ROLE OF ADRENERGIC INNERVATION IN DISTRIBUTION OF SYSTEMIC AND CORONARY FRACTIONS OF LEFT VENTRICULAR EJECTION WITH RAISED INTRAAORTIC PRESSURE

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KEY WORDS: left ventricular ejection; coronary fraction; systemic fraction; intraaortic pressure; adrenergic innervation of the heart.

Pressure loading in the aorta is one of the factors determining the left ventricular stroke ejection level [1, 6, 8, 9]. As was shown previously [2, 3] during pressor responses increasing the pressure load on the left ventricle, redistribution of blood is observed between the coronary and systemic circulations, with deviation of a considerable volume of blood into the coronary system. This shunting of blood into the coronary system affects the level of the total left ventricular ejection, calculated as the sum of the systemic and coronary fractions (SF and CF). This approach to the problem assumes the greatest importance when cardiac ejection is estimated from SF, disregarding the coronary blood flow.

The aim of this investigation was to study the effects of a measured rise of intraaortic pressure on changes in SF and CF of left ventricular ejection during β-adrenoreceptor blockade by propranolol (Obsidan).

EXPERIMENTAL METHOD

Acute experiments were carried out on cats anesthetized with chloralose (50 mg/kg) and pentobarbital (20 mg/kg), with an open chest and artificially ventilated. SF of the left ventricular ejection was judged on the basis of measurements of volume velocity of blood flow in the ascending aorta (distally to the origin of the coronary arteries) by means of a vascular transducer (diameter 7 mm) of an RKÉ-2 electromagnetic flowmeter. CF was determined by measuring the outflow from the coronary sinus, multiplied by 3/2, by the method described previously [2, 3]. The intraaortic systolic pressure (AP_1) was gradually raised by increasing the resistance in it with an occluder, located distally to the transducer of the electromagnetic flowmeter (Fig. 1). The occluder consisted of a loop, wrapped around the ascending part of the aorta, and a micrometer system. The thread consisted of Kapron tape 0.8 mm in diameter. Successive adjustment of the micrometer system by 1 mm led to an increase of AP_1 by 1.5-60 mm Hg. The results were grouped on the basis of levels of all parameters corresponding to a rise of AP_1 by 30 mm Hg. The results of elevation of the intraaortic pressure were analyzed before and during β-adrenoreceptor blockade within the same pressure ranges. AP_1 was recorded proximally to the site of the occluder, through a catheter (diameter 0.6-1 mm), passed through the right carotid artery to the base of the aorta. The systemic blood pressure in the femoral artery (AP_2) was recorded simultaneously. Contractility of the heart was estimated by recording the first derivative of intraventricular pressure (dp/dt max), by means of an MN-7M analog computer, on the systolic pressure curve in the left ventricle, and the end-diastolic pressure (EDP) in the left ventricle also was recorded. The degree of filling of the ventricle also was judged from the measurements of the last parameter. Pressure in the left ventricle was measured by means of a catheter passed through the auricle of the left atrium. All pressures were recorded by means of a pressure transducer of the PDP-400p type. All parameters were recorded simultaneously on N-3021 and N-338 automatic writers. The results were subjected to statistical analysis by Student's t test. The β-adrenoreceptors of the heart and vessels were blocked by propranolol, injected in a dose of 1 mg/kg into the animal's femoral vein.

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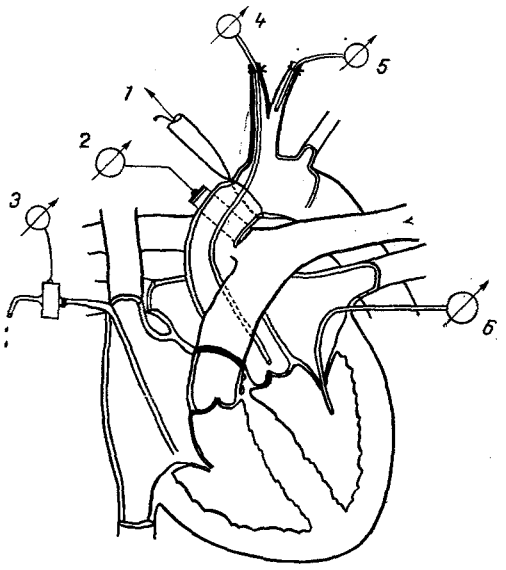

