EFFECT OF CONTRACTION RATE ON BLOOD SUPPLY TO THE ISOLATED RAT HEART

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UDC 612.172.1:612.172.2]-085.23

A change in the contraction rate of the isolated rat heart perfused with oxygenated Krebs-Henseleit solution within the range from 180 to 420 beats/min is not followed by changes in the hydraulic resistance of the coronary vessels. In experiments in which the isolated rat heart was perfused under constant pressure with donor's blood an increase in the heart rate from 120 to 300 beats/min had no significant effect on the coronary blood flow. An increase in the heart rate from 300 to 360-420 beats/min, however, caused a definite increase in the coronary blood flow. The blood supply to the heart calculated per single contraction fell progressively with an increase in the heart rate from a considerably lower than normal level to the normal level for that species of animal, and then remained constant. Stabilization of the blood supply to the heart calculated per single contraction (0.011–0.012 ml/g per contraction) occurred when the normal heart rate for rats was reached. After comparing their results with those obtained by other investigators, the authors suggest that the blood supply to the heart is constant within the range of near-normal contraction rates for different species of animals and man, with a value of about 0.01 ml/g contraction.

The degree of dilatation of the blood vessels in a skeletal muscle and the duration of the postcontraction hyperemia are determined by the rate of contraction of the muscle fibers and are independent of the character of the contractions or the amount of work performed by the muscle [1]. According to Rosenblueth et al. [11], if the heart rate is constant the coronary blood flow is also independent of the external work done by the heart. It can accordingly be postulated that the heart rate is an important factor determining the state of the coronary vessels.

In the investigation described below the effect of the heart rate on the blood supply to the isolated rat heart was studied. The relationship between the two parameters has not been studied in this particular experimental object.

EXPERIMENTAL METHOD

Albino rats weighing 250-300 g received heparin (500 units) by intraperitoneal injection 30-60 min before the beginning of the dissection and 25% urethane solution (0.65 ml/100 g body weight) 5-10 min before the beginning of the experiment. The animals were intubated and artificial respiration was applied, after which the thorax and the pericardial cavity were opened. All vessels approaching the heart except the aorta and pulmonary artery were tied with a single ligature. Perfusion with oxygenated (95% O_2 + 5% CO_2) Krebs-Henseleit solution [11] or with donor's blood was carried out under constant pressure of 70 mm Hg through a metal cannula introduced into the aorta. The outflowing blood or perfusion fluid was led via a thin vinyl chloride tube inserted into the pulmonary artery to a photoelectric drop recorder [3]. Blood was taken from the donor's carotid artery by means of a control-led volume pump [2] and led into a chamber

Laboratory of Regulation and Biophysics of the Circulation, Institute of Normal and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician V. N. Chernigovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 75, No. 5, pp. 5-8, May, 1973. Original article submitted May 31, 1972.

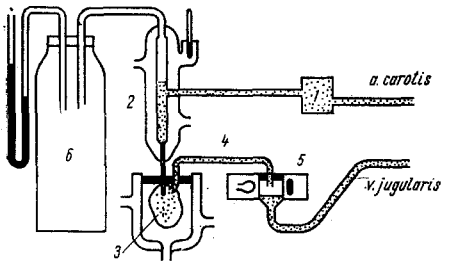

Fig. 1

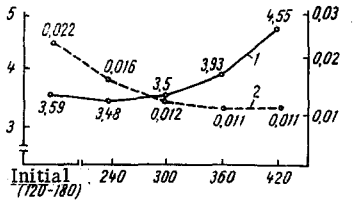

Fig. 2

Fig. 1. Diagram of apparatus for perfusion of the isolated rat heart under constant pressure with donor's blood: 1) pump; 2) vessel of small capacity with heating jacket; 3) heart in constant-temperature chamber; 4) tube draining blood from pulmonary artery; 5) photoelectric drop recorder; 6) damping vessel with control manometer.

Fig. 2. Dynamics of coronary blood flow per minute (1) and blood supply to isolated rat heart calculated per single contraction (2) with a change in heart rate under conditions of stabilized perfusion pressure. Abscissa, heart rate, beats/min; ordinate, on left, coronary blood flow (in ml/g per minute), on right, blood supply to heart calculated per single contraction (in ml/g per contraction).

about 2 ml in volume from which it passed to the blood vessels of the isolated heart, then to the drop recorder and, finally, back to the donor's jugular vein. A constant perfusion pressure was ensured by connecting the small chamber with a large damping vessel, the volume of which was 2 liters (Fig. 1). The output of the pump was regulated so that the blood level in the chamber remained practically the same. The heart rate was fixed by electrical stimulation. One electrode was the metal cannula in the aorta, the other a special needle fixed to the apex of the heart. Perfusion of the heart and oxygenation of the Krebs-Henseleit solution were carried out at a stabilized temperature (37°C).

