THE INFLUENCE OF THE CARDIAC CONTRACTILE FUNCTION ON THE REALIZATION OF THE SYMPATHETIC EFFECT

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In studying the mechanisms which condition compensation in the failing cardiovascular system, the question of the influence of cardiac hyperfunction on the realization of cardiac sympathetic and parasympathetic effects is of considerable interest. The literature data on this question are contradictory [2, 4, 9, 10]. However, not long ago, F. Z. Meerson, T. M. Dmitrieva [6], and V. I. Kapel'ko [3], in experiments on nonanesthetized rabbits with closed thoraces, demonstrated that during increasing compensatory hypertrophy of the heart, conditioned by gradual aortic stenosis, the vagus effect becomes weak and there is an emancipation of the heart from the influence of the vagus nerve which is more significant the greater the degree of stenosis. In the present report we studied the influence of increasing compensatory cardiac hypertrophy on the size of the sympathetic effect.

EXPERIMENTAL

The work was carried out on the hearts of 40 frogs prepared according to Vetokhin [1]. Cannulae were placed into the inferior vena cava and in one of the aortic arches and the preparation was arranged so that the heart received uninterrupted perfusion. A vertical glass tube connected with the arterial cannula and fixed vertically permitted alteration of the pressure in the aorta from 4 to 28 cm of water in the first series of experiments and from 14 to 44 cm of water in the second series, the level of venous pressure during the entire experiment being held strictly constant. We prepared the sympathetic branch by the usual method at the level of the 2nd and 3rd ganglia and placed it on thin platinum electrodes. For stimulation an SIF-3 electrostimulator was used; stimuli were given for 15 sec, the duration of impulse was 2 msec, the voltage 10 V, frequency 8 cps. Cardiac contractions were recorded with an Engelmann lever key on a smoked kymograph drum. The stroke volume was determined by collecting the liquid ejected by the heart in a measuring tube. The stroke work W_{str} was calculated according to the formula:

$$W_{str} \text{ (in g-cm)} = \text{stroke volume (in ml)} \cdot \text{height of water column (in cm)}.$$

The inotropic sympathetic effect was estimated according to the amplitude, stroke volume, and stroke work; the chronotropic effect, according to the rate of contraction.

For a quantitative estimate of the sympathetic effect we used two indices: 1) the absolute sympathetic effect—the difference between maximal value of the index of contractile function on a background of stimulation of the sympathetic nerve and the corresponding value before stimulation, expressed in absolute numbers; 2) the relative sympathetic effect—the ratio of maximal value of the index of contractile function on a background of stimulation to the corresponding value before stimulation, expressed in percent.

RESULTS

Investigation of the changes in cardiac contractile function with increase in aortic pressure has shown that with an increased cardiac load the amplitude and frequency of contractions and also the value of the stroke volume, decrease, returning to normal or subnormal levels when the load is removed. With increase in load the cardiac work

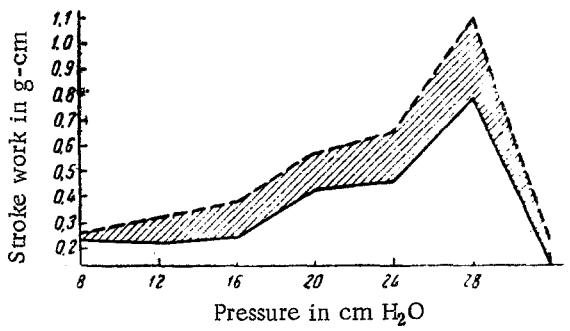

Fig. 1. Changes in the sympathetic effect (stroke work) during increased aortic pressure. Explanation in the text.

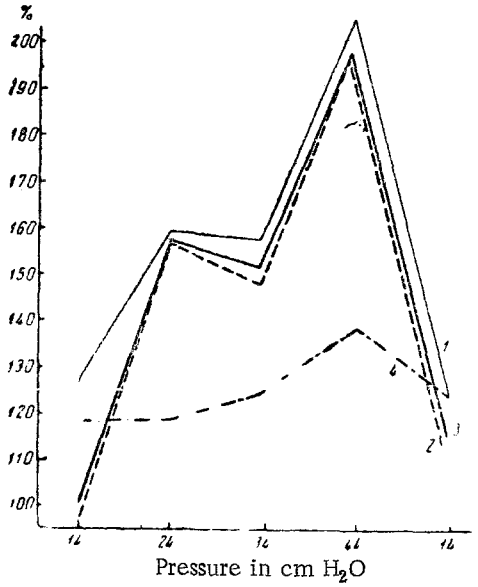

Fig. 2. Changes in the relative sympathetic effect (with various indices) with increased aortic pressure.

increases considerably, reaches a maximum, and then falls sharply. Thus, increase in aortic pressure altered regularly the level of cardiac contractile function. Stimulation of the sympathetic nerve to a certain degree of load was irregular compared to the original background.

