, 2) n = 7, 3) n = 6, Ca^{++}; d) 3 h after burning (n = 9).

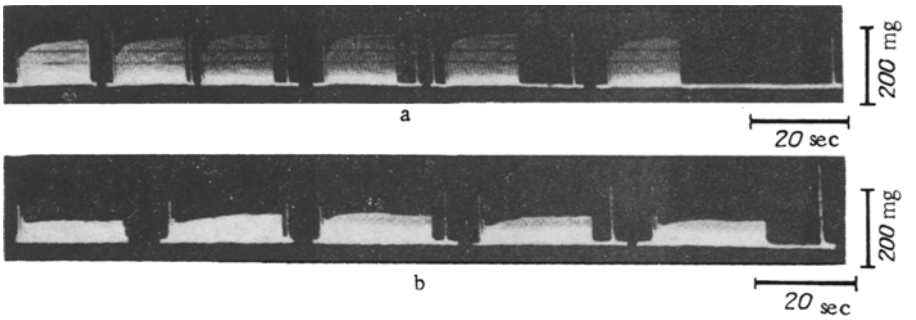

Fig. 3. Poststimulation potentiation on rabbit papillary muscle. Frequency of conditioning stimulation 1 Hz. a) Control, delay time of testing pulse: 0.5, 2, 5, 8, 15, and 60 sec; b) burns, delay time of testing pulse: 0.5, 2, 5, 8, and 15 sec.

ence was biphasic for only 50% of the preparations tested (Fig. 2c) and in the other experiments an increase in the frequency of stimulating pulses from 0.1 to 2 Hz led to a progressive decrease in the amplitude of contractions (Fig. 1b), as reflected in the "monophasic" f—P curve illustrated in Fig. 2c. In all papillary muscles isolated 3 h after burning the frequency—strength dependence was monophasic and the amplitude of contractions at a frequency of 2 Hz was reduced by 50-70% compared with the initial amplitude measured at 0.1 Hz.

It was interesting to study whether the "monophasic" relationship between frequency and strength of myocardial contraction in burned rabbits would change under the influence of an increase in the external Ca^{++} ion concentration. As Fig. 2c shows, a twofold increase in the external Ca^{++} concentration led to conversion of the monophasic dependence into biphasic (six experiments). In some experiments the reversibility of the changes in the contractile properties of the myocardium was studied in the burned animal. For this purpose the effect of prolonged perfusion of the preparations with normal Tyrode solution was examined. Experiments showed that perfusion of the preparation for 3-4 h led to restoration of the biphasic relationship between frequency of stimulation and strength of contractions of the preparation (five experiments).

Special attention was paid to the study of poststimulation potentiation of the contractions. In the papillary muscles of the animals of the control group the amplitude of contractions during repetitive stimulation at a frequency of 1 Hz increased and stabilized at a constant level. The response to testing stimulation applied 0.5-180 sec after the end of the

volley of conditioning stimuli differed only a little from the amplitude of the last contraction in the repetitive series (Fig. 3a). A different picture was obtained in experiments on the papillary muscle of the burned rabbits. In this case, during repetitive stimulation of the preparation the amplitude of contraction decreased, but after the end of repetitive stimulation it increased, and the longer the interval between the last pulse and the testing stimulation the greater the increase observed (Fig. 3b). PSP was most marked in papillary muscles isolated 3 h after thermal injury to the animal (100% of preparations tested). After burn shock lasting in the region of 1 h PSP was observed in only 50% of experiments. PSP also was observed in 50% of preparations isolated from the heart 10 min after burning.

The results demonstrate conclusively that thermal trauma has a significant effect on the properties of the myocardial cells, and that the degree of changes in cardiac function in burns is directly proportional to the duration of burn shock. In some experiments simultaneously with the recording of mechanical activity of the preparation, potentials were recorded intracellularly. No significant differences were found between the action potentials of the myocardial cells. This indicates that in burn shock it is mainly the mechanism coupling excitation with contraction that is disturbed. Only further research will show the nature of this disturbance. However, the great similarity between changes in the frequency—strength relationship in the myocardium in burn shock and the disturbances observed following blocking of the calcium channels in the surface membrane by means of compound D-600 cannot be ignored [7]. The fact that an increase in the external calcium concentration restores the biphasic f—P dependence is evidence in support of the hypothesis that this similarity is not accidental.

The hypothesis that toxic substances secreted into the blood stream during burn shock [6, 8, 11] are bound by certain membrane receptors, and consequently damage the system of calcium channels, seems very tempting. If this is true, it will have to be accepted that the binding of these "burn toxins" is quite stable, for to rinse the preparation it must be perfused with normal Tyrode solution for 3-4 h.

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