Effect of Acute Hypoxia in Pregnant Females on Contractile Activity of Lymphatic Vessels in the Offspring

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Delayed consequences of acute hypoxia were studied in 60-day-old rat pups. The animals were exposed to acute hypobaric hypoxia on day 10 of embryogenesis. The offspring of intact females served as the control. Reactivity of mesenteric lymphatic vessels to norepinephrine was studied by vital microscopy. The frequency and duration of lymphatic vessel contractions in males significantly increased compared to the control. In females the duration of norepinephrine-induced lymphatic vessel contractions increased, while the frequency and amplitude of contractions and basal vascular tone did not differ from the control.

Key Words: *prenatal hypoxia; contractility of lymphatic vessels*

Physiologists and physicians pay much attention to the under normal conditions and protective response in disease. Lymphatic vessels are highly sensitive to a variety of vasoactive substances, endogenous regulators [3], and oxygen tension [1]. Acute hypobaric hypoxia (AHH) is a universal damaging factor modulating activity of the organism. Delayed consequences of prenatal hypoxia in the offspring are of considerable interest. The negative effect of prenatal hypoxia may develop in various periods of postnatal ontogeny [2,5-9].

Here we studied delayed consequences of acute prenatal hypoxia in the offspring of females exposed to AHH in the early period of pregnancy. We assayed the reaction of lymphatic vessels to norepinephrine (1×10^{-6} M).

MATERIALS AND METHODS

Females were exposed to AHH on day 10 of pregnancy (period for generation of organs and systems). The animals were placed in flow altitude chamber and elevated to a "height" of 11,500 m over 1 min. Contractile activity of lymphatic vessels was assayed in rat pups at the age of 2 months. The offspring of intact females served as controls. Experiments were performed on 60-day-old males and females.

The effect of norepinephrine on contractile activity of lymphatic vessels was studied by a modified method of vital microscopy of mesenteric vessels [4]. After laparotomy the animals were maintained on a thermostatic table at 37°C. The intestinal loop and mesentery were placed on a waveguide table of a microscope. The mesentery was kept moistened and warm by continuous perfusion of physiological saline. A water immersion lens (×30) was put on the surface of the mesentery. The area of a moist chamber was 1.5 cm^2. We examined the lymphatic vessel (diameter 60-150 μ) localized within the chamber and exhibiting no motor activity. The image was projected on a monitor of a Matritsa industrial television device and recorded with a video recorder.

The device was equipped with a MBI-11 microscope, VSR-2 rectifier, FEU-35 photomultiplier, FMEL-1F photometric heads, I-338-1P automatic recorder, telemonitor, and video recorder.

Norepinephrine in a concentration of 1×10^{-6} mol/liter (0.2 ml, Sigma) was applied to a mesenteric lymphatic vessel. Application of physiological saline ser-

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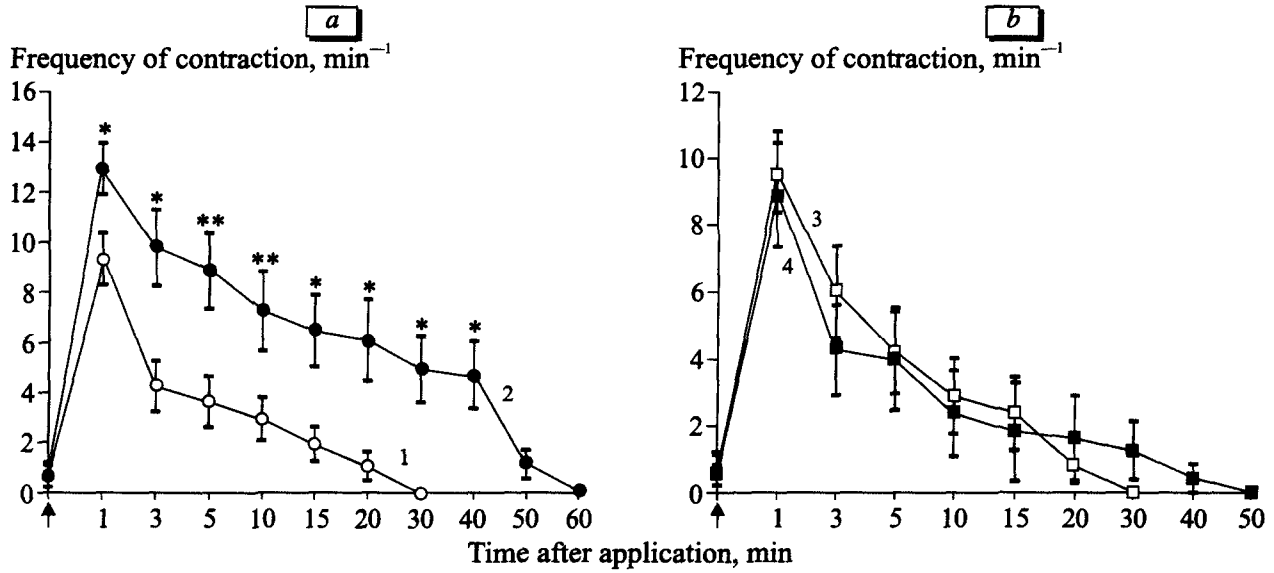

Fig. 1. Norepinephrine-induced (10^{-6} mol/liter) contractions of lymphatic vessels in male (*a*) and female rat pups (*b*) exposed to acute prenatal hypoxia. *1, 3*) control (*a*, n=15; *b*, n=10). *2, 4*) prenatal hypoxia (*a*, n=13; *b*, n=11). Arrow: application of norepinephrine. *p<0.05 and **p<0.005 compared to the control.

ved as the control. We recorded the frequency (contractions per minute) and amplitude of phasic contractions (% of the initial lumen of non-contracted vessels), changes in the basal tone (% of the initial lumen of non-contracted vessels), and duration of the reaction (spontaneous vascular activity after norepinephrine application). The results were analyzed by nonparametric Wilcoxon—Mann—Whitney test (Statistica software).

RESULTS

Changes in the frequency and duration of lymphatic vessel contractions induced by norepinephrine were studied in 60-day-old male (group 1, n=13) and female offspring (group 2, n=11) of females low resistant to AHH. The number of these pregnant females was highest. Control measurements were performed on male (n=15) and female offspring (n=10) from females not exposed to AHH.

The frequency of lymphatic vessel contractions in group 1 animals significantly increased over the 1st minute after application of norepinephrine (p<0.05). On the 1st and 10th minutes the positive chronotropic effect attained 130 and 250% of the control level (p<0.01). We also observed prolongation of the effect (Fig. 1, *a*). Changes in the amplitude of contractions and basal vascular tone did not differ from those in control animals. The latency of the response in treated and control rats was 10-15 sec.

Application of norepinephrine had no effect on the frequency and amplitude of contractions, basal vascular tone, and latency of the response in group 2 rats. However, the period of norepinephrine-induced changes in treated rats increased from 30 min to 50 min (p<0.01, Fig. 1, *b*).

The sympathoadrenal system is one of the stress-realizing systems, which perform adaptive function (centralization of blood flow, maintenance of systemic blood pressure, and mobilization of energy reserves). Pronounced and long-lasting changes in the sympathoadrenal system play a negative role. Lymphatic vessels are characterized by extremely high sensitivity to stress factors. These data suggest that stress accompanied by activation of the sympathoadrenal system impairs adaptive function in the offspring of females exposed to AHH. Pathological changes persist up to the period of maturity and are most pronounced in males.

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