Fig. 1. Scheme of experiment with external occlusion of ascending aorta. 1) Occluding device, 2) transducer of electromagnetic flowmeter for measuring systemic fraction of cardiac ejection, 3) transducer of electromagnetic flowmeter for measuring coronary fraction, 4) catheter for measuring aortic pressure, 5) catheter for measuring systemic arterial pressure, 6) catheter for measuring pressure in left ventricle.

EXPERIMENTAL RESULTS

The effect of β-adrenoreceptor blockade on the distribution of blood between SF and CF in response to a gradual rise of AP_1, created by occlusion of the aorta, was investigated in 10 experiments. In the course of these experiments AP_1 was gradually raised by between 0 and 90 mm Hg, with the β-adrenoreceptors intact (Fig. 2a) and after their blocking by propranolol (Fig. 2b). A gradual rise of AP_1 led to an increase in SF, which gradually returned to its initial level after a further rise of AP_1 (Fig. 3a). In the presence of β-adrenoreceptor blockade, when AP_1 was raised by amounts up to 60 mm Hg no significant differences were observed in the increase in SF compared with its changes before blockade. With a rise of AP_1 from 61 to 90 mm Hg, unlike in animals with intact β-adrenergic innervation, SF rose sharply ($p < 0.05$).

Under blockade conditions, when AP_1 was increased by more than 30 mm Hg a fall of dp/pt max was observed, whereas when β-adrenoreceptors were intact, dp/dt max increased within the same limits. Thus changes in contactile activity are among the factors responsible for the formation of changes in SF, with the β-adrenoreceptors intact and within this range of AP_1.

Propranolol significantly reduced the initial dp/dt max ($p < 0.05$). As was shown previously [4, 5], a rise of aortic pressure accompanied by a lower level of contractile activity leads to reduction of cardiac ejection, whereas if accompanied by a higher level of contractile activity, cardiac ejection is increased. In the present experiments, with a rise of AP_1, SF increased more the lower the initial level of contractile activity. A definite role in the changes in SF in response to an increase in the load under β-blockade conditions is thus played, not by contractile activity, but by another factor, which is evidently the diastolic filling of the left ventricle.

EDP in the left ventricle served as the indicator of diastolic filling in the present experiments. With a rise of AP_1, EDP increased progressively, whether the β-receptors were intact or blocked. However, the rise of EDP under blockade conditions occurred in response to smaller aortic loads. With an increase of AP_1 from 61 to 90 mm Hg, the increase in EDP was significantly greater ($p < 0.05$) than with the β-receptors intact. This more marked rise of EDP led to changes in SF under blockade conditions within this same range of AP_1.

