Adrenergic Reactivity of Visceral Veins in Hypoxia and Hypothermia

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Adrenoreactivity of veins in skeletal muscle to norepinephrine decreased, while reactivity of intestinal veins remained virtually unchanged during combined exposure to hypoxia and hypothermia. In skeletal muscles cooling enhanced the direct effect of hypoxia on vascular smooth muscle cells, while in the intestine hypothermia prevented hypoxia-induced endothelial dysfunction, as it did under normothermic conditions. The results of experiments on the intestine indicated possible protective effect of hypothermia with respect to hypoxia-induced damage, and experimental findings on muscles showed potentiation of the direct effect of oxygen deficiency on venous smooth muscles.

Key Words: *adrenoreactivity of visceral vein; hypoxic hypoxia; hypothermia; norepinephrine; gastrocnemius; small intestine*

Hypothermia and oxygen deficiency modify vascular adrenergic reactions in mammals [7,11]. Changes in adrenergic reactivity of vascular smooth muscles are usually studied under conditions of exposure of the organism to only one extreme factor, hypoxia or hypothermia. These studies were performed on large arterial segments and rarely on vein preparations [10,11]. Though artificial cooling is used in practical surgery for protection from hypoxic damage to organs, reports about combined effect of hypoxia and hypothermia on the sensitivity of vascular smooth muscles to vasoactive substances are scanty [7].

It was previously shown that hypoxia caused less expressed shifts in precapillary resistance and postcapillary resistance in feline gastrocnemius muscle after cooling to 30°C in comparison with hypoxic exposure under normothermic conditions; in the small intestine, shifts in the precapillary resistance were also less pronounced, but postcapillary resistance increased [4,5]. Mechanisms of changes in the sensitivity of visceral veins to oxygen deficiency in hypothermia are unknown.

Changes in the sensitivity of vascular smooth muscles during hypothermia-hypoxia are most likely realized via the adrenergic mechanisms, *i. e.* increased blood catecholamine concentrations and increased sensitivity of mammalian vascular smooth muscle cells to these substances caused by graded hypothermia.

We studied changes in the sensitivity of visceral veins to norepinephrine under conditions of combined and separate exposure to hypoxia and hypothermia.

MATERIALS AND METHODS

Experiments were carried out on 12 cats (2.5-4 kg) narcotized with nembutal (30-40 mg/kg intramuscularly). The gastrocnemius (shin preparation) and small intestine (jejunum and ileus) were denervated and perfused autonomously with autoblood (constant perfusion volume mode). Changes in bloodflow resistance in arteries and veins in response to intraarterial bolus injection of norepinephrine (10 μg) in 0.1 ml 6% dextrane (Polygluquine) were evaluated by arterial [9] and venous [2,3,12] resistography under conditions of normothermia and normoxia, hypoxia (10% O_2 in nitro-

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TABLE 1. Effects of Hypoxia and Hypothermia on Venous and Arterial Reactions to Norepinephrine in Cats

Perfusion pressure, mm		Baseline values	Hypoxia	Hypothermia	Hypoxia+hypothermia
Veins	muscle	4	5.5	5.2	2.5
	intestine	2.2	4.1	2.2	2.8
Arteries	muscle	53	69	49	40
	intestine	51	25	38	42

gen at the 10th min of exposure), cooling to 30.0±0.3°C at a rate of 0.07±0.02°C/min, and then during combined exposure to hypoxia and hypothermia. Blood clotting in perfusion tubes was prevented by intravenous heparin (1500-2000 U/kg). The animals were cooled in a tank with circulating ice-cold water (0°C). The data were statistically processed using Student's t test, the differences were considered significant at $p<0.05$.

RESULTS

Norepinephrine increased venous resistance under conditions of normoxia and normothermia, this increase being more pronounced in the skeletal muscle than in the intestine (Table 1). Hypoxia at normal temperature enhanced adrenergic reactions in muscle and intestinal veins, the absolute increase in venous resistance was less pronounced in the muscle (Table 1), while the relative increase was less expressed in the intestine (Fig. 1). This increase in the reactivity of visceral veins to norepinephrine under conditions of hypoxic hypoxia is in line with published data that norepinephrine potentiated contraction of vascular segments from the femoral, pulmonary, and major subcutaneous veins in dogs under conditions of oxygen deficiency [10]. Denudation canceled this effect. It can be assumed that hypoxia suppressed basal production of relaxing endothelial factor(s), which led to a more pronounced constrictive reaction of veins to norepinephrine. Hypoxia induced only functional changes in venous endotheliocytes, because venous response to norepinephrine returned to baseline 10 min after termination of hypoxic exposure.

