ADAPTIVE FUNCTION OF THE SYMPATHETIC INNERVATION OF THE CEREBRAL VESSELS DURING RAPID CHANGES IN SYSTEMIC ARTERIAL PRESSURE

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UDC 612.181.4-06:612.143

KEY WORDS: adaptation; hemorrhage; hypotension; hypertension; reinfusion.

One aspect of the problem of regulation of the cerebral circulation that is not yet quite clear is the functional role of postganglionic sympathetic fibers from the superior cervical ganglion which run toward the cerebral vessels. Detailed histological data are available on the adrenergic efferent innervation of different parts of the cerebral vascular bed [7]. However, opinions on the function of this vascular innervation vary from the complete rejection of its role in the regulation of the cerebral blood flow [12] to acceptance of a nervous-reflex mechanism as the only regulator of the cerebral circulation during falls of systemic arterial pressure and changes in the blood gas composition [14].

It has been suggested [3, 13] that the sympathetic innervation of the cerebral vessels may be important in protection of the blood vessels during a rapid rise of arterial pressure. In sudden arterial hypertension stretching of the cerebral vessels by the increased intravascular pressure disturbs the close connections between the endothelial cells of these vessels and may cause edema or rupture of the blood–brain barrier [10]. An increase in the sympathetic vasoconstrictor tone may prevent such disturbances [6, 9]. It should be pointed out that these facts are in agreement with Orbeli's views [4] on the adaptive influence of the sympathetic nervous system on organs and tissues.

The object of this investigation was to study the role of the sympathetic innervation of the cerebral vessels in widening the range of adaptation of the cerebral circulation in arterial hypertension.

If an increase in the systemic arterial pressure is created against the background of self-regulating dilatation (relaxation of the walls) of the cerebral vessels after hemorrhagic hypotension, a serious disturbance of the cerebral circulation or even hemorrhages into the brain tissue can evidently be expected. During hypotension, however, reflex activation of the sympathetic nervous system should also be expected. This determined the approach used to study the problem, which included histological analysis of disturbances of the cerebral circulation in desympathized and intact cerebral hemispheres after corresponding hemodynamic loads.

EXPERIMENTAL METHOD

Experiments were carried out on rats of both sexes weighing 200-300 g, under superficial ether anesthesia. The blood pressure was measured by means of an electromanometer through a cannula introduced into the brachial artery. The cerebral vessels were desympathized by unilateral removal of the superior cervical ganglion.

In series I hemorrhagic hypotension was created in four animals by withdrawing 2-2.5 ml of blood into a syringe connected to a catheter in the abdominal aorta. The arterial pressure was lowered in the course of 20-30 sec from its initial level (100 ± 5 mm Hg) to 40 ± 5 mm Hg, after which it was raised by rapid reinfusion of blood to 145 ± 7 mm Hg.

In series II (four rats) hypertension was created without preliminary hypotension by injection of 2-2.5 ml of dextran into the abdominal aorta.

Laboratory of Physiology of the Cerebral Circulation, Professor A. L. Polenov Leningrad Neurosurgical Research Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. N. Chernigovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 90, No. 11, pp. 543-546, November, 1980. Original article submitted March 17, 1980.

