CHANGES IN MORPHOMETRIC PARAMETERS OF THE CEREBRAL MICROCIRCULATION IN EXPERIMENTAL HYPERTENSION

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KEY WORDS: cerebral microcirculation; hypertension.

In hypertension vascularization in various tissues is reduced: in muscle, skin, mesentery, the sclera of the eye, etc. [5-7]. A decrease in the density of the vascular network of the brain has been found in hypertensive rats, together with a decrease in the number of capillaries in the cerebral cortex of persons with essential hypertension [1, 2]. The decrease in density of the vascular network in the brain may lead to the formation of ischemic zones in brain tissue which, in turn, cause activation of the sympathetic system [2]. The development of ischemia in the brain stem is known to be a powerful factor activating the sympathetic system. Accordingly the further study of cerebral vascularization in hypertension is of great importance.

The aim of this investigation was to make a more detailed study of the reduction in density of microvessels in the brain stem by hypertensive rats. Special attention was paid to the study of the distribution of vessels of different caliber in the brain of hypertensive animals compared with normal.

EXPERIMENTAL METHOD

Histological sections through the brain stem of spontaneously hypertensive rats (SHR) and also of rats with experimental renal hypertension (RHR) [4], weighing 190-250 g, were studied. In the course of the experiment the arterial pressure (BP) was measured in the caudal artery by an eletroplethysmographic method.

The cerebral vessels of animals anesthetized with hexobarbital (100 mg/kg body weight, intraperitoneally) were injected intravitally with ink, after preliminary dialysis against Tyrode's physiological saline. Immediately before the experiment heparin was added to the ink in a concentration of 100 IU/ml ink. The injection was given through the ascending aorta under a pressure corresponding to BP of each animal, over a period of 3 min. The brain was then removed, fixed, and embedded in celloidin. Serial sections 20 μm thick were cut from the celloidin block. Unstained cleared sections alternated with sections stained with cresyl violet. The degree of filling of the vessels with ink was monitored in unstained sections 100 μm thick. Unstained sections 20 μm thick were studied by the TAC texture analysis system (Ernst Leitz, West Germany). A television picture of the preparation studied was analyzed by a specially devised program, whereby the total area of the vessels, their total length, the number of fragments of vessels in the field of vision, the area and length of vessels of a given diameter, the area of the field in which the measurement was made, the relative length of the vessels (per unit volume of tissue), and the mean diameter of the vessels could be determined simultaneously [3]. The results were subjected to statistical analysis and printed out in digital and graphic form. In this investigation microvessels under 15 μm in diameter were studied.

EXPERIMENTAL RESULTS

Intracerebral microvessels were studied in hypertensive rats with stable systolic BP of 155-165 mm Hg. BP of the control rats was 100-120 mm Hg. The experimental results are given in Table 1.

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TABLE 1. Changes in Morphometric Parameters of Cerebral Microcirculation in Hypertensive Rats (M ± m)

Group of animals	Number of preparations	Number of fields measured	Mean number of fields in preparations	Relative length of vessels, mm/mm³	Diameter of vessels, μm	Area of vessels/area of field, %
Control	48	1909	40±1,6	544±12,7	7,9±0,25	7,96±0,22
SHR	35	1650	47±2,1	459±15	6,96±0,27	6,0±0,2
P				<0,001	<0,05	<0,001
RHR	42	1513	36±1,0	468,8±9,2	7,2±0,26	6,25±0,13
P				<0,001	<0,05	<0,001

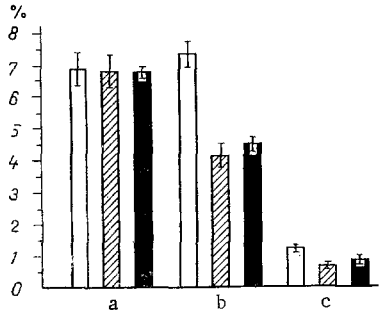

Fig. 1. Distribution of areas of microvessels of different diameters in brain of control and hypertensive rats: a) vessels under 5 μm in diameter, b) vessels from 6 to 10 μm in diameter, c) vessels from 11 to 15 μm in diameter. Unshaded columns – control, obliquely shaded – SHR, black columns – RHR.

