EXPERIMENTAL DETERMINATION OF OPTIMAL PARAMETERS FOR STIMULATION OF A MUSCLE AUTOGRAFT FOR USE IN DYNAMIC CARDIOMYOPLASTY

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The first attempts to use unprepared skeletal muscle to support the disabled myocardium were unsuccessful because of the inability of the muscle autograft to function adequately with the heart contracting in response to pulsed electrical stimulation [2, 7, 8, 11]. The results of investigations [10] of the molecular, biochemical, and histochemical changes taking place in a muscle autograft during long-term stimulation, and also of electrophysiological studies leading to the discovery of the development of resistance of the skeletal muscle tissue to fatigue during long-term pulsed electrical stimulation made it possible subsequently to use skeletal muscle for reconstructive operations on the heart in clinical practice [2, 6, 9, 11]. A new method of surgical treatment of the heart failure syndrome, which has been developed in the last decade, is dynamic cardiomyoplasty [1, 4, 6, 7, 10]. The results of experimental and clinical studies have now given all grounds for optimism so far as the future for the technique of dynamic cardiomyoplasty is concerned, in the light of approaches to the surgical treatment of critical heart failure [1, 3-5, 7]. However, several problems still remain unsolved, one of them being optimization of the regimes and parameters of stimulation of the muscle graft supporting the irreversibly damaged myocardium.

The aim of this investigation was to elaborate the optimal conditions and regimes of stimulation of an untrained muscle graft for use in the operation of dynamic cardiomyoplasty.

EXPERIMENTAL METHOD

Altogether 32 acute experiments were undertaken on mongrel dogs of both sexes weighing 16-30 kg, disregarding chronobiological factors. In all experiments barbiturate anesthesia was used; no muscle relaxants were given at any stage of the operation because of their uncontrollable action on skeletal muscle. All experiments were carried out with observance of accepted ethical principles and existing regulations for work with laboratory animals. The left latissimus dorsi muscle (LDM) was mobilized by a technique developed by ourselves, with preservation of the fixation point in the region of insertion of its tendon into the humerus and of the thoracodorsal neurovascular bundle [5]. A stimulating electrode of the original "STIMINAK-04" muscle stimulator (USSR, developed at the Department of Electronics of the Moscow Engineering Physics Institute, under the direction of Doctor of Technical Sciences I. A. Dubrovskii [3]) was applied to the (thoracodorsal) nerve to the latissimus dorsi. The pulsed electrical stimulator used in the experiments enabled the investigation to be carried out with both asynchronous and cardiosynchronized modes of stimulation, in multiples of between 1:1 and 1:8 relative to the R-wave of the ECG. It is possible to work with this apparatus on modes of single stimulation or "burst" stimulation with between 1 and 8 pulses in the burst, and with a pulse duration of between 0.07 and 0.6 msec, a following frequency of pulses in the "burst" of between 10 and 100

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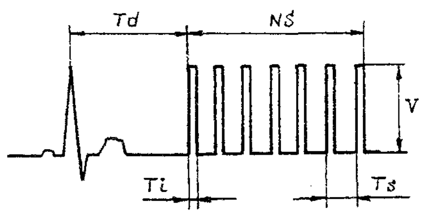

Fig. 1

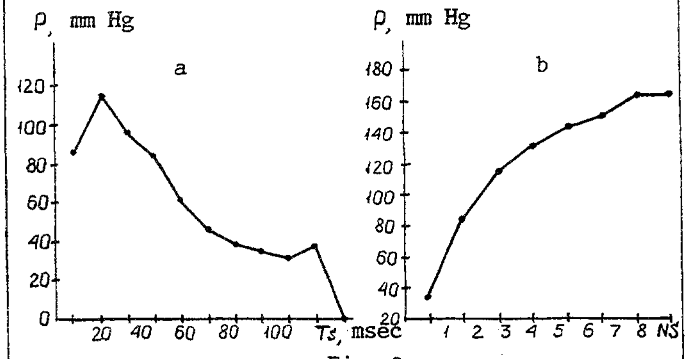

Fig. 2

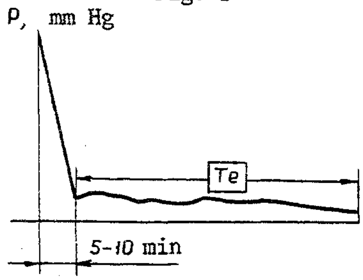

Fig. 3

Fig. 1. Characteristics of stimulation schedule. T_d) Delay time of "burst" relative to R wave, NS) number of pulses in "burst," Ti) pulse duration, Ts) duration of intervals between pulses in "burst."

Fig. 2. Changes in pressure in balloon depending on interval between pulses (a) and their number in "burst" (b). P) Pressure in balloon, NS) number of pulses in "burst," Ts) interval between pulses.

Fig. 3. Pressure curve in balloon depending on time of stimulation of muscle graft. T_e) Time of coming out on a "plateau."

