PHYSIOLOGY

Resistive and Metabolic Functions of Intestinal and Skeletal Muscle Blood Vessels in Hypoxic Animals Exposed to Hypothermia

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UDC616.34−008.9+616.74+008.9]−02:615.832.9]−07

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 115, № 3, pp. 227−229, March, 1993
Original article submitted September 9, 1992

Key Words: *intestine; skeletal muscle; hypothermia; hypoxia*

It has been shown earlier [2-5] that the effect of hypoxia on the indexes characterizing the resistive function (the precapillary and postcapillary resistance to blood flow) and the metabolic function (the capillary filtration coefficient and mean capillary pressure) of rat skeletal muscle and small intestine [3,5] is markedly reduced in controlled (30°C) total body hypothermia in comparison with the effect of the same stimulus on the blood vessels in normothermia. From this evidence a conclusion was drawn about the protective effect of total body hypothermia on the skeletal muscle structures of the organ vessels in exposure to hypoxia.

The aim of this study was to investigate the resistive and metabolic functions of the skeletal muscle and small intestine in exposure to both stimuli but in reverse order: the effect of hypothermia in experimental hypoxic hypoxia.

MATERIALS AND METHODS

The experiments were carried out on 32 male and female cats weighing 3 to 5 kg, narcotized with urethane (1 to 1.1 g/kg) with the use of heparin (1500-2000 IU/kg). The gastrocnemius muscle (tibia preparation) or the small intestine (ileum and jejunum) were isolated from the general circulation, the nerve connections with the organism being preserved intact).

The blood vessels of the preparations were continuously perfused with blood taken from the femoral artery. The precapillary and postcapillary resistance to blood flow, the capillary filtration coefficient, and the mean capillary hydrostatic pressure were measured by methods described earlier [1]. The hydrostatic perfusion pressure (110 to 120 mm Hg) and the venous drain pressure were set at the level of 6 and 10 mm Hg for the small intestine and the gastrocnemius muscle respectively, that is, within the normal physiological range for cat blood vessels [6].

Hypoxic hypoxia was induced by using a gas mixture containing 10% oxygen and 90% nitrogen in the normal respiration rate. The animals were cooled to 30°C at the rate of 0.06±0.02°C by being placed in a special water bath with a water temperature of 0°C. For a comparison of the changes in the indexes of the vascular functions studied caused by exposure to hypothermia in hypoxic hypoxia the animals cooled previously to 30°C were restored to normothermia (37°C) by raising the water temperature to 35-45°C at the rate of 0.066±0.02°C/min. Hypoxia

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0007−4888/93/0003−0231$12.50

TABLE 1. Baseline Indexes of Resistive and Metabolic Functions of Skeletal Muscle and Intestinal Vessels: Precapillary Resistance (R_a), Postcapillary Resistance (R_v), Mean Capillary Pressure (P_c), and Capillary Filtration Coefficient (CFC)

Experimental conditions	Organ	Index			
		R_a	R_v	P_c, mm Hg	CFC, ml·100 g/min mm Hg
		mm Hg/100 g/ml·min			
Normoxia, normothermia:					
Before exposure to hypoxia	Intestine	3.54±0.24	0.52±0.02	18.0±0.8	0.050±0.07
	Muscle	7.32±0.64	0.50±0.06	16.8±0.8	0.027±0.002
Before exposure to hypothermia	Intestine	3.54±0.24	0.52±0.02	18.0±0.8	0.050±0.007
	Muscle	7.32±0.64	0.52±0.02	16.8±0.8	0.027±0.002
Before exposure to hypoxia, after body heated to 37°C	Intestine	3.7±0.37	0.42±0.02	17.3±0.84	0.041±0.007
	Muscle	7.27±0.45	0.55±0.06	17.5±1.0	0.026±0.005
Hypoxic background before exposure to hypothermia	Intestine	5.46±0.13	0.54±0.04	20.1±1.15	0.058±0.004
	Muscle	9.35±0.56	0.70±0.05	20.6±0.7	0.039±0.007

was then induced and at the 10th min the animals were cooled again. The vascular function indexes were determined [1] for separate and combined presentation of the hypothermic and hypoxic stimuli. The changes in the indexes were measured in percentage of the baseline values presented in Table 1.

