ROLE OF OXYGEN EXTRACTION FROM CORONARY BLOOD IN REGULATION OF THE MYOCARDIAL OXYGEN SUPPLY

E. B. Novikova and O. V. Tskitishvili

UDC 612.133.1:612.261]:612.127.2

KEY WORDS: coronary blood flow; coronary vascular tone; vasomotor regulation.

The oxygen supply to the myocardium is made to correspond to its load by vasomotor regulation, which varies with the coronary blood flow. Extraction of oxygen from the blood under these circumstances as a rule remains stable. An increase in extraction during adaptive reactions has been observed only during inadequate coronary perfusion, and, in particular, against the background of a stabilized coronary volume blood flow [8] or limitation of the expansion reserve of the coronary vessels [2]. However, it is not clear whether these changes are the result of an emergency situation, in which vasomotor responses are unable to maintain parity between the oxygen consumption and supply, or whether the extraction mechanism must be regarded as a physiological factor in the regulation of the myocardial blood supply. In that case, like any regulatory mechanism, its influence on the process cannot be confined to one direction only, but it must be activated in cases when the oxygen supply is adapted to conditions of reduced loading on the heart.

The aim of this investigation was to determine how oxygen extraction from the coronary blood changes in response to strengthening and weakening of cardiac activity in different states of vasomotor regulation.

EXPERIMENTAL METHOD

Experiments were carried out on mongrel dogs weighing 10-15 kg under pentobarbital anesthesia (35 mg/kg). The circumflex or anterior descending coronary artery was perfused through a glass cannula from the subclavian artery of the test dog or from the carotid artery of a donor dog. A cannula was introduced into the coronary sinus through the right atrium and tied there with a ligature. Blood from the sinus was returned through a transparent cuvette into the femoral vein. To determine the velocity of the coronary inflow and outflow, the flow detector of a "Biotronix" electromagnetic flowmeter or a bubble flowmeter of the authors' own design [3, 4] was used. Meanwhile the pressure in the left ventricle and right atrium, the coronary perfusion pressure and, in some cases, the cardiac output were recorded. The electromagnetic detector was placed on the pulmonary artery. The oxyhemogram of coronary venous blood was recorded synchronously with all the parameters, using the 036M oxyhemograph. The partial pressure of oxygen was determined in blood samples on a micro-Astrup apparatus (Radiometer, Denmark). A six-channel "Cardiovar-VI" electrocardiograph and a Mingograph-804 instrument were used as recorders. The load on the heart was varied by changing the heart rate. It was increased by electrical stimulation of the heart through an electrode inserted into the right atrium; it was slowed by stimulating the vagus nerves or changing the rhythm of electrical stimulation after destruction of the sinus node (ESL-2 stimulator). The state of the vasomotor regulation was altered by acting on the initial tone of the coronary vessels, the level of which was judged from the peak of reactive hyperemia after occlusion of the coronary artery for 10 sec. The tone was altered by varying the coronary perfusion pressure or the partial pressure of oxygen in the arterial blood.

EXPERIMENTAL RESULTS

The results of an experiment with electrical stimulation of the heart, increasing the heart rate from 150 to 320 beats/min (113%), are given in Fig. 1. During tachycardia the

All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR E. I. Chazov.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 95, No. 1, pp. 3-5, January, 1983. Original article submitted February 19, 1982.

0007-4888/83/9501-0001$07.50

outflow from the coronary sinus increased from 16 to 38.5 ml/min (140%). This increase in blood flow took place despite a fall of pressure in the left ventricle and, correspondingly, in the coronary perfusion pressure, for the coronary bed was under autoperfusion conditions. The oxyhemoglobin concentration in blood from the coronary sinus was virtually unchanged. There were only small fluctuations with a tendency toward an increase (2-4%). The increased oxygen demand of the heart was entirely satisfied by the increase in the coronary blood flow as a result of the vasomotor response. The expansion reserve of the coronary system in this experiment exceeded 200%. Proportional changes in the blood flow during quickening of the heart rate were observed previously [5], as also was a small decrease in extraction [9], which could be the result of a marked increase in the linear velocity of the blood flow in the capillaries and a decrease in the time required for oxygen diffusion. Comparison of the effects of tachycardia, with different levels of initial coronary vascular tone, showed that correlation between the heart rate and blood flow weakens with a decrease in tone. With a decrease in the peak of reactive hyperemia from 150 to 80% the coefficient of correlation r decreased from 0.84 to 0.47 and the coefficient b in the regression equation decreased from 0.34 to 0.12. During gradual weakening of the vasomotor responses the oxygen concentration in the coronary venous blood began to fall. The effect of tachycardia during reactive hyperemia, amounting to 100%, is shown in Fig. 2. Quickening of the heart rate from 90 to 200 beats/min (122%) caused an increase in blood flow in the circumflex coronary artery perfused from a donor from 11 to 14 ml/min and a decrease in the oxygen concentration in blood from the coronary sinus from 48 to 22%. Although the expansion capacity of the coronary vessels was not completely exhausted, tachycardia led to utilization of the oxygen reserve.