Hz, and with pulse amplitude of 3, 6, and 9 V, discretely. With this stimulator, a "burst" of pulses can be delayed relative to the R-wave by between 10 and 1000 msec (Fig. 1). From our point of view, implantation of a single muscle electrode into the region of entry of the neurovascular bundle into the muscle tissue is optimal, for with an increase in the number of electrodes, if these are sutured to the periphery of the muscle graft, the force of contraction is virtually unchanged, but at the same time, excessive trauma to the muscle tissue takes place. After mobilization of LDM it was firmly fixed around a specially made silicone balloon (volume 100 ml), filled with physiological saline and connected to a pressure transducer. After the muscle loop had been formed around the balloon, a basic pressure of 100 mm Hg was created in it and stimulation of LDM began. The pressure in the balloon was measured and the ECG and mean arterial pressure of the animal were monitored on a "Mingograf-7" apparatus (Siemens-Elema, Germany). The experiments were conventionally divided into three series. Common to all three series of experiments was the initially chosen heart rate (120 beats/min), which is the average value for the experimental animals used. In series I contractile activity of the muscle graft was studied alternately, depending on (1) pulse length (Ti), (2) the pulse following frequency in the "burst" (Ts), and (3) the number of pulses in a "burst" (NS); the amplitude of the pulses remained unchanged at 3 V (Fig. 1). In the experiments of series II the optimal delay of the "burst" of pulses (T_d) at the chosen heart rate of 120 beats/min and with values of Ti, Ts, and NS determined in the experiments of series I, was investigated (Fig. 1). In series III of the experiments, long-term stimulation of the untrained LDM graft was studied, using regimes determined in the first series of experiments, but with different amplitudes and frequencies of stimulation (Table 1). The hemodynamic parameters determining optimal perfusion and metabolic aspects of function of the isolated LDM muscle graft, were maintained throughout the investigation at the mean physiological level.

EXPERIMENTAL RESULTS

The criteria for evaluation of contractile activity of the muscle graft was the difference between the basic pressure in the balloon and its peak amplitude value during stimulation of the muscle graft.

In the course of the experiments it was found that a pulse of duration between 0.07 and 0.6 msec did not significantly affect the contractile activity of the muscle graft.

The study of dependence of the force of contraction of the muscle graft on pulse following frequency in the burst showed that the optimal interval between pulses (Ts) was 20 msec (Fig. 2a).

The results relating to dependence of the rise of pressure in the balloon during stimulation of the muscle graft on the number of pulses in the "burst" are given in Fig. 2b. The optimal number of pulses in the "burst" was seven, because any further increase in their number did not cause a significant change in skeletal muscle contractility.

It was shown that the optimal delay (T_d) ought to be 250 msec, with a natural heart rate of 120 beats/min.

The third series of experiments was conducted at four different frequencies of contraction of LDM: 120/min (1:1), 60/min (1:2), 30/min (1:4), and 15/min (1:8). We used these frequencies with different amplitudes of pulses, and with previously chosen values Ti = 0.5 sec, Ts = 20 msec, and NS = 7. All the experiments showed a tendency for pressure in the balloon to fall progressively relative to the initial values, with the establishment of a distinctive period of relatively constant pressure ("plateau"), which lasted throughout the period of the investigation (2 h). The criteria for evaluation were the time taken to reach the "plateau" (T_e) and also the initial and established values of pressure in the balloon during stimulation (Fig. 3).

Table 1 gives the mean values of the rise of pressure in the balloon during stimulation of the muscle graft in accordance with the program described above, and with the following pulse amplitudes: 9, 6, and 3 V. In all cases of prolonged stimulation, whatever the amplitude and frequency of the pulses, the time taken to reach a "plateau" was about equal, namely 5-10 min. However, the pressure level during establishment of the stable period was directly dependent on the frequency of contractions and on amplitude.

For the analysis of the results, the optimal amplitude and frequency of stimulation of the untrained muscle graft for prolonged and effective contractile working of the muscle, the following parameters were chosen: amplitude 6 V and frequency of stimulation 15-30 pulses/min.

As a result of our previous experiments [4-6] and on the basis of data in the literature [1, 2, 7, 11], we consider that preliminary training of the skeletal muscle, as a result of which the muscle fibers undergo "transformation" from quickly fatigued into resistant to fatigue, serves no useful purpose.

The reason is that to achieve complete transformation during continuous and progressive electrical stimulation, a muscle requires 6-8 weeks, whereas retransformation takes place in the course of 2-3 weeks. Stimulation of the muscle autograft as a rule begins on the 9th-14th day after the operation of dynamic cardiomyoplasty, and it is therefore logical to suggest that during this time the previously trained muscle will lose its properties acquired in the course of training. It can be concluded that the method cannot give effective assistance to the damaged heart in the early periods after the operation and, consequently, patients for dynamic cardiomyoplasty must be selected from those having a definite reserve of myocardial contractility.

TABLE 1. Pressure in Balloon During Contraction of LDM as a Function of Amplitude and Frequency of Stimulation per Minute

Interval between stimuli, min	Frequency of stimulation, pulses/min											
	15			30			60			120		
	Amplitude of pulses, V											
	3	6	9	3	6	9	3	6	9	3	6	9
1	150	200	250	140	170	220	140	150	200	120	140	90
10	55	50	10	35	40	9	25	30	8	20	25	5
60	47	47	5	20	32	4	15	25	2	10	20	2
120	42	45	3	15	30	1,5	5	20	1	5	8	0,5

We also showed that a disturbance of diastolic filling of the left ventricle during cardiosynchronized stimulation can be achieved by a change in the delay time after the R wave and in the number of pulses in the "burst," depending on the heart rate. This requires the creation of a new dialogic stimulator, to be implanted into the patient during performance of myoventriculoplasty operations.

From the point of view of optimization of the hemodynamic parameters of the heart-muscle complex, the optimal initial training schedule of stimulation is a burst of seven pulses, each from 0.07 to 0.6 msec in duration, with a frequency of 30-50 Hz, an amplitude of 6 V, and a burst following frequency of 15-30/min.

A definite schedule and parameters of stimulation can be suggested both as initial stimulation in the immediate postoperative period and as the hemodynamically most effective, and least exhausting to the skeletal muscle. Certain parts of the investigation described above can be successfully used under clinical conditions during operations on patients for whom the use of traditional methods of surgical treatment is associated with a high degree of risk and of death, and they can also be used to design and make myocardial stimulators for use in the operation of dynamic cardiomyoplasty.

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