The microvascular network of the hypertensive animals had lower density, as shown by a decrease in relative length of the vessels. This decrease in SHR was 15.6%, whereas in RHR the relative length of the microvessels was reduced by 13.8% compared with the control. The ratio of the area of the vessels to the area of the field in which the measurement was made was considerably reduced under these circumstances: In SHR the ratio was 24.6% less, and in RHR 21.5% less than in the control; a decrease in the mean diameter of the microvessels also was observed: by 11.9 and 8.9% respectively.

Thus in both spontaneous and experimental renal hypertension, the characteristics studied showed changes in the same direction.

Analysis of the distribution of the area of the vessels studied depending on their caliber showed that the fraction of vessels 6-10 μm and 11-15 μm in diameter per unit volume of tissue (Fig. 1) was reduced, possible evidence that some of these vessels were excluded from the circulation. If this exclusion was complete, the smaller vessels supplied by these vessels must also have been excluded. However, as will be clear from the diagram in Fig. 1a, the fraction of the smallest vessels (under 5 μm in diameter) was unchanged. If the possibility of complete exclusion of vessels over 5 μm in diameter is ruled out, it must be suggested that the decrease in the fraction of these vessels took place on account of a decrease in their diameter and, consequently, their transfer into a category of vessels with smaller caliber (under 5 μm). This, in turn, should have led to an increase in the fraction of vessels under 5 μm in diameter. Since the total area of these vessels remained unchanged, a certain proportion of them evidently became closed and completely excluded from the circulation. The fact will be noted that this process of exclusion of small vessels in both spontaneous and renal hypertension was limited to a certain minimal level, corresponding to the control. This may indicate that even under pathological conditions, the number of functioning vessels of small caliber is kept constant.

The results thus confirmed the fact described previously, that the density of the vascular network is reduced in hypertension. It must be pointed out that in this series of experiments the degree of reduction in den-

sity was not as great as was described previously. However, the fact that there was a change in the vascular network in an investigation conducted by the method of examination of preparations which we adopted, confirms the previous results. Our data indicate some specific structural changes in the vessels in hypertension. The structural changes observed can evidently be explained by two processes: a decrease in caliber of the vessels and complete closing of some arterioles and capillaries. The change in the vascular network is an important fact which must evidently affect the pathogenesis of hypertension.

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CHANGES IN PULMONARY MICROVESSELS OF RATS WITH BRONCHIOLO-ALVEOLAR FIBROSIS INDUCED BY INTRABRONCHIAL INJECTION OF TRYPSIN

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The interest of research workers has recently been drawn to interstitial diseases of the lungs (IDL), which are characterized by diffuse septo-alveolar fibrosis and alveolitis [6, 10]. All IDL are characterized not only by immunopathological processes of various kinds [6, 9], but also by systemic lesions of the microcirculation and the development of an alveolar-capillary block, which is the cause of the patients' death [8, 10]. Meanwhile the histogenesis of these lesions and, in particular, relations between specific (immunopathological) and nonspecific (regenerative) changes in the microvessels in IDL has not been adequately studied.

It was accordingly decided to study changes in the microvessels of the lungs in experimental bronchiolo-alveolar fibrosis induced by intrabronchial injection of trypsin.

EXPERIMENTAL METHOD

Experiments were carried out on 35 noninbred albino rats of both sexes weighing 260-320 g, into which 0.5 ml of a solution of trypsin (from Spofa, Czechoslovakia) in a concentration of 50 mg in 1 ml of isotonic sodium chloride solution was injected intrabronchially under ether anesthesia by tracheotomy. The animals were killed 1, 3, 5, 8, 10, and 15 days after the injection (five to seven rats at each time). Pieces of the lungs were fixed for light and electron microscopy by the usual methods [5, 7]. Serial frozen sections 5-7 μm thick for immunomorphological investigations were stained by the direct Coons' method with luminescent serum against rat globules, and also by the method of Goldwasser and Shepard to reveal complement [2]. The vascular system of the lungs was injected with a mixture of ink and gelatin in two or three animals at each time post mortem [5].

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