EFFECT OF HYPOTHERMIA ON THE DEVELOPMENT OF NEUROGENIC PULMONARY EDEMA

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The effect of hypothermia on the development of pulmonary edema produced by bilateral division of the vagus nerves in the neck was studied in experiments on guinea pigs and rats of both sexes. Hypothermia was found not to protect the animals against disturbances of permeability of the air–blood barrier of the lungs or against the development of pulmonary edema. Conditions facilitating the development of tissue hypoxia were created (a decrease in cytochrome oxidase activity in the myocardium and succinate dehydrogenase activity in the lungs) during the development of edema.

KEY WORDS: hypothermia; vagotomy; pulmonary edema; tissue enzymes.

Pathological states in which artificial hypothermia has been demonstrated are sometimes complicated by pulmonary edema, worsening the prognosis considerably [1, 3, 6]. There are a few reports in the literature on the effect of hypothermia on pulmonary edema, but only on those types caused by exposure to ammonium chloride and serum and to hyperbaric oxygen [2, 4, 8–10].

EXPERIMENTAL METHOD

Experiments were carried out on 168 sexually mature albino rats and 54 guinea pigs of both sexes. Pulmonary edema was induced in the tracheotomized animals by one-stage bilateral division of the vagus nerves in the neck. The animals were cooled in a refrigerator until their rectal temperature was 23.3–19.6°C (measured with the TMS-2 electrothermometer). The permeability of the pulmonary air–blood barrier was determined with the aid of Evans' Blue [5, 11]. The degree of blood filling of the lungs was investigated by Meijer's method [12] with Serebrovskaya's modification [7]. The arterial pressure, respiratory movements, and ECG were recorded. Macroscopic changes in the thoracic organs were observed in animals killed 2 h after vagotomy, the pulmonary coefficient (the ratio between the weight of the lungs in mg and the body weight in g) was determined and the weight of the dry residue of the lungs obtained. In special experiments the activity of cytochrome oxidase and succinate dehydrogenase (using neo- and blue tetrazolium salts) and also the acetylesterase activity (using paranitrophenyl acetate as the substrate) were investigated in the heart and lungs in special experiments.

EXPERIMENTAL RESULTS

At the moment of division of the vagus nerves in the uncooled rats and guinea pigs the arterial pressure rose by 20–30 mm and then fell a little, after which it remained stable until the end of the experiment. The respiration acquired the typical character of vagus dyspnea. The heart rate fell considerably (from 468.2 ± 11.7 to 335.0 ± 39.2/min; $P < 0.01$). Changes in atrioventricular and intraventricular conduction appeared. The results in Table 1 show that pulmonary edema developed in the vagotomized rats and guinea pigs as a result of an increase in permeability of the pulmonary air–blood barrier. The blood filling of the lungs was unchanged.

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TABLE 1. Pulmonary Coefficient, Dry Residue, Blood Filling, and Permeability of Air–Blood Barrier of the Lungs of Rats and Guinea Pigs after Bilateral Vagotomy under Conditions of Normothermia and Hypothermia (M±m)

Experimental conditions	Group of animals	No. of animals	Pulmonary coefficient (in mg/g)		Dry residue (in %)		Blood filling of lungs (in ml/100 g dry tissue)		Permeability of air–blood barrier (in mg Evans' Blue/kg wet weight of tissue)	
			rats	guinea pigs	rats	guinea pigs	rats	guinea pigs	rats	guinea pigs
Normothermia	Control (tracheotomy)	7	7,24±0,8	8,06±0,53	20,25±0,25	19,60±0,47	55,87±0,88	52,20±8,99	10,78±2,44	21,45±3,90
	Experimental (vagotomy +tracheotomy)	7	10,60±1,28	10,51±1,12	17,96±1,00	16,60±0,85	54,91±0,99	65,50±9,49	46,09±11,54	62,30±14,05
Hypothermia	Control (tracheotomy)	7	7,08±1,06	9,77±0,60	20,53±0,23	19,40±1,19	65,01±10,02	80,16±14,33	11,42±1,42	19,50±4,20
	Experimental (vagotomy +tracheotomy)	7	10,11±2,06	11,91±1,89	19,19±2,01	17,99±0,97	69,69±7,01	62,91±6,89	44,50±10,50	41,75±14,33
Levels of probability of difference (P) between diifferent groups of animals			$P_{1-2}<0,01$ $P_{1-3}>0,5$ $P_{2-4}>0,5$ $P_{3-4}>0,1$	$P_{1-2}<0,02$ $P_{1-3}<0,05$ $P_{2-4}>0,5$ $P_{3-4}>0,2$	$P_{1-2}<0,05$ $P_{1-3}>0,1$ $P_{2-4}>0,5$ $P_{3-4}>0,1$	$P_{1-2}<0,02$ $P_{1-3}>0,5$ $P_{2-4}>0,1$ $P_{3-4}>0,05$	$P_{1-2}>0,5$ $P_{1-3}>0,05$ $P_{2-4}<0,05$ $P_{3-4}>0,5$	$P_{1-2}>0,1$ $P_{1-3}<0,05$ $P_{2-4}>0,1$ $P_{3-4}>0,1$	$P_{1-2}<0,01$ $P_{1-3}>0,5$ $P_{2-4}>0,5$ $P_{3-4}<0,01$	$P_{1-2}<0,02$ $P_{1-3}>0,5$ $P_{2-4}>0,1$ $P_{3-4}<0,01$