The temperature of the blood used for the perfusion of the muscle and intestinal vessels was maintained at the level of the animal's body temperature by the use of a heat exchanger and an ultrathermostat (U 15°, Germany). The temperature of the blood for the perfusion of the muscle and the intestine was measured with the transducers of a TPEM–1 electrothermometer. The above-mentioned indexes were recorded with an H–327–8 recorder. The material obtained was processed with the use of Student's *t* test.

RESULTS

Exposure to hypoxic hypoxia in both vascular regions studied (skeletal muscle and intestine) resulted in a decrease in the precapillary and postcapillary resistance to blood flow by 18.6±5.1, 21.3±9.5 and 17.7±4.3, 20.3±2.7%, respectively (Figs. 1, 2) compared with the baseline values presented in Table 1, the capillary filtration coefficient reflecting the number of functioning capillaries (with intact microvascular permeability) being increased by 30.2±13.2% in the skeletal muscle and by 23.6±3.2% in the intestine. Exposure to the above-mentioned stimuli resulted in a reduction of the mean capillary pressure in the skeletal muscle by 7.1±1.7% and in the intestine by 7.1±3.5%.

Exposure to hypothermia in normoxia increased the precapillary and postcapillary resistance to blood flow in the muscle and intestine by 47.0±21.8, 34.9±6.7 and 32.5±19.8, 26.6±7.3%, respectively (Figs. 1, 2). Some differences between the organs were found with regard to the changes in the capillary filtration coefficient, the latter being increased in the muscle (by 26.0±8.1%) and decreased in the intestine (by 17.9±3.2%).

It should be noted that the order of exposure to the stimuli was not essential to the nature of the changes in the vascular functions studied, since in the control series of experiments with the reverse order of exposure to the stimuli (exposure to hypothermia followed by exposure to hypoxia) the results obtained were comparable in terms of the qualitative and quantitative changes in the indexes of the resistive and metabolic functions of the vessels in both regions.

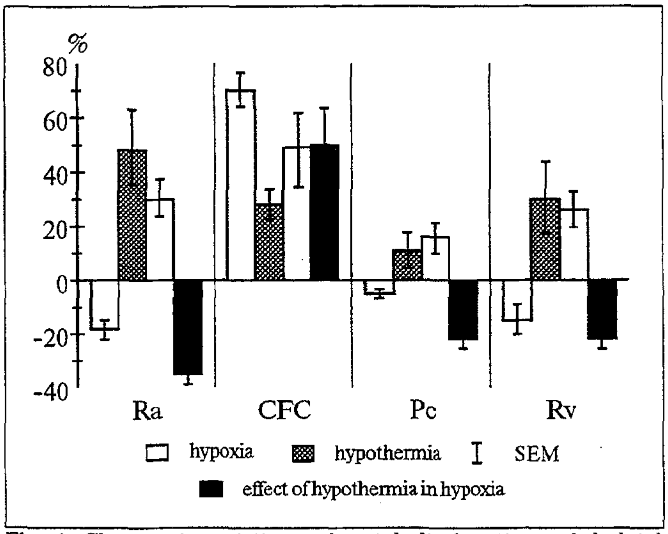

Fig. 1. Changes in resistive and metabolic functions of skeletal muscle blood vessels in separate and combined exposure to hypoxia (10% O_2 in nitrogen) and acute cooling of the body to 30°C, % of baseline values. R_a: precapillary resistance; R_v: postcapillary resistance; CFC: coefficient of capillary filtration; P_c: mean capillary hydrostatic pressure.

