DOI 10.1007/s10517-016-3155-2

GENERAL PATHOLOGY AND PATHOPHYSIOLOGY

Influence of High Blood Pressure on Microcirculation in Cerebral Cortex of Young Rats

I. B. Sokolova, I. V. Sergeev, and D. P. Dvoretskii

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 160, No. 9, pp. 276-278, September, 2015
Original article submitted November 5, 2014

We studied the density and structure of the microvascular network of the pia mater, the blood flow rate and oxygen saturation in the sensorimotor cortex of young spontaneously hypertensive rats (SHR). The density of the microvascular network in hypertensive animals was by ~1.4 times lower than in normotensive Wistar-Kyoto rats (control) and arteriolar bed density was lower by ~1.9 times. The blood flow rate in tissue and oxygen saturation in the sensorimotor cortex in SHR rats were significantly lower than in control animals.

Key Words: *arterial hypertension; microcirculation; brain; pial arterioles; blood flow speed*

Chronic hypertension leads to thickening of the walls of cerebral arterioles, narrowing of their lumen, obliteration, and plasmorrhages [1,8,9,11] that in turn leads to vascular wall abnormalities up to necrosis.

Arterial hypertension is a highly prevalent disease associated with serious complications, significantly impairing quality of life, and often leading to disability in not only elderly, but also in young active patients. Therefore, the investigation of the effects of hypertension on various structures of the body with consideration of previous findings but using modern technical approaches [10,12] seems to be promising.

Here we studied changes in the density and structure of the microvascular network, blood flow rate in the sensorimotor cortex (SMC) and tissue oxygenation against the background of arterial hypertension in manifesting in young age.

MATERIALS AND METHODS

The experiments were carried out on 4-5-month-old male Wistar-Kyoto rats (n=20; controls) and 5-month-old hypertensive male SHR rats (n=20). The rats were kept under standard vivarium conditions with natural light and free access to water and food. The experiments were carried out in accordance with the rules adopted by European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (1986).

Visualization and monitoring of the microvascular network of pia mater above SMC was carried out using a television instrument for *in vivo* studies of microcirculation. In zoletil-anesthetized (20 mg/kg, Virbac) animals, the parietal bone and the dura mater were removed. The brain surface was continuously irrigated with saline (37°C); the body temperature was maintained at 37°C throughout the test. The mean blood pressure in Wistar-Kyoto rats was 105-120 mm Hg and in SHR rats it was around 170-190 mm Hg.

The animals were placed under a ×40 lens of a videomicroscope, through which the structure and density of microvascular bed of SMC pia mater was observed. The significance of differences was assessed by Mann–Whitney test ($p \leq 0.05$).

The blood flow rate in SMC and oxygen saturation of the tissue in the region of interest (SO_2) were evaluated by a complex multi-functional laser diagnostics "LAKK-M" (LAZMA). The blood flow and

Laboratory of Physiology of Cardiovascular and Lymphatic Systems, I. P. Pavlov Institute of Physiology, Russian Academy of Sciences, St. Petersburg, Russia. ***Address for correspondence:*** sib@kolt.infran.ru I. B. Sokolova

SO_2 were recorded above the entire SMS area. The significance of differences was assessed by Student's *t* test ($p \leq 0.05$).

RESULTS

The density of the entire microvascular network in SHR rats was by 1.4 times lower and the density of the arteriolar portion was lower by 1.9 times, (Fig. 1). A difference in the structure of the microvascular network of the pia mater in the control and hypertensive animals was found: in Wistar-Kyoto rats, the arterioles, capillaries and venules constituted 40.2 and 59.8%, respectively, while in SHR rats, the corresponding values were 29.5 and 70.5%.

This significant decrease in the number of microvessels and especially arterioles per unit of area could have a negative impact on cerebral metabolism. Oxygen supply to brain tissue is determined by a large number of parameters: partial oxygen pressure (pO_2) in the arterial blood, blood flow rate in cerebral vessels, tissue oxygen consumption, density of the microvascular bed, etc. The main gas exchange occurs in arterioles and capillaries. pO_2 is high in ~70% cerebral cortex volume (pO_2=15-45 mm Hg) and low in less than 10% of the brain tissue (pO_2=0-10 mm Hg) [2]. The increase of the distance between the arterioles and capillaries shifts this ratio toward lower pO_2 values. The decrease in the density of arteriolar and capillary compartments of the microvascular network leads to the formation of ischemic regions in the cerebral tissue.

