CORONARY BLOOD FLOW DYNAMICS IN RATS

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In recent years the problem of adequate recording of the coronary blood flow in relatively large animals has been solved perfectly successfully with the aid of ultrasonic and induction systems, under acute and chronic experimental conditions [1, 6, 7]. However, in small animals, and rats in particular, the study of the dynamics of the coronary blood flow presents definite difficulties, due to the small size of the flow and the high heart rate.

The aim of this investigation was to study the possibility of using high-frequency ultrasound to study coronary blood flow dynamics in rats.

EXPERIMENTAL METHOD

This paper gives the results of a study of coronary blood flow dynamics carried out by means of a specially made ultrasonic high-frequency transducer. The use of such a transducer has made it possible to solve some problems related to blood flow measurement in blood vessels under 300 μ in diameter, located on the surface of the myocardium, which contracts with a frequency of 300-500 beats/min. This transducer, measuring 1.5×2.0 mm, was developed on the basis of an ultrasonic instrument [2], made in the Bioengineering Laboratory of the Research Institute of has made it possible to measure the coronary blood flow by a contact method through the myocardial surface. A miniature piezoelectric crystal made of the titanozirconium salt of lead, 0.5 mm^2 in area, and working on a frequency of 26.8 MHz, was used as the sensitive element. This element, an emitter of ultrasound, receives ultrasound waves reflected from the blood cells. The difference in the frequency of these two processes arising during movement of the blood is determined by the frequency of the doppler signal, which is proportional to the blood flow rate and is recorded in the form of a flow curve. Experiments were carried out on male Wistar rats weighing 200-250 g, on which thoracotomy was performed under general anesthesia (pentobarbital sodium 60 mg/kg, intravenously) and artificial ventilation of the lungs with air. To determine cardiac output and to undertake phase analysis, an ultrasonic transducer of bandage type, working on a frequency of 13.4 MHz, was applied to the ascending aorta. The transducer was calibrated in units of volume velocity of the blood flow and was used in investigations of cardiac output on conscious rats, conducted jointly with O. S. Medvedev during the last 10 years [3]. The coronary blood flow transducer was used to scan the myocardium in the region of the descending branch of the left coronary artery. The coronary artery was located by means of the acoustic signal and the optimal position of the transducer on the heart was determined. The transducer was fixed to the myocardial surface by means of a ligature, but in some experiments acrylic glue (MK-2) was used. The coronary blood flow dynamics was studied under conditions of relative physiological rest and also during different procedures: coronary occlusion for 0.2-1 min, asphyxia, and administration of the vasodilator dipyridamole in doses of 0.5-2.0 mg/kg. The drug was injected through a catheter implanted into the femoral vein.

EXPERIMENTAL RESULTS

The investigations showed that the coronary blood flow in rats is pulsatile in character. Under these circumstances two types of coronary blood flow curve were most probable: the first was close to rectangular and was re-

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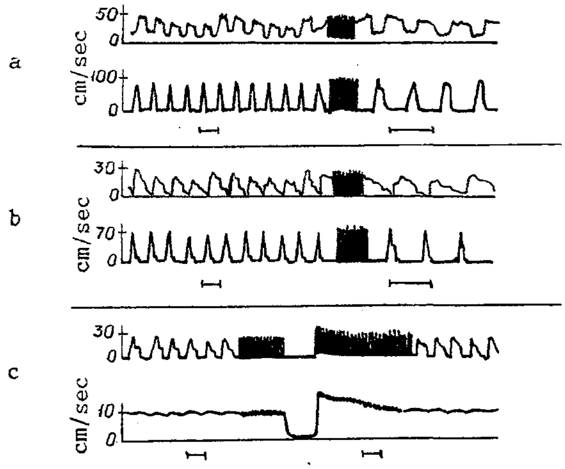

Fig. 1. Correlation between shape and magnitude of coronary blood flow with cardiac ejection (a and b) and response of coronary blood flow to occlusion of middle coronary artery for 30 sec (c). a, b) (from top to bottom): coronary blood flow in left descending artery, blood flow in ascending aorta, time scale 0.25 sec; c) (from top to bottom): coronary blood flow in left descending artery, mean coronary flow rate, time scale 0.25 and 20 sec.