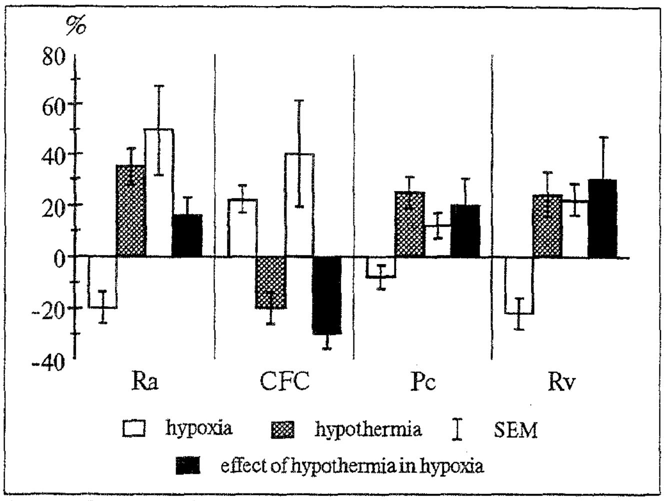

Fig. 2. Changes of resistive and metabolic functions of intestinal vessels in separate and combined effect of hypoxic stimulus and body hypothermia, % of baseline values. Notation as for Fig. 1.

This proved to be important for the interpretation of the subsequent measurements of the vascular function index changes when the hypothermic animals had to be restored to normothermia (due to the methods used in the experiments) by raising their body temperature from 30 to 37°C. After that, exposure to hypoxia resulted in an increase rather than a decrease in the precapillary and postcapillary resistance and capillary pressure; in the muscle these indexes increased by 30±12.5, 28.9±12.3 and 17.9±6.4%, whereas in the intestine they increased by 52.6±17.7, 26.6±5.6, amd 15.9±3.9%. In both organs exposure to hypoxia after heating to 37°C resulted in an increase of the capillary filtration coefficient (the microvascular metabolic function), which correlated with the indexes recorded in the initial exposure to hypoxic hypoxia.

Exposure to hypothermia in hypoxia affecting the organ vessels led to marked changes in the indexes of the vascular functions. Thus, hypothermia (30°C) in hypoxia caused a sharp fall in the precapillary resistance to the blood flow in the muscle by 27.9±10.3%, whereas in the experiments on the intestine this index increased by 13.2±3.6% (Figs. 1, 2). The capillary filtration coefficient was increased in the muscle by 51.8±19.4% compared with the baseline value, whereas in the intestine it was decreased by 27.2±8.3%. Unlike the capillary filtration coefficient the postcapillary resistance was found to be lower in the muscle by 15.0±4.6 and 21.6±2.0%, respectively, whereas in the intestine it was 35.6±18.2 and 24.8±12.5% higher (Figs. 1, 2).

The evidence suggests that exposure to hypothermia in hypoxia resulted in a dilatation of the arteries (a decrease in the precapillary resistance to blood flow), "precapillary sphincters" (an increase in the capillary filtration coefficient), and veins (a decrease in the postcapillary resistance of cat skeletal muscle, whereas in the intestine a similar effect resulted in a constriction of both arterial and venous vessels of the skeletal muscles [1]. The vascular response differences between the organs are probably associated with the fact that skeletal muscle belongs to the "membrane" organs, whereas the intestine is considered to be among "the nucleus" organs of the organism.

Exposure to hypothermia in normoxia resulted in higher indexes of the resistive (precapillary and postcapillary resistance) and metabolic (capillary filtration coefficient and mean capillary pressure) functions in the muscle and intestine (Figs. 1, 2), whereas in hypoxia (at the 10th min of inhalation of the hypoxic mixture) the sensitivity of the skeletal muscle arteries and veins to the effects of hypothermia was found to be qualitatively different: the precapillary and postcapillary resistance to blood flow were decreased (Fig. 1).

