

Smooth Myocytes of Cerebral Arteries in Acute Phase of Experimental Hypertension

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Abstract

Using cytological, histochemical and morphometric methods, the changes of smooth myocytes of cerebral arteries was studied in 12 pups with experimental hypertension induced by coarctation as compared to the normal characteristics of these cells established in 10 control animals. It was established that hypertension induced hypertrophy and polyploidy of leiomyocytes of the circular muscular layer in the tunica media of the coronary arteries, that was manifested as the increase in their nuclear DNA content and in the numbers of binuclear cells. After the elimination of hypertension, which was previously established in the cordial vasculature, the tendency for reversal of the changes in nuclear and cytoplasmic linear parameters of the cells examined was observed. However, the nuclear DNA content and the number of polyploidy leiomyocytes in the coronary arteries remained practically unchanged. The latter indicates that the polyploidy of leiomyocytes in the coronary arteries is irreversible.

Keywords: Hypertension; Smooth myocytes; Structure of cell population

Abbreviations

SM: Smooth Myocytes; MSU: Moscow State University; MOS: Micrometer Ocular Screw

Introduction

The study of smooth myocytes (SM) of cerebral vessels with sudden developing hypertension is of considerable theoretical and practical interest, dictated by the possibility of acute hemodynamic disturbances in the cerebral pool [1,2]. One of the reasons for the latter is the rupture of the vascular wall, the strength of which largely depends on the state of the cells of the middle envelope [3,4]. Certain prospects in the assessment of adaptive morphogenesis of the tissue components of blood vessels, opens the narrowing of the aorta in a limited area in animals, accompanied by an increase in blood pressure in the prestenotic zone, including the cerebral region [5]. In the available literature, information about the structure of smooth myocytes of the arteries of the brain in hypertension is scarce and contradictory¹.

¹a search was carried out for the electronic resources of the Russian National Library and PubMed NCBI for the period from 1990 to 2019.

The purpose of the work is to analyze the structural transformations of smooth myocytes of the cerebral arteries in the emergency stage of experimental hypertension.

Materials and Methods

The hemodynamic model of aortic coarctation was obtained operatively in experiments on 12 puppies (3-6 months old) according to the previously developed method [6]; 10 dogs were used as controls. After 5 days, in the emergency stage of the pathological process [7], animals were taken out of the experiment by bloodletting under anesthesia. A mercury manometer measured blood pressure in the carotid artery and assessed its hemodynamic parameters in the cerebral pool from its value. The outer and inner diameter (d) of the middle cerebral artery were determined with a MOS-1-15 × screw ocular micrometer; the thickness of the middle shell was calculated [8]. The objective criterion for the strength of the vessel wall is the permissible tensile stress (σ), which was obtained by the formula: $\sigma = pd / 2\delta$, where p is blood pressure, δ is wall thickness [9]. Isolated GM media of the middle cerebral artery was isolated by the method of targeted alkaline dissociation [10], the preparations were stained according to Felgen (hydrolysis in 5 N HCl at 37°C for 12 minutes). The

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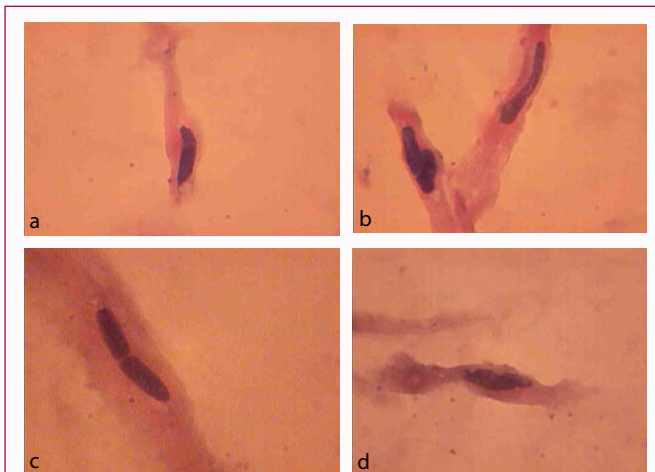


Figure 1: Isolated smooth myocytes of the middle cerebral artery of dogs in the control (a) and emergency stage of hypertension (b - d). Cell hypertrophy (b, c), binuclear myocytes (b, c) uneven cytoplasm density (d), vacuolization of nuclei (b, d). Alkaline cell dissociation. Stained with hematoxylin-eosin. About. 90, ok. 10.

eyepiece micrometer measured linear parameters of the nucleus and cytoplasm of the SM; their area (S) and volume (V) were derived by equalities: $S = 0.785 \times LT$ and $V = 0.523 \times LT^2$, where L is long, T is the cross section [8]. According to the calculated volumes, the index of the nuclear-cytoplasmic ratio was estimated. The proportion of binuclear forms in the population of the SM was taken into account. The DNA content in the nuclei of mononuclear vascular myocytes was analyzed on a MIF-K cytometer (MGU) at a wavelength of 580 nm. Quantitative data were processed by the method of variation statistics. The significance of differences was judged by the value of Student's t-test.