TABLE 2. Changes in Enzyme Activity in Lung and Heart Tissues of Rats after Bilateral Vagotomy under Conditions of Normothermia and Hypothermia (M ± m)

Experimental conditions	Group of animals	No. of rats	Cytochrome oxidase activity (in mg tetrazolium/g wet weight of tissue)		Succinate dehydrogenase activity (mg tetrazolium/g wet wt. of tissue	Succinate dehydrogenase activity (mg tetrazolium/g wet wt. of tissue	Acetylesterase activity (in micromoles paranitrophenol per gram wet wt. of tissue)	
			in the lung	in the heart	in the lung	in the heart	in the lung	in the heart
Normothermia	Control (tracheotomy)	7	0,811±0,113	1,638±0,228	0,158±0,030	0,791±0,081	24,94±2,40	11,16±1,16
	Experimental (vagotomy + tracheotomy)	7	0,861±0,169	1,576±0,226	0,158±0,009	0,894±0,125	21,24±1.31	15,69±1,59
Hypothermia	Control (tracheotomy)	7	0,847±0,063	2,091±0,200	0,163±0,017	0,815±0,119	17,30±1,46	15,96±1,19
	Experimental (vagotomy + tracheotomy)	7	0,795±0,085	1,734±0,150	0,113±0,014	0,982±0,053	18,55±1,28	21,55±1,72
Levels of probability of difference (P) between different groups of animals			$P_{1-2}>0,5$ $P_{1-3}>0,5$ $P_{2-4}>0,5$ $P_{3-4}>0,5$	$P_{1-2}>0,5$ $P_{1-3}>0,05$ $P_{2-4}>0,2$ $P_{3-4}>0,05$	$P_{1-2}=1$ $P_{1-3}>0,5$ $P_{2-4}<0,05$ $P_{3-4}<0,01$	$P_{1-2}>0,2$ $P_{1-3}>0,5$ $P_{2-4}>0,2$ $P_{3-4}>0,1$	$P_{1-2}<0,05$ $P_{1-3}<0,01$ $P_{2-4}<0,05$ $P_{3-4}>0,2$	$P_{1-2}<0,001$ $P_{1-3}<0,01$ $P_{2-4}<0,01$ $P_{3-4}<0,01$

Vagotomy under hypothermic conditions led to a smaller (by 5-20 mm) increase in the arterial blood pressure. The respiration rate of the animals decreased just as during normothermia. The heart rate fell from 151.0 ± 5.0 to 123.0 ± 18.8/min ($P < 0.05$). Slowing of atrioventricular conduction and ventricular extrasystoles were observed on the ECG. Vagotomic pulmonary edema developed under these conditions also as a result of a substantial increase in the permeability of the pulmonary air–blood barrier.

Investigation of the enzyme activity in the tissues of the rats (Table 2) showed that under normothermic conditions vagotomy did not change the cytochrome oxidase or succinate dehydrogenase activity in either the lungs or the myocardium. In the hypothermic animals a decrease in cytochrome oxidase activity in the heart and succinate dehydrogenase activity in the lungs was observed after vagotomy. The development of vagotomic pulmonary edema in the uncooled rats was accompanied by a marked decrease in acetylesterase activity in the lungs and an increase in its activity in the heart. Vagotomy carried our during hypothermia did not significantly change the activity of this enzyme in the lungs, but considerably increased it in the heart muscle.

Hypothermia thus does not prevent disturbance of the permeability of the air–blood barrier of the lungs and the development of pulmonary edema after vagotomy. Hypothermia creates conditions that may facilitate the development of tissue hypoxia and, in particular, a decrease in the cytochrome oxidase activity in the myocardium and succinate dehydrogenase activity in the lungs during the development of neurogenic pulmonary edema.

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