The qualitative differences observed in the sensitivity of the arteries and veins to the hypothermic stimulus in normoxia and hypoxia suggest that the hypothermic responses of the visceral vessels depend on the degree of saturation of the blood with oxygen.

In the experiments on the intestinal vessels the qualitative changes found in the vascular indexes in normoxia and hypoxia were the same when the animals were exposed to hypothermia. However, with both hypothermia and hypoxia the capillary filtration coefficient was found to be higher in the muscle, while in the intestine it was lower; this, however, corresponded to the change in this index in hypothermia alone, suggesting a weak correlation between the sensitivity to hypothermia of the "precapillary sphincters" of the skeletal muscle and the intestine on the one hand and the oxygen supply of the body on the other (Figs. 1, 2).

The evidence of the protective effect of the earlier exposure to hypothermia against the hypoxic effect on the vascular functions (both resistive and metabolic) found in previous experiments [3-5] has not been confirmed for the presentation of both stimuli in reverse order. In other words, hypoxic hypoxia does not have any "protective" effect against hypothermia affecting the vessels and their resistive and metabolic functions.

Thus, the combined effect of both stressors (hypoxia and hypothermia) on the experimental animals and their visceral vascular functions depends on the order of presentation of the stimuli, this being responsible for either a positive or a negative cross-resistance of the smooth muscle structures forming the metabolic microvascular function.

REFERENCES

1. B. I. Tkachenko (Editor), *Integration of Vascular Functions* [in Russian], Leningrad (1984).

2. A. A. Nurmatov, Yu. A. Kudryashov, and B. I. Tkachenko, *Fiziol. Zh. SSSR*, **72**, № 4, 517-523 (1988).
3. A. A. Nurmatov, Yu. A. Kudryashov, B. I. Tkachenko, and V. G. Bachkova, *Ibid.*, № 1, 70-75 (1988).
4. B. I. Tkachenko, A. A. Nurmatov, and Yu. A. Kudryashov, *Byull. Eksp. Biol. Med.*, **104**, № 9, 285-287 (1987).
5. B. I. Tkachenko, A. V. Samoilenko, Yu. A. Kudryashov, *et al.*, *Fiziol. Zh. SSSR*, **76**, № 12, 1682-1689 (1990).
6. B. Oberg, *Acta Physiol. Scand.*, **71**, № 2-3, 233-247 (1967).

PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

Effect of Cod-Liver Oil with a High Content of Polyunsaturated Fatty Acids (Eikonol) on Myogenic Tone and Vasoconstrictory and Vasodilatatory Responses of Isolated rat Caudal Artery

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UDC 615.324:665.214.1].015.4.076.9

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 115, № 3, pp. 229—231, March, 1993
Original article submitted November 18, 1992

Key Words: *cod-liver oil; tone; diet; α- and β -reactivity; resistive artery*

Recent studies have shown that a diet enriched with unsaturated fatty acids, eicosapentaenoic (20:5 n=3) and docosahexaenoic (22:6 n=3) possesses an antiarrhythmic effect and reduces the morbidity rate in acute myocardial infarction [3,8]. The antiatherogenic [5,10] and hypotensive [7,9] effects of this diet have been demonstrated. However, the influence of a diet enriched with polyunsaturated fatty acids (PUFA) and, in particular, with the nutritional supplement eikonol, containing a high concentration of the indicated PUFA, on the properties of resistive arteries, the tone and reactivity of which directly determine the blood pressure, has not yet been investigated.

The aim of the present study was to assess the influence of a PUFA-enriched diet (with the nutritional supplement eikonol added) on myogenic tone, $\alpha-$ and β $-$reactivity, and the extent of the endothelium-dependent dilatation of the isolated rat resistive artery.

MATERIALS AND METHODS

Male Wistar rats weighing 300 g were used for the experiments. The animals were fed standard

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(Presented by N. R. Paleev, Member of the Russian Academy of Medical Sciences)