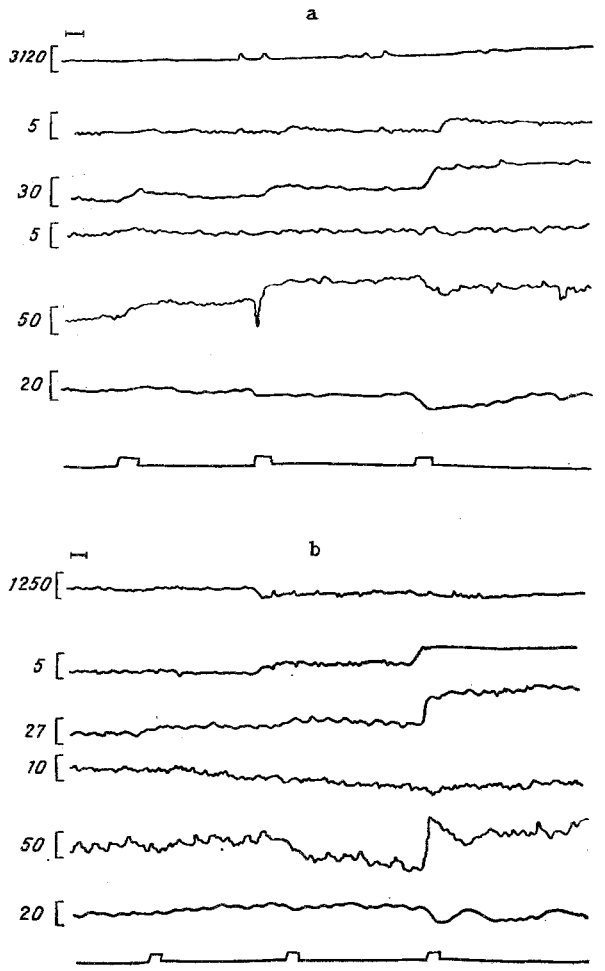

Fig. 2. Changes in parameters of hemodynamics with different degrees of aortic occlusion. a) Before, b) during β-adrenoreceptor blockade. On curves from top to bottom: time marker (10 sec), dp/dt max, in mm Hg/sec, envelope); EDP in left ventricle (in mm Hg), systolic pressure in ascending aorta (in mm Hg), CF) in ml/min, SF of left ventricular ejection (in ml/min), systolic arterial pressure in femoral artery (in mm Hg), marker of degrees of occlusion.

Unlike in our previous investigations [2, 3], in response to rise of AP_1, CF did not increase significantly (the highest values were 2-3 times lower). Although with an increase of intraaortic pressure above 60 mm Hg an increase in CF took place, which was commensurate in magnitude with the change in SF, it also was less than the maximal shifts observed previously [2, 3]. Against the background of β-adrenoreceptor blockade a decrease was observed in CF during a rise of AP_1 within the range from 0 to 60 mm Hg (Fig. 2b; Fig. 3b). Whether this decrease of CF was connected with reduction of myocardial contractility, or whether the latter was itself due to a decrease in CF because of negative coronary inotropic effects [1], is not yet clear. However, with a rise of pressure in the aorta of between 1 and 30 mm Hg dp/dt max remained unchanged, but the coronary blood flow was reduced. It may therefore be suggested that the reduction of contractility in response to subsequent degrees of elevation of intraaortic pressure was due to reduction of the coronary blood flow, which can regulate the strength of the cardiac contractions independently of adrenergic mediator levels [1].

The reduction of CF could also be due to reflex α-adrenergic constriction in response to activation of arterial baroreceptors, for AP_2 proximally to the occluder fell progressively during the blockade. Whereas in animals with intact β-receptors influences realized through the β-adrenoreceptors of the coronary vessels predominate, when they are blocked, influences on α-receptors become predominant [10], and their excitation may lead to spasm of the coronary arteries [7].

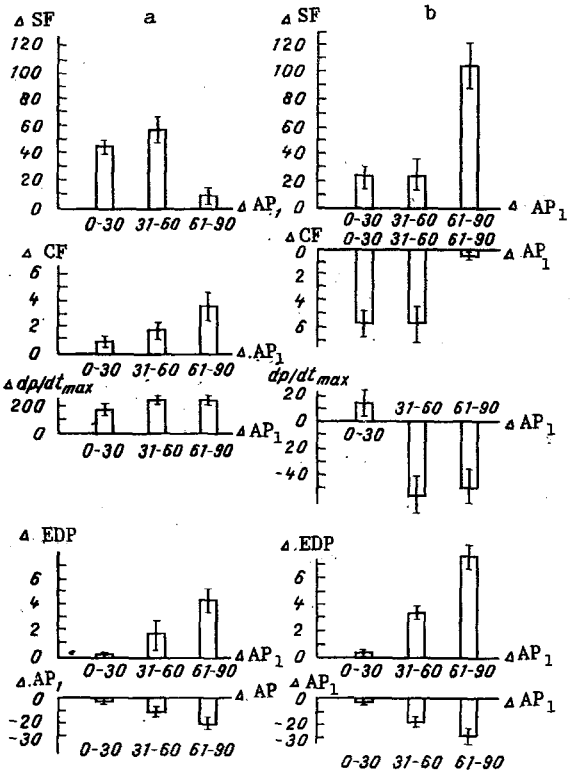

Fig. 3. Changes in systemic (ΔSF, ml/min) and coronary (ΔCF, ml/min) fractions of left ventricular ejection, dp/dt max (in mm Hg/sec), EDP in left ventricle (ΔEDP, mm Hg), and femoral arterial pressure (ΔAP_2, mm Hg) with different degrees of aortic occlusion (ΔAP_1, mm Hg). a) Before, b) during blockade.