Investigation of the sympathetic effect showed that with increased load on the heart the inotropic sympathetic effect increases. In the majority of experiments the inotropic sympathetic effect reached maximum at an aortic pressure of 24 cm of water and with subsequent increases in pressure it fell slightly; however, in certain experiments and with the highest pressure used (44 cm of water) the value exceeded the starting value. Figure 1 presents the dynamics of changes in the sympathetic effect at mean values of cardiac work in the first of experiments. The solid line reflects the change in the normal; the dotted line, a background of stimulation of the sympathetic nerve; the hatched area, the dynamics of change in absolute sympathetic effect. It is evident that with increase in pressure from the initial value to 20 cm of water the absolute sympathetic effect—"supplementary" work—increases approximately twofold (from 0.048 ± 0.015 to 0.145 ± 0.038) and with an increase to 24 cm of water, fivefold (to 0.246 ± 0.038). A tendency toward increase is found also for "supplementary" amplitude and stroke volume the increase of these two indices appeared to be statistically invalid, however.

The value of the relative sympathetic effect is clearly increased with increasing cardiac load. The dynamics of change in this index, in terms of mean relative values for amplitude, stroke volume, stroke work, and rate for the second series of experiments are presented in Fig. 2. This increase for the inotropic index is not statistically valid.

Change in the chronotropic sympathetic effect, both absolute and relative, was negligible.

Evaluating the results obtained, one must first dwell on the changes in the contractile function of the heart with progressive increases in aortic pressure. Myocardial tension is the main index of contractile function by which the level of metabolic processes in the myocardium is measured [7]. With this known assumption the tension (T) may be calculated on the basis of data for intraventricular pressure (P), cardiac radius (r), and thickness of the ventricular wall (S) at the moment of isometric tension:

$$T = \frac{P \cdot r}{2S}.$$

In our experiments as the pressure was increased, the radius of the heart did not decrease and the thickness of the myocardial wall was changed negligibly; thus, as the load on the heart increases the tension of the heart also increases, accompanied by a fall in the amplitude of contraction and stroke volume. Up to a certain load level the heart maintains the increase in cardiac work. Under extraordinary loads, when the stroke length and volume have fallen to a minimum, the increased myocardial tension is opposed by the fluid pressure in the aorta, but almost or completely fails to move this fluid—the work in this case sharply declines and subsequently approaches zero. Consequently, progressive increase in myocardial tension is the main and most constant change in the contractile function of the heart and may be regarded as the most probable reason for the change in the sympathetic effect. The data thus obtained indicate that under conditions of hyperfunction, the inotropic sympathetic effect is increased; this continues until such time as the increase in load does not lead to a sharp drop in the contractile ability of the heart.

Change in the sympathetic effect during increase of the myocardial tension may be conditioned to some degree by three factors: 1) change in the amount of mediator elaborated by the nerve endings, 2) change in the reactivity of the adrenoreceptor, and 3) change in the exchange of mediator by the parasympathetic nervous system —acetylcholine, under these conditions. It is necessary to study the role of these factors in special experiments. In addition, one should keep in mind that the complex biochemical movements which take place in the myocardium under the influence of sympathetic nerve stimulation are extremely similar to those metabolic changes which take place during cardiac hyperfunction. The latter is accompanied by an increase in myocardial tension. In both instances glycogen breakdown is increased, ATP exchange is intensified, oxygen requirement is increased, potassium concentration is altered, etc. [5, 8]. It therefore may be stated that, if as a result of increased load myocardial metabolism is "tuned up" on the basis of hyperfunction, the energy reserve of the heart is mobilized, the cardiac reaction to the augmented sympathetic impulses improved, and the sympathetic effect increased.

We dwelt on the investigations by E. N. Speranskaya and coauthors [2, 9], in which a decrease in the sympathetic effect was noted when the intraventricular or atrial pressure was increased. It must be remembered that in these studies, in distinction from our experiments, the cannula in which the increase of pressure was created was introduced not into the aortic arch but, by passing the spiral valve, directly into the ventricle; thus, not the systolic but the diastolic intraventricular pressure was increased. It is known that in the intact organism the ventricular diastolic pressure, like that of the atria, is increased only in extraordinary situations and is a sign of cardiac insufficiency (failure). Under these conditions, with profound exhaustion of the energy reserves of the myocardium, the heart is not in condition to fully reproduce the reaction requiring a considerable energy expenditure—the sympathetic effect must be decreased, which the authors did observe.

In our experiments, evidently, we did not have such an extreme situation. In estimating the increase in sympathetic effect in our studies, it must be remembered that data previously obtained in our laboratory has shown that in similar conditions there occurs a weakening of the negative vagal effect [3, 6]. These facts in toto permit us to regard the changes in cardiac reactivity to extracardiac neural influences during hyperfunction as a single adapative process—the predominance of cardiac reactivity to sympathetic influences. This allows for an increase in the contractile function of the myocardium, which in conditions of high loads plays an important role in the maintenance of normal circulation.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
