EFFECT OF ENDOTHELIUM-DEPENDENT STABILIZATION OF THE PRESSURE DROP IN SMALL ARTERIES

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UDC 612.143.014.49

KEY WORDS: endothelium-dependent vasodilatation; pressure gradient stabilization; small arteries

According to the generally accepted view, the resistance of arteries carrying blood to organs is low and likewise it undergoes only minor changes during both constriction and dilatation of the intramural vascular bed [8]. However, this view is unacceptable in view of the large number of times by which the blood flow can be increased. For instance even at rest, the average pressure in the femoral artery of cats is ~10% lower than the average pressure in the arch of the aorta [7]. Hence it is clear that for a fivefold increase in flow rate, as is the case during heavy muscular work, arteries cannot always behave simply as passive tubes, the pressure drop in which is proportional to the blood flow.

In experiments on rats the pressure drop of blood was measured during its movement from the arch of the aorta to the distal end of a comparatively small artery, in order to discover the effect of self-stabilization of the pressure drop during changes in blood flow [3]. This effect indicates the high powers of adaptation of the afferent arteries. The aim of this investigation was to continue the study of this effect on a single vessel, namely the rat saphenous artery.

EXPERIMENTAL METHOD

Experiments were carried out on 14 Wistar rats weighing 350-450 g, anesthetized with pentobarbital (50 mg/kg). Blood clotting was prevented in injection of heparin (1500 U/kg intravenously).

The scheme of the principal experiments is shown in Fig. 1. A cannula 6 was inserted into the distal end of the left saphenous artery 1 (internal diameter 0.3 mm), and blood from it was pumped through an electromechanical flow control system 5 into the right femoral vein. The design of the apparatus was described previously [2]. In the experiments of series I a cannula was inserted into the superficial epigastric artery 2 in order to record pressure in the proximal end of the saphenous artery. The popliteal artery 3 was ligated. The pressure in the distal end of the saphenous artery was recorded through a thin polyethylene tube 7, which was passed into the artery through the lumen of the cannula 6. The pressure drop on the saphenous artery was measured with a differential-manometric pressure transducer 8 (DMI-06). The systemic pressure was recorded by means of a W102 RFT electromanometer (East Germany), connected to a catheter passed through the brachial artery to the arch of the aorta.

EXPERIMENTAL RESULTS

The characteristic curve of changes in the pressure drop (P) on the saphenous artery in response to a stepwise increase in the blood flow (Q) in it is given in Fig. 2a. During a stepwise increase in blood flow the pressure drop on the saphenous artery rose sharply, but after 5-6 sec it began to fall, and reached a new stationary value after ~20 sec, which was only a little higher than the initial value. On the basis of these characteristic times of development of the response of the vessel, we investigated the quasistatic relationship between blood flow and pressure drop (Q–P). For this purpose, the blood flow was

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 0007-4888/89/0006-0750$12.50 © 1989 Plenum Publishing Corporation

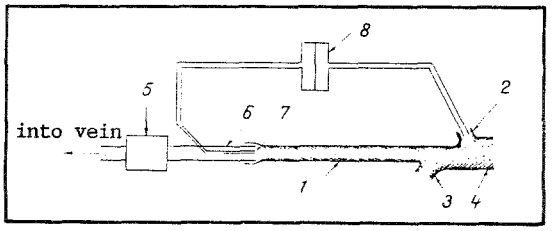

Fig. 1. Scheme showing experimental method. 1) Saphenous artery; 2) superficial epigastric artery; 3) popliteal artery; 4) femoral artery; 5) flow control system; 6) outlet cannula; 7) thin polyethylene tube; 8) differential-manometric transducer.

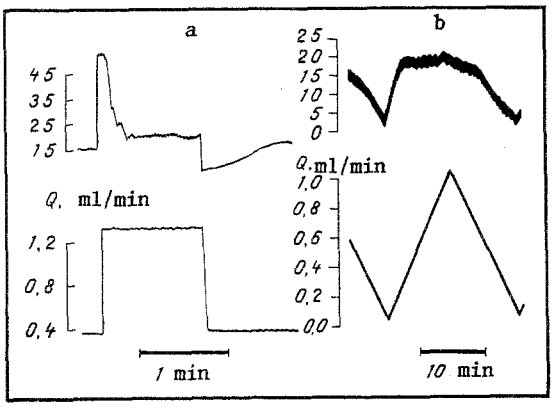

Fig. 2. Changes in pressure drop P on saphenous artery during rapid stepwise (a) and slow "sawtooth" (b) changes in blood flow. From top to bottom: pressure drop, mm Hg; blood flow (in ml/min). Time marker: for a – 1 min, for b – 10 min.