Cooling to 30°C did not change the reactions of visceral veins to norepinephrine in comparison with the baseline values (Table 1). Previous data [8] and new findings suggest that cooling to 30°C does not essentially modify the reactivity of visceral veins in mammals.

Combined exposure to hypoxia and hypothermia drastically (2-fold) suppressed the response of muscle vein to norepinephrine, the reactivity of intestinal veins only little changed (Table 1). Adrenoreactivity of muscle veins decreased more than 2-fold compared to normoxia-normothermia (Fig. 1).

Therefore, combined exposure to hypoxia and hypothermia drastically decreased adrenoreactivity of skeletal muscle veins, while the reactivity of intestinal veins remained virtually unchanged. This suggests that cooling enhanced the direct effect of hypoxia on venous smooth muscle cells in skeletal muscle and prevented hypoxia-induced endothelial dysfunction in the intestine, as it did in normothermal animals exposed to hypoxia. Experiments on the intestine revealed a protective effect of hypothermia against hypoxia, while experiments on skeletal muscle demonstrated that hypothermia potentiated the effect of oxygen deficiency on venous smooth muscles.

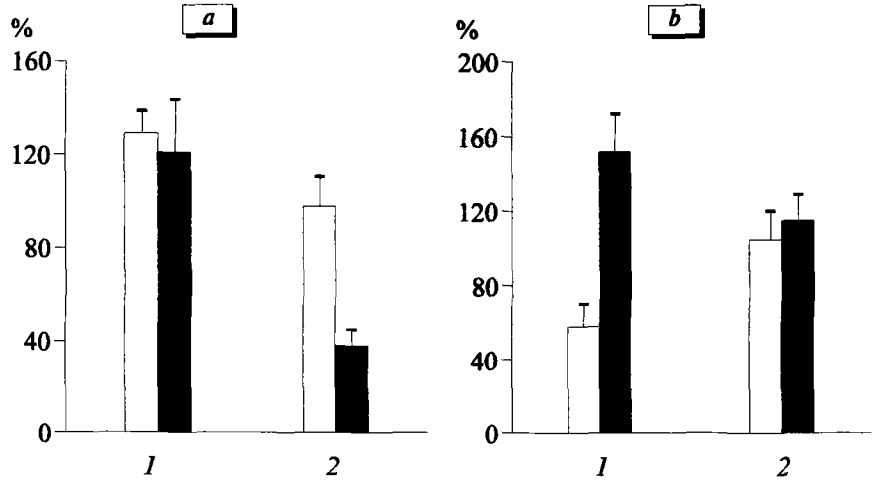

Fig. 1. Adrenergic reactions of arteries (light bars) and veins (dark bars) in skeletal muscles (*a*) and small intestine (*b*) under conditions of hypoxia (*1*) and hypothermia-hypoxia (*2*). Reactions in normoxia-normothermia (*1*) and normoxia-hypothermia (*2*) are taken as 100%.

Hypoxia at normal temperature virtually did not change the reactions of gastrocnemius arteries to norepinephrine, while the respective parameter in the small intestine decreased 2-fold in comparison with the baseline values (Table 1). Hence, the above-mentioned stimulation of adrenergic reactions in visceral veins under conditions of hypoxia and normothermia is little expressed in skeletal muscle arteries, while in the intestinal arteries the sensitivity of smooth muscles cells to adrenergic stimulation was considerably suppressed in hypoxia (Fig. 1). This probably confirms a direct effect of hypoxia on smooth muscles in intestinal arteries [1], i.e. suppression of their adrenergic reactivity. Hypothermia virtually did not change the reaction of muscle arteries to norepinephrine, and the reactions of the intestinal arteries only tended to decrease. Our findings in skeletal muscle arteries in hypothermia coincide with the results obtained on muscle and intestinal veins. Combined exposure to hypothermia and hypoxia little changed the adrenergic reactions of muscle and intestinal arteries in comparison with hypothermia alone (Fig. 1). Our data suggest that whole-body cooling protects the body from hypoxic hypoxia by modifying adrenergic sensitivity of arterial smooth muscles.

Venous and arterial reactions in the small intestine indicate that moderate (30°C) cooling protects vascular smooth muscle cells from hypoxia. The mechanisms underlying the drastic decrease of adrenergic reactivity of veins in skeletal muscles under conditions of hypoxia and hypothermia remain to be investigated.

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