It is not clear what caused replacement of vasomotor regulation under these conditions in extraction. It can be tentatively suggested that the fall in tone of the vessels located in different layers of the myocardium took place unequally. This suggestion is supported by results showing that during tachycardia, against the background of initial dilatation of the coronary system, the ratio of the endocardial blood flow to the epicardial flow falls progressively [6, 7]. Vessels of the outer layers evidently preserve their ability whereas vessels of the inner layers lose it. Reactive hyperemia gives only the mean overall characteristics of the expansion reserve of all vessels in the territory studied. The coronary venous outflow similarly contains blood from vessels that differ in tone and oxygen level. The changes in oxygen extraction revealed by the experiments evidently arise in response to a combination of increased oxygen demand with loss of their expansion reserve by vessels of a smaller or greater part of the myocardium, and they are thus compensatory.

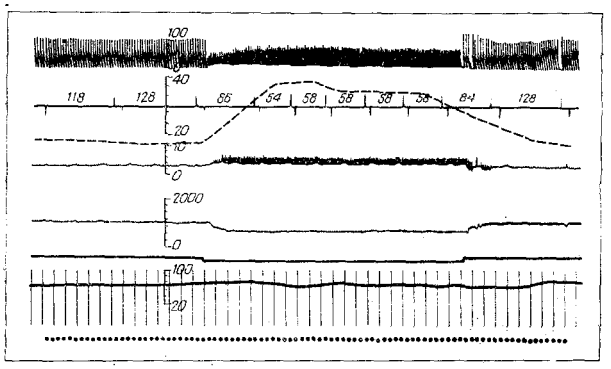

Fig. 1. Effect of tachycardia on velocity of coronary blood flow and oxygen concentration in coronary venous blood under normal conditions. From top to bottom: pressure in left ventricle (in mm Hg); rate of outflow of blood from coronary sinus: numbers between pulses of bubble flowmeter represent time (in sec) during which 3.4 ml of blood flows; broken line represents velocity of coronary blood flow (in ml/min); pressure in right atrium (in mm Hg); velocity of blood flow through pulmonary artery (in ml/min); marker of electrical stimulation; oxyhemogram of blood flowing from coronary sinus.

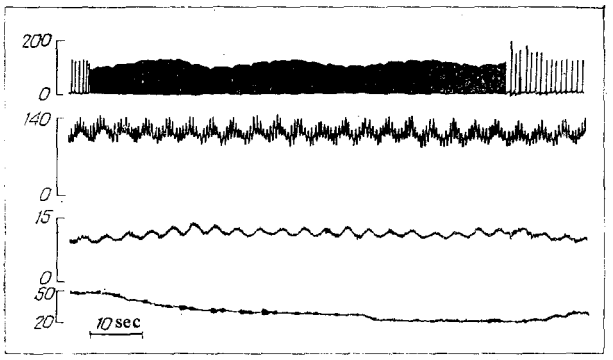

Fig. 2. Effect of tachycardia on velocity of coronary blood flow and oxygen concentration in coronary venous blood after reduction of coronary expansion reserve. From top to bottom: pressure in left ventricle (in mm Hg); coronary perfusion pressure (in mm Hg); velocity of inflow into circumflex coronary artery (in ml/min); oxyhemogram of blood in coronary sinus.