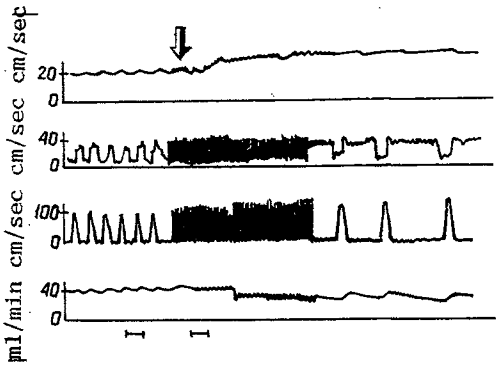

Fig. 2. Effect of asphyxia on coronary blood flow and cardiac ejection in rats. From top to bottom: mean coronary blood flow rate, blood flow in coronary artery, blood flow in ascending aorta, cardiac output, time scale 0.25 and 20 sec. Arrow indicates beginning of asphyxia.

corded, as a rule, at high flow rates (Fig. 1a). This form of curve is characteristic of flows in diastole with peak rate of 40-50 cm/sec and higher, and taking place against the background of a large constant component. The blood flow in systole in this case may amount to 30-50% of the peak values. These values of the coronary blood flow usually corresponded to high linear flow rates in the ascending aorta (100 cm/sec and higher). With diastolic flow rates of not more than 15-20 cm/sec the shape of the curve was triangular, with a steep leading edge (Fig. 1b). The value of the flow in systole was very small and had the appearance of separate pulsations or was completely absent. In that case, values of the linear blood flow rate in the ascending aorta were low (not more than 70-90 cm/sec).

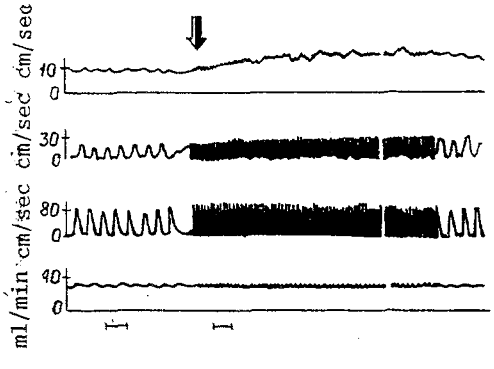

Fig. 3. Action of dipyridamole (1.0 mg/kg, intravenously) on coronary blood flow and cardiac ejection. Legend as to Fig. 2. Arrow indicates beginning of injection of drug.

Examination of the coronary blood flow rate curves for a period of 1-3 min showed some degree of variability during different cardiac cycles in the same animal. These blood flow oscillations were associated with the phases of respiration (Fig. 1a, b). The peak flow rate was doubled. It is important to note that the responses of coronary blood flow rate and cardiac ejection rate were synchronous, the former being more marked.

To assess the dynamics of the myocardial blood supply, the coronary artery was occluded for 20-60 sec, to be followed by reperfusion, which was performed distally to the site of the transducer. At the initial moment of reperfusion the increase in pulse blood flow rate was 20-30%, but not more than 50% of the level before occlusion. The increase in the mean rate was greater, namely by 40-50%, but not more than 100% (Fig. 1c). Incidentally, the change in mean flow rate characterizes most fully the response of the volume velocity of the blood flow. Usually the blood flow was restored in the course of 30-60 sec. On repetition of these procedures the effect of a peak of reactive hyperemia virtually disappeared. This was evidently due to adaptation of the myocardium. It is important to note that responses of recovery of the blood flow which we observed in rats and dogs are fully comparable. However, the value of the peak of reactive hyperemia in rats was smaller, probably due to the smaller size of the region of blood supply of the heart muscle in rats compared with dogs [4].