 0007-4888/80/9011-1510$07.50

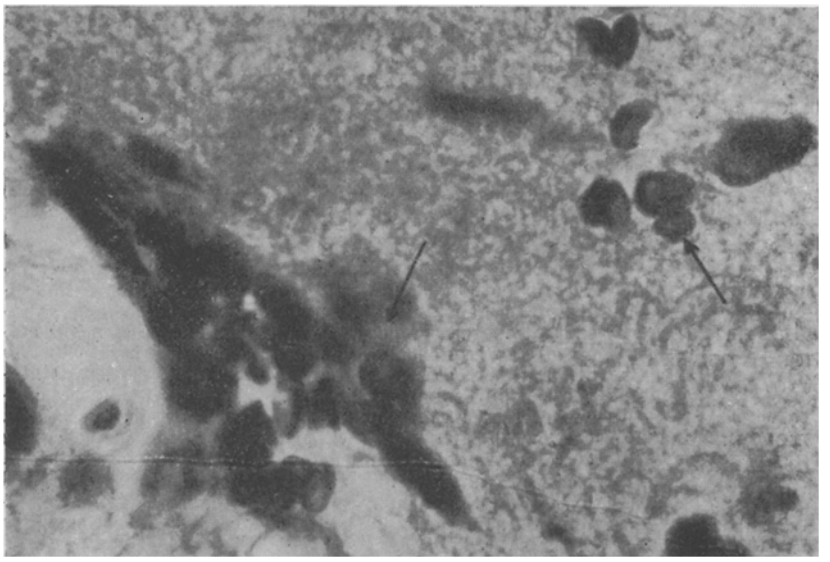

Fig. 1. Multiple tiny hemorrhages in the parietal cortex of the desympathized cerebral hemisphere of a rat: erythrocytes (arrows) in brain tissue. Hematoxylin–eosin, 1200×.

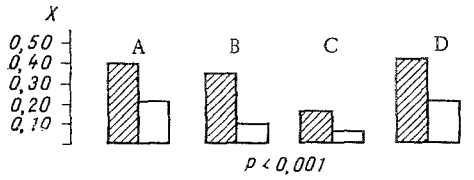

Fig. 2. Mean number of hemorrhages ($\bar{X}$) per histological section in desympathized (shaded columns) and innervated (unshaded columns) rat cerebral hemispheres. A) In whole hemisphere; B) in frontal lobe; C) in temporal lobe; D) in parietal lobe.

In series III (control) the only intervention was removal of the superior cervical ganglion on one side.

In the experiments of series I and II the systemic arterial pressure was measured not earlier than 1 h after removal of the superior cervical ganglion.

At the end of the experiment the animals were killed by injection of ether into the heart. The brain was fixed in 10% formalin solution and then embedded in paraffin wax. Serial sections, 10-15 μ thick, were stained with hematoxylin–eosin, and every 10th section was studied.

EXPERIMENTAL RESULTS

In the two experimental series, an increase in size of the perivascular spaces and some loosening of the structure of the brain tissue around the parenchymatous vessels were observed in the rostromedial portions of the rat brain. Hemorrhages were found only in series I (with preliminary hypertension). Injury to the vessel walls was found in the arteriolar system. The hemorrhages were mainly diapedetic in character (Fig. 1). The greatest disturbance of the cerebral circulation occurred in the precapillary and capillary systems. The mean number of hemorrhages in the denervated and intact cerebral hemispheres is shown in Fig. 2.

In the denervated half the mean number of hemorrhages per histological section (0.393) was twice that on the intact side (0.200). In all regions of the denervated half of the brain, where hemorrhages were present, their mean number was significantly higher than in

the corresponding regions on the innervated side. The largest number of hemorrhages was observed in the rostromedial region of the brain at the junction of the frontal, temporal, and parietal lobes; no hemorrhages were observed in the brain stem and in the occipital lobes.

In control experiments operative trauma during dissection and removal of the superior cervical ganglion did not lead to injury to the brain tissue or to disturbance of the integrity of the vessel wall.

During a fall of systemic arterial pressure (experiments of series I), caused by artificial hemorrhage, self-regulatory dilatation of the cerebral vessels and simultaneous reflex activation of the sympathetic nervous system should be expected [2]. It has been shown [8] that the self-regulation curve during hemorrhagic hypotension in the desympathized half of the brain is shifted to the left. Consequently, vascular tone in the innervated half of the brain during hemorrhagic hypotension, when considerable activation of the sympathetic nervous system takes place, is higher than the vascular tone of the desympathized half.

The number of hemorrhages in the denervated half of the brain, which was twice that in the intact half, is evidence that the sympathetic innervation of the cerebral vessels is of great physiological importance for widening the range of adaptive powers of the vessel wall in the cerebrovascular system in response to a rapid rise of systemic arterial pressure — the self-regulation curve is shifted to the right.