With an increase of AP_1 by 61-90 mm Hg against the background of β-adrenoreceptor blockade, the value of CF was unchanged. This may be assumed to be a manifestation of different mechanisms of change of CF with different degrees of aortic occlusion under these conditions. Possibly with a very small degree of aortic occlusion the baroreceptor mechanism is more prominent, but with an increase in the degree of occlusion the α-adrenergic reduction of the blood flow is balanced by an increase due to passive stretching of the vessels by the increased pressure.

Some investigators [11, 12] reject any role of a baroreceptor mechanism in the changes in coronary blood flow following aortic occlusion in dogs. In their experiments propranolol did not affect the increase in coronary blood flow during aortic occlusion. However, in their experiments aortic occlusion caused an increase in systolic pressure in the left ventricle, by a degree commensurate with the increase of systolic pressure in the aorta above 60 mm Hg in the present experiments.

The redistribution of blood flow between the systemic and coronary circulations, in response to a mechanical increase of the load on the heart by the intraaortic pressure, thus differs from its redistribution in response to a rise of pressure caused by a reflex or humoral mechanism [2, 3]. Occlusion of the aorta giving the same (about 50 mm Hg) or even greater degrees of rise of intraaortic pressure caused a much smaller "leak" of blood into the coronary system than was observed under the influence of vasoactive drugs [2].

This redistribution is affected by the level of neurogenic activity. Under conditions preventing realization of β-adrenergic influences an increase is observed in the deviation of blood into the systemic vascular bed, accompanied by a decrease in the volume reaching the coronary circulation.

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EFFECT OF ATRIOPEPTIN ON ADRENERGIC MECHANISM CONTROLLING VASCULAR TONE

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KEY WORDS: atriopeptin; smooth muscles; vascular tone.

The hypotensive effect of atriopeptin and some ways in which the peptide acts on smooth-muscle cells of blood vessels have been described in the literature [2-5].

The aim of this investigation was to study the effect of atriopeptin on one concrete mechanism of regulation of smooth muscle tone, namely the adrenergic mechanism. Considering the importance of the problem of the regional circulation, it was decided to investigate this problem on the vascular smooth muscle of several organs, differing in its initial functional properties.

EXPERIMENTAL METHOD

Contractile activity of smooth muscles of isolated preparations of cerebral and pancreatic arteries, the portal vein, and the aorta was recorded during constant-temperature perfusion with Krebs' solution, by means of mechanical to electrical transducers, under auxotonic conditions, by the method described previously [1]. The action of atriopeptin, noradrenalin, and other drugs aimed at modifying the initial functional state of the cell membranes was studied. A synthetic analog of atriopeptin of type I, II, and III, obtained in the Laboratory of Peptide Synthesis, All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR, was used.

EXPERIMENTAL RESULTS

Under the initial conditions, i.e., on the addition of atriopeptin (in a concentration of 10^{-10} to 10^{-7} M) to standard Krebs' solution, no changes in tone and spontaneous contractile activity took place in the smooth musculature of the blood vessels to the organs and the aorta (n = 27). Meanwhile the smooth muscles tested were activated sufficiently well by noradrenalin (10^{-6} M) and by a 40 M solution of potassium ions. If smooth muscle tone was first increased by means of these activators, atriopeptin caused relaxation in preparations of the aorta (10^{-7} M) and of the portal vein (10^{-10} M), but as before, it did not change smooth muscle tone in the basilar artery of the vein and the artery of the pancreas (Table 1, Fig. 1).

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