The next stage of the work was to study the dynamics of the blood flow during asphyxia. Asphyxia which, as we know, is accompanied by hypoxia and hypercapnia, led in most experiments to an increase of the coronary blood flow (Fig. 2). This took place approximately 15-20 sec after obstruction of breathing. The greatest increase in blood flow was recorded at average flow rates, namely by 30-50%, but not more than 100% of the initial level. The increase in pulse blood flow rate was smaller (20-30%). The increase in pulse blood flow took place on account of an increase in the blood flow rate in diastole; the systolic blood flow also increased. The shape of the blood flow curve in this case was close to rectangular. In some experiments asphyxia was accompanied by bradycardia, which appeared 1.5-2 min after the beginning of exposure. This led to a change in shape of the pulse blood flow curve, which was manifested as lengthening of the diastolic flow phase. During bradycardia the values of the coronary blood flow rate showed no significant change, the cardiac output fell, and the peak rate of ejection of blood into the aorta and the stroke volume increased. In some experiments, at the very beginning of asphyxia, the increase in the coronary blood flow was negligible, and after 1-1.5 min it fell significantly. However, on the whole the character of the responses of the coronary blood flow in rats, at both peak and average flow rates, was similar to that observed in cats [5].

Incidentally, in similar investigations which we conducted previously on cats and dogs, we used bandange transducers of fixed diameter. The results given in this paper characterize the response of the linear blood flow rate in which changes in diameter of the coronary artery were disregarded.

To test that, in principle, the volume velocity of the coronary blood flow can be determined by taking measurements through the myocardial surface, experiments were carried out with vasodilators. One such preparation was dipyridamole. If dipyridamole was injected intravenously in a dose of 1.0 mg/kg, an increase in coronary blood flow was observed (Fig. 3). The peak pulse blood flow rate increased by 10-15%, and the mean flow rate increased by 20-30%. The peak blood flow values were observed at the 3rd-5th minutes after injection of the drug, and they persisted for 30 min. Under these circumstances no changes in cardiac ejection or linear and volume velocity of the blood flow in the aorta were observed. The results of these experiments show that when the blood supply to the myocardium is assessed, some idea can be obtained of the values of the linear blood flow rate, especially at its average values, when the blood supply to the myocardium is assessed.

The investigations described above were carried out with the aid of transducers in which the piezoelectric element was set at an angle of 45° to the myocardial surface. The piezoelectric element probably works at the same angle to the surface of the coronary artery also, for usually the main branches of these vessels are arranged almost parallel to the myocardial surface. This makes it possible to measure the linear blood flow rate. With ultrasound of a frequency of 26.8 MHz the sensitivity of the doppler signal to linear velocity was 240 Hz/cm/sec. The resolving power of the frequency detector of the ultrasonic instrument under these circumstances was about 0.3 cm/sec. During working on the middle coronary artery the signal to noise ratio was usually 30-40 dB or higher, thus guaranteeing sufficient reliability of recording the shape of the coronary blood flow curve.

Thus the technique of high-frequency ultrasound, which possesses high sensitivity, guarantees reliable measurement of the coronary blood flow in rats. Its use can be particularly effective in combined investigations of the dynamics of cardiac activity, both in the healthy animal and if lesions of the cardiovascular system of various kinds are present.

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FUNCTIONAL STATE OF THE HEMATOPOIETIC SYSTEM IN DIFFERENT STAGES OF CCl_4-INDUCED LIVER FIBROSIS IN MICE

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It was shown previously that functional activity of the Kupffer cells is depressed in CCl_4-induced fibrosis in the liver [1-3]. Besides macrophages in other locations, the Kupffer cells play a most active role in the regulation of hematopoiesis, for they secrete GM-CSF [3, 4, 15], erythropoietin, IL-1, TNFα, and PGE I and PGE II. The transition from fibrous transformations into the irreversible form is associated with a decrease in the degree of mononucle-

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