increased slowly (over a period of 10 min) at a constant rate from 0 to 1 ml/min. The characteristic trace of one experiment is given in Fig. 2b. The bottom curve represents blood flow in the saphenous artery (in ml/min), the top curve represents blood flow in the saphenous artery (in ml/min), the top curve the pressure drop in the same artery (in mm Hg). Nonzero values of the pressure drop on the artery when the blood flow as arrested are due to the existence of a small "leakage" flow through branches of the saphenous artery. Clearly, there exists a region of blood flows in which the pressure drop rises proportionally to flow (Q from 0 to 0.30 ± 0.05 ml/min; n = 11) and a region of stabilization of the pressure drop (Q > 0.3 ml/min), in which the artery adapts itself to changes of blood flow by changing its own lumen. To discover the relationship between these regions with physiological values of blood flow in the saphenous artery, an additional series of experiments was carried out. A flowmeter [6], consisting of a segment of polyethylene tube (internal diameter 0.76 mm, length 5 mm), with side tubes welded to it in order to measure the pressure drop on the tube, was inserted into the femoral artery. The value of this pressure drop, reached by a DMI-06 transducer, characterized the blood flow in the femoral artery. To calibrate the flowmeter, at the end of each experiment its distal end was connected to the flow control system [2], so that the recorded pressure drop could be correlated with the blood flow in the femoral artery. During rapid compression of the distal end of the saphenous artery the blood flow in the femoral artery fell sharply by 0.3-0.35 ml/min (n = 3), i.e., by the value of the blood flow in the saphenous artery. The background blood flow in this artery, estimated by this method (0.3-0.35 ml/min), corresponded to the beginning of the region of stabilization of the pressure drop (Fig. 2b).

The study of the mechanisms of adaptation of comparatively large arteries of cats and dogs to changes in blood flow [1, 4] confirmed the following view of the mechanism of this response [10]. Increase in blood flow in artery → increase in shear stress on endothelium →

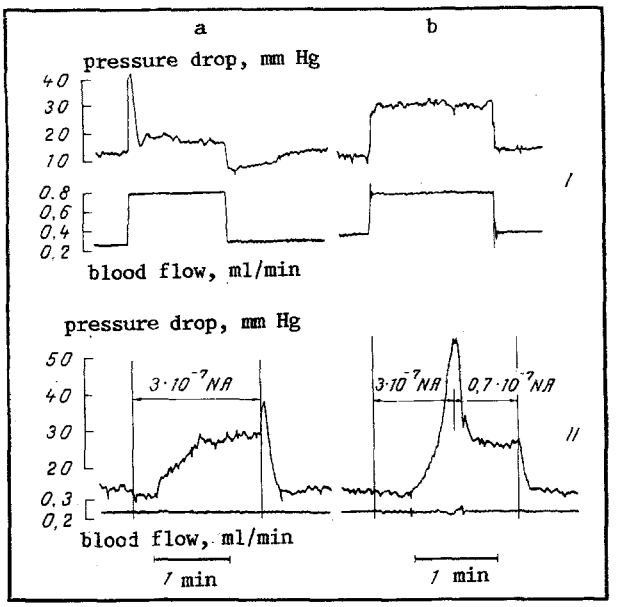

Fig. 3. Response of saphenous artery to stepwise changes in blood flow (I) and intra-arterial injections of noradrenalin solution (II) before (a) and after (b) functional injury to the endothelium. In I and II below: pressure drop (in mm Hg), blood flow (in ml/min). Arrows indicate time of intra-arterial injection of noradrenalin, showing its concentration in blood flowing through the artery. Time marker 1 min.

increase in its deformation → increased synthesis by endothelial cells of a factor inducing relaxation of the muscular coat of the artery. To determine the role of the endothelium in the case of the saphenous artery in rats, we used functional inactivation of endotheliocytes, by exposing the intima of the vessels briefly to a 0.3% solution of H_2O_2 [9]. In these experiments the pressure in the proximal end of the saphenous artery was recorded through a cannula introduced into the popliteal artery. The catheter introduced into the superficial epigastric artery was used initially to wash out the blood from the saphenous artery with physiological saline, and then to inject the H_2O_2 solution into it in the course of 60 sec. After resumption of the blood flow, a solution of noradrenalin was injected through this same catheter in order to detect the degree of preservation of contractility of the artery.