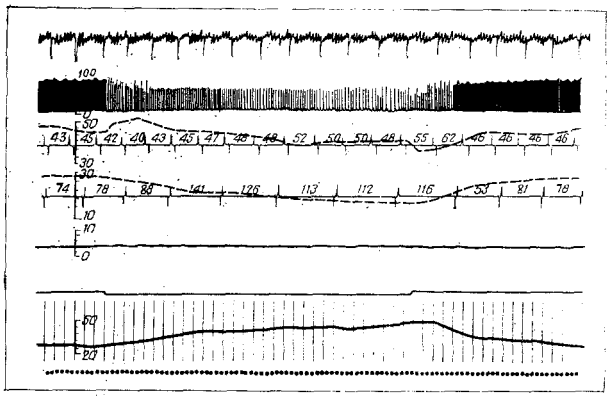

Fig. 3. Effect of slowing of the heart on velocity of coronary blood flow and oxygen concentration in coronary venous blood after reduction of coronary expansion reserve. From top to bottom: coronary perfusion pressure (in mm Hg); pressure in left ventricle (in mm Hg); velocity of inflow into circumflex coronary artery and outflow from coronary sinus (Fig. 1); pressure in right atrium (in mm Hg); marker of stimulation of right vagus nerve; oxyhemogram of coronary venous blood.

However, investigations of extraction during slowing of the heart rate showed that this activation of the extraction mechanism can also be observed when there is no need for additional oxygen.

During fully effective vasomotor regulation, provided by the large expansion reserve of the coronary system, slowing of the heart led to construction of the coronary vessels and to a proportional reduction in blood flow. However, even with a very small decrease in initial tone, the effect of bradycardia changed. The result of an experiment in which slowing the heart rate from 200 to 100 beats/min was caused by stimulation of the right vagus nerve (12 V, 15 Hz) is given in Fig. 3. During bradycardia the blood flow in the circumflex coronary artery, perfused from a donor animal, decreased from 45.5 to 41 ml/min (10%), whereas the outflow from the coronary sinus decreased from 27.6 to 17.2 ml/min (37%). The reason for the greater change in outflow was that, besides an increase in coronary resistance, the fall of pressure in the left ventricle, on which the perfusion pressure in that part of the coronary system that was under autoperfusion conditions depended,

also affected it. During the effect of bradycardia the oxygen concentration in the coronary venous blood rose from 34 to 50%. Reactive hyperemia in this case was about 70%. Since the level of vascular tone is not the limiting factor for a decrease in oxygen supply, it can be postulated that the fall of tone affects the sensitivity of the coronary microvessels to the tissue oxygen level. Possibly the most sensitive arterioles, closest to the capillaries, are the first to be excluded from local regulation of the blood flow during a fall in tone of the coronary vessels. The residual expansion reserve will be exhibited by vessels of larger diameter. Vasodilatation also may lead to the opening of pathways with a lower resistance and may give rise to functional shunting of the blood, as a result of which it will pass through fewer nutritive capillaries [1]. As a result the accuracy of vasomotor regulation is reduced and the oxygen supply will be changed on account of its movement along the concentration gradient. This mechanism may perhaps operate not only when the oxygen demand of the heart decreases, but also when it increases.

The results show that the extraction mechanism for changing the oxygen supply to the myocardium may be activated at a comparatively early stage of depression of the coronary expansion reserve and may participate in local regulation simultaneously with the vasomotor mechanism.

LITERATURE CITED

1. E. M. Ginzburg, L. I. Serebryakova, A. V. Mazaev, et al., Kardiologiya, No. 8, 97 (1980).
2. E. B. Novikova, Vestn. Akad. Med. Nauk SSSR, No. 1, 76 (1980).
3. S. A. Yur'ev and E. B. Novikova, Kardiologiya, No. 1, 79 (1965).
4. S. A. Yur'ev, Biofizika, No. 1, 184 (1965).
5. H. S. Badeer, Acta Cardiol., 18, 356 (1963).
6. R. M. Ball and R. J. Bache, Cir. Res., 38, 60 (1976).
7. L. Becker, Am. J. Physiol., 230, 1072 (1976).
8. P. Somani, A. R. Laddu, and H. F. Hardman, J. Pharmacol. Exp. Ther., 175, 577 (1970).
9. H. R. Weiss, Am. J. Physiol., 236, H231 (1979).