The development of essential hypertension adversely affects the parameters of microcirculation, such as blood flow rate in the cerebral tissue. In the SMC of SHR rats, the tissue blood flow rate (29.1±0.9 pf. units) was significantly lower ($t \leq 0.05$) than in the same brain area in Wistar–Kyoto rats (33.4±1.0 pf. units). Our results on the effect of hypertension on blood flow in the brain agree with previously reports [5-7]. Almost all researchers observed the decrease in blood flow in different brain structures in patients with hypertension.

We found statistically significant ($t \leq 0.05$) decrease in SO_2 in the SMC tissue of SHR rats (91.7±0.4% *vs.* 93.4±0.4% in the control) resulting from reduced density of the microvascular network and blood flow rate.

Thus, essential hypertension leads to significant violations of the basic parameters of microcirculation in the brain: density of microvascular network in the cerebral tissue and blood flow rate even in young animals. It has been previously shown that reactivity of pial arteriolar wall in the hypertensive animals also is also impaired [3,4]. The pathological changes in the microcirculation can lead to serious disease such as encephalopathy, formation of sites of the diffuse ischemic tissue in the brain, which is indirectly confirmed by the decrease in oxygen saturation of the SMC in SHR rats.

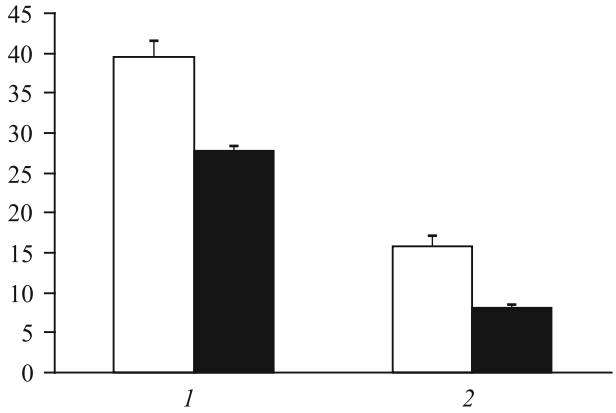

Fig. 1. Density of the entire microvascular network (*1*) and its arterial portion (2) in the SMC pia mater in normotensive and hypertensive rats. Light bars: Wistar-Kyoto rats; dark bars: SHR rats. Ordinate: density of microvascular network (number of microvessels per unit area).

Activation of therapeutic angiogenesis in the cerebral cortex of hypertensive animals could be a method of controlling hypertensive angiopathy.

REFERENCES

1. N. F. Vereshchagin, V. A. Morgunov, T. S. Gilevskaya, *et al*., *Pathology of the Brain in Atherosclerosis and Arterial Hypertension* [in Russian], Moscow (1997).
2. E. P. Vovenko and A. E. Chuikon, *Ross. Fiziol. Zh*., **95**, No. 7, 673-687 (2009).
3. D. P. Dvoretskii, O. N. Ryzhikova, and V. N. Shuvaeva, *Regionar. Krovoobr. Mikrocirk.*, No. 1, 75-81 (2002).
4. O. N. Ryzhikova, V. N. Shuvayeva, A. V. Kostylev, and D. P. Dvoretskii, *Bull. Exp. Biol. Med*., **143**, No. 2, 184-186 (2007).
5. L. L. Beason-Held, A. Moghekar, A.B. Zonderman, *et al*., *Stroke*, **38**, No. 6, 1766-1773 (2007).
6. W. Dai, O. L. Lopez, O. T. Carmichael, *et al*., *Stroke*, **39**, No. 2, 349-354 (2008).
7. J. R. Jennings, M. F. Muldoon, C. Ryan, *et al*., *Neurology*, **64**, No. 8, 1358-1365 (2005).
8. J. R. Jennings and Y. Zanstra, *Neuroimage*, **47**, No. 3, 914-921 (2009).
9. R. N. Kalaria, *Nutr. Rev*., **68**, Suppl. 2, S74-S87 (2010).
10. S. Paiardi, L. F. Rodella, C. De Ciuceis, *et al*., *Clin. Hemorheol. Microcirc.*, **42**, No. 4, 259-268 (2009).
11. C. S. Rigsby, D. M. Pollock, and A. M. Dorrance, *Microvasc. Res*., **73**, No. 3, 198-205 (2007).
12. C. Sierra, *Panminerva Med.*, **54**, No. 3, 179-188 (2012).