In series II (without preliminary artificial hemorrhage) the initial vascular tone in both the intact and the desympathized half of the brain was higher than in series I; the vascular bed of the brain could withstand systemic hypertension without disturbance of the integrity of the vessel walls. In this case unilateral desympathization itself (without subsequent activation of the sympathetic nervous system) did not lead to any significant difference in the resistance of the blood vessels of the two halves of the brain in response to arterial hypertension. This is in agreement with the view [11] that the background sympathetic tone of the cerebral vessels is unimportant.

The ability of the cerebral vessels to produce self-regulatory responses of a change in perfusion resistance to sudden hypertension thus depends on their initial tone. The possibility cannot be ruled out that in some special circumstances, when vascular tone in one or other region of the brain is sufficiently high and the sensitivity of the blood vessels in that region to catecholamines is increased, its response to hypertension accompanied by increased sympathetic activation may be spasm.

The different number of hemorrhages in different regions of the brain (Fig. 2) can be explained both by the different density of the sympathetic innervation and by the different thickness of the vessel walls [1, 7]. These same circumstances can evidently also explain why the perfusion resistance of the somatic vessels in response to direct stimulation of sympathetic nerves increases several times more than the perfusion resistance of the cerebral vessels [5].

The varied and contradictory opinions expressed in the literature on the function of the sympathetic innervation of the cerebral vessels can perhaps be explained on the grounds that the contribution of background activity of the sympathetic nervous system to the creation of the tone of the walls of the cerebral circulation corresponding to an average level of systemic arterial pressure is unimportant, and only preliminary natural or artificial enhanced activation of the sympathetic nervous system can reveal the adaptive character of its influence on regulation of the cerebral blood flow in response to subsequent hemodynamic loads.

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CHANGES IN OXYGEN SUPPLY LEVELS IN RATS AFTER EXCHANGE BLOOD TRANSFUSION WITH PERFLUORODECALIN EMULSION

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UDC 615.384.015.4:612.26

KEY WORDS: blood gases; oxygen consumption; organofluorine emulsions; perfluorodecalin.

The creation of oxygen-transporting blood substitutes on the basis of organofluorine compounds (OFC) is attracting the attention of scientists in different countries [4]. The use of OFC for these purposes is dependent on their chemical inertness and increased ability to dissolve oxygen and other gases [11]. Usually OFC emulsions are studied on the whole organism or on isolated organs. However, the problem of the adequacy of the oxygen supply to the whole organism or to a perfused organ actually on account of the OFC emulsion is most frequently avoided and indirect indices are used in the calculation: the period of survival of the animals, the secretory function of the organ, and other indices [9, 10].

The object of the present investigation was to study the oxygen supply to the whole organism during exchange blood transfusion in rats with perfluorodecalin (PFD) emulsion. On the basis of these data the oxygen-transport properties of this medium can be assessed.

EXPERIMENTAL MATERIALS AND METHODS

Emulsions were obtained by an ultrasonic method using centrifugation to remove large particles. A 5% solution of a copolymer of ethylene oxide and propylene oxide, containing 0.15 M NaCl, was used as the emulsifier.

The PFD content in the emulsions was 20 ± 1 vol. %. The relative viscosity was lower than that of blood, namely 2.8 ± 0.5 cP; the concentration of the fluorine ion in the emulsions varied between limits of $0.6 \cdot 10^{-4}$ and $5.5 \cdot 10^{-4}$ M. The mean particle diameter in the different samples of PFD emulsions did not exceed 0.22-0.25 μ. The pH of the emulsions immediately before the beginning of the biological experiment was corrected by sodium bicarbonate solution to 7.4. The value of LD_{50} of the PFD emulsions was determined in experiments on albino mice and calculated by the method of Miller and Tainter [1].

Indices of the oxygen supply to the body were determined in acute experiments using a model of exchange blood transfusion in rats anesthetized intraperitoneally with sodium hydroxybutyrate (800 mg/kg) mixed with hexobarbital (40 mg/kg). Exchange transfusion was carried out by means of a hand-operated perfuser, pumping blood from the femoral artery and injecting emulsion synchronously into the femoral vein at the rate of 0.5-1 ml/min.

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