EXPERIMENTAL RESULTS AND DISCUSSION

In 12 experiments in which the isolated rat heart perfused with oxygenated Krebs-Henseleit solution worked satisfactorily for several hours, a change in the heart rate within the range from 120 to 360 beats/min had virtually no effect on the outflow of perfusion fluid and, consequently, on the hydraulic resistance on the coronary vessels.

Presumably the absence of changes in hydraulic resistance of the coronary vessels with an increase in the heart rate is due to loss of their myogenic tone. However, an increase in the volume velocity of outflow of perfusion fluid following the injection of acetylcholine (10^{-7}) and papaverine (10^{-5}) into the perfusion fluid showed that the myogenic tone of the coronary vessels of the isolated heart remains sufficiently high under the conditions used in these experiments. Preservation of the myogenic tone of resistive blood vessels under similar conditions is also confirmed by the findings of Ushida and Bohr [12].

Vander Veen and Willebrands [13] concluded from their experiments in which the rat heart was perfused with oxygenated Krebs-Henseleit solution that an increase in the heart rate is accompanied by a proportionate increase in the oxygen consumption and the rate of outflow of perfusion fluid. However, analysis of the figure given by these workers shows that within the frequency range from 180-360 beats/min the rate of outflow of perfusion fluid, contrary to this conclusion, was virtually unchanged.

It can be postulated on the basis of these results that the quantity of oxygen dissolved physically in the perfusion solution is sufficient to satisfy the increasing demand of the heart, with an increase in its rate of contraction, as the result of an increase in the coefficient of oxygen extraction without any significant increase in the volume velocity of flow of the perfusion fluid. Evidence in support of this hypothesis is given by the experiments of Fisher and Williamson [8], who showed that if the heart is perfused with oxygenated saline, satisfaction of the oxygen demand sharply increased as the result of 2,4-dinitrophenol takes place by its more complete extraction, where the volume velocity of perfusion is not significantly altered.

These results show that the isolated rat heart preparation, perfused with oxygenated saline, is not a suitable object with which to study the relationship between the hydraulic resistance of the coronary vessels, on the one hand, and the oxygen consumption of the heart and its output on the other.

Accordingly, in the next series of six experiments the relationship between the blood supply of the heart and its rate of contraction were studied during perfusion of the coronary vessels with donor's blood under constant pressure.

It can be concluded from the results given in Fig. 2 that an increase in the rate of contraction of the isolated heart for the 120-180 to 300 beats/min is not accompanied by any significant change in the volume velocity of the blood flow. This conclusion at first glance is contrary to the results of other investigations [5, 9, 10] which showed that with an increase in the heart rate the coronary blood flow rises. It should be noted, however, that in these investigations which were conducted on dogs the heart rate was changed from near-normal values to values much above the typical level for this species of animal. In the present experiments on rat hearts the contraction rate was changed from values considerably below normal to the level characteristic for this species of animal. If, however, the isolated rat heart was made to contract at a higher rate (from 300 to 420 beats/min) the coronary blood flow would increase (Fig. 2).

An increase in the heart rate is thus accompanied by an increase in the coronary blood flow when the heart rate reaches the typical level for that particular species of animal and then exceeds it.

The coronary arterio-venous oxygen difference is known to be high at the normal heart rate, and the energy requirements of the myocardium which increase as a result of quickening of the heart rate are satisfied chiefly through an increase in the coronary blood flow.

In the present experiments the value of the coronary blood flow per single contraction of the isolated rat heart at first decreased progressively with an increase in the heart rate from a level much below normal to the level characteristic of this species of animal, and then remained constant (Fig. 2).

Stabilization of the blood supply to the heart calculated per single contraction (0.011–0.012 ml/g per contraction) was observed when the heart rate reached the normal level.

If the results obtained by other workers [4, 6, 7] in experiments on dogs with different heart rates are converted in the same way, it will be seen that in the animals of this species the blood supply to the heart is 0.009–0.012 ml/g per contraction. A similar calculation performed on the data of Torriggiani et al. [14] shows that the coronary blood flow in healthy persons and in patients with thyrotoxicosis is also about 0.01 ml/g per contraction.

It can therefore be postulated that the blood supply to the heart within a near-normal range of contraction rates is constant for animals of different species and for man, with a value of about 0.01 ml/g per contraction.

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