Research results

Blood pressure in the carotid artery in dogs 5 days after coarctation of the aorta increases 1.6 times (up to 128 mm Hg; control - 82 mm Hg.). The pressure of blood flowing into the cerebral pool also increases in the same way. The emergency stage of development of the pathological process is accompanied by a significant narrowing of the lumen of the middle cerebral artery, indicating an increase in its tone. In the experiment, the vessel lumen is reduced by 1.5 times ($d = 538 \pm 12.2 \mu\text{m}$, the control is $832 \pm 11.4 \mu\text{m}$; $p < 0.01$), and the size of the middle shell increases 1.4 times to $75.2 \pm 2.6 \mu\text{m}$ (control $52.4 \pm 2.3 \mu\text{m}$; $p < 0.01$). The permissible tensile stress of the arterial wall drops 1.4 times ($\sigma = 128 \times 538/2 \times 75.2 = 458$ units; control: $\sigma = 82 \times 832/2 \times 52.4 = 651$ units).

Isolated SM of the middle cerebral artery in conditions of acute hypertension are distinguished by blurring of boundaries, uneven cytoplasm density, nucleus vacuolization (Figure 1). A morphometric study reveals a change in the structure of the vascular myocyte population (Table 1). The cell length increases by 1.2, the cross section - by 1.3, the area and volume increase by 1.5 and 2.0 times. The same pattern was found when measuring their nuclei: the length

Table 1: Morphometric analysis of isolated smooth myocytes average canine cerebral artery in control and experiment ($\bar{x} \pm s_x$).

Group animals	Lc, μm	Tc, μm	Ln, μm	Tn, μm	Sc, μm^2	Vc, μm^3	Sn, μm^2	Vn, μm^3
Control	48,5 \pm 1,5	14,1 \pm 0,5	16,8 \pm 0,3	7,5 \pm 0,2	536 \pm 12,8	5043 \pm 66,5	98,93,6	494 \pm 8,4
AAG	57,1 \pm 1,6**	18,3 \pm 0,7*	19,2 \pm 0,4*	8,2 \pm 0,2*	820 \pm 16,3*	10001 \pm 89,0*	124 \pm 6,7**	675 \pm 14,2*

Note: AAG - emergency stage of arterial hypertension; Lc is the cell length; Ln is the length of the core; Tc is the cross section of the cell; Tn is the cross section of the nucleus; Sc is the cell area; Sn- is the area of the nucleus; Vc - cell volume; Vn is the core volume. The differences are significant: * at $P < 0.01$; ** when $P < 0.02$.

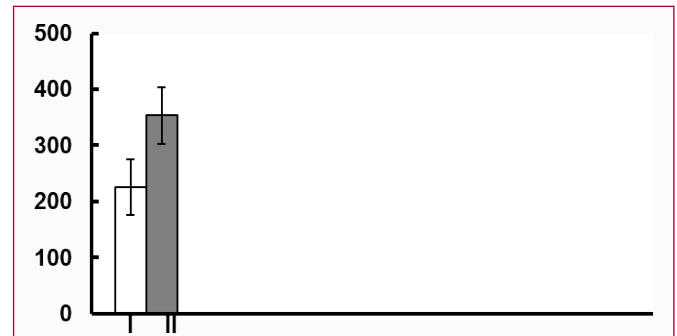


Figure 2: The DNA content in the nuclei of isolated smooth myocytes of the middle cerebral artery of dogs in the control (I) and the emergency stage of hypertension (II). On the ordinate axis - the value of the indicator (used). Vertical bars are standard error values.

and transverse dimensions become larger by 1.1; area and volume - respectively 1.3 and 1.4 times. SM nuclear-cytoplasmic relations are reduced 1.6 times. An increase in the share of binuclear forms in the SM population to $0.6 \pm 0.04\%$ was noted, while the initial level was $0.3 \pm 0.02\%$ ($p < 0.01$). Cytophotometric analysis indicates an increase in the amount of DNA in the nuclei of mononuclear myocytes (Figure 2).

Results and Discussion

The study showed that the experimental narrowing of the aorta in a limited area causes a significant increase in blood pressure in the cerebral pool. At the same time, the lumen narrowing and thickening of the middle cerebral artery are recorded. The proposed original mathematical analysis of the parameters of blood pressure, internal diameter and size of the membranes indicates a decrease in the allowable stress on the rupture of the walls of cerebral vessels. This can lead to a progressive weakening of the strength of the latter and the formation of aneurysms [11].

The emergency stage of hypertension is accompanied by alternative changes in the vascular myocytes of the middle sheath of the arteries of the large brain. Quantitative assessment of the SM states an increase in cell size and a decrease in the nuclear cytoplasmic index. Obviously, the ratio of different types of SM in the population is determined by the functional need [3] and is a reaction to the hemodynamic changes that occur. In our laboratory, it was previously shown [12] that the acute phase of experimental aortic coarctation causes submicroscopic transformations of the SM arteries: swelling and clearing of the matrix, fragmentation and focal degradation of mitochondrial cysts, destruction of the outer cell membrane.

The study of isolated vascular myocytes revealed signs of intracellular regeneration [7]: an increase in the proportion of binuclear forms and the amount of DNA in the nuclei of mononuclear SM. Considering reports of intensive DNA synthesis in SM nuclei on days 3-4 after vascular stenosis and that dividing cells may linger in prophase [13], the latter event should be considered as one of the mechanisms of polyploidy [14].

Thus, the transformation of the SM population of the middle membrane of cerebral arteries, which is observed in the emergency stage of hypertension, leads to a decrease in the allowable stress on the rupture of their wall. Prerequisites for the destruction of vessel membranes are created, the possibility of hemorrhages and the development of acute cerebral circulation is initiated, which is confirmed in clinical observations [6].

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