The results of one experiment are given in Fig. 3. Control traces are shown on the left. Changes in pressure drop on the artery during a stepwise change of blood flow are shown above. The response of the vessel in intra-arterial injection of noradrenalin (blood concentration $3 \cdot 10^{-7}$ g/ml) is shown below. Corresponding curves obtained after passage of 0.3% H_2O_2 through the vessel shown on right. The response of stabilization of the pressure drop disappeared completely, whereas sensitivity to noradrenalin actually increased. Other investigators have observed the same phenomenon [11]. This result suggests that in the artery tested, the endothelium plays a role in the mechanism of adaptation to the blood flow. The degree of adaptation to changes in blood flow in arteries of other orders and of other species of animals requires further study. All that can be suggested at present is that the following phenomena are linked with the effect of stabilization of the pressure gradient in arteries which has been discovered: 1) maintenance of a high reserve of growth of blood flow in intensively working organs; 2) stabilization of pressure in certain parts of the vascular bed despite a change of blood flow, which is very important for the resistive and, in particular, for the exchange regions of the vascular bed; 3) maintenance of the phase of rapid closure of blood flow collaterals when the main pathways are occluded [5]. If the effect also is manifested at the level of the smallest arteries, this will reveal its important role in the regulation of the resistive part of the vascular bed.

LITERATURE CITED

1. A. M. Mel'kumyants, E. S. Veselova, and V. M. Khayutin, Byull. Éksp. Biol. Med., No. 8, 7 (1981).
2. V. P. Nikol'skii and A. N. Rogova, Byull. Éksp. Biol. Med. (in press).
3. V. P. Nikol'skii, A. N. Rogova, and V. M. Khayutin, Byull. Éksp. Biol. Med. (in press).
4. V. Smieshko, V. M. Khayutin, M. Gerova, et al., Fiziol. Zh. SSSR, No. 2, 596 (1979).
5. V. M. Khayutin, Control of Activity of Visceral Systems [in Russian], Leningrad (1983), pp. 180-195.
6. R. A. Jaffe and M. J. Free, J. Appl. Physiol., 32, No. 4, 571 (1972).
7. E. Kanzow, Y. Yansen, and D. Dieckhoff, in: Vascular Smooth Muscle, E. Betz (ed.), Berlin (1972), pp. 80-83.
8. M. F. O'Rourke, Arterial Fucntion in Health and Disease, Edinburgh (1982).
9. U. Pohl, J. Holtz, R. Busse, et al., Hypertension, 8, No. 1, 37 (1986).
10. S. Rodbard, Perspect. Biol. Med., 13, 507 (1970).
11. C. Verrecchia, R. Sercombe, and J. Seylaz, Clin. Exp. Pharmacol. Physiol., 12, No. 2, 169 (1985).

STATE OF THE OXYGEN TRANSPORT FUNCTION OF BLOOD IN RABBITS WITH HYPERTHERMIA

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UDC 616.152.21-092:612.57]-092.9-07

KEY WORDS: hyperthermia; affinity of hemoglobin for oxygen; oxyhemoglobin dissociation curve

When the mechanisms ensuring a balance between the oxygen demand of an organism and its demand during the development of exogenous hyperthermia are studied, most attention has been paid to the investigation of the circulation and respiration [1, 2]. The study of the acid-transport function (ATF) of blood has been reduced to determination of the partial pressure (pO_2) and concentration (cO_2) of oxygen and the degree of saturation of the arterial and venous blood with oxygen (sO_2) [1, 10]. The affinity of hemoglobin for oxygen has not actually been determined during hyperthermia, although the possible position of the oxyhemoglobin dissociation curve (ODC) and the effect of factors responsible for its shift under these circumstances have been discussed. The state of the ATF of the blood during the first few hours after the end of exposure to heat has received even less study.

The aim of this investigation was to determine parameters characterizing ATF of mixed venous blood, including the affinity of hemoglobin for oxygen (P_{50}), in different phases of hyperthermia.

EXPERIMENTAL METHOD

Exogenous hyperthermia was simulated in 25 noninbred rabbits of both sexes weighing 2.5-3.5 kg. Under ether anesthesia a catheter was introduced through the jugular vein into the right atrium. The position of the catheter was verified after the experiment at autopsy. The rabbit's rectal temperature was measured 1 h after recovery from the anesthetic and an initial blood sample was taken. The animals were placed in a heat-insulated chamber, which was supplied with hot air, but their movements were in no way restricted. Heating took place under conditions of controlled hyperthermia: In the course of 30-45 min the body temperature rose to 42°C, at which level it was maintained for the next 30-45 min, after which the animal

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0007-4888/89/0006-0753$12.50 © 1989 Plenum Publishing Corporation