EFFECT OF THE ACETYLCHOLINE SYSTEM ON PATHOGENESIS OF PULMONARY COMPLICATIONS AFTER SHOCK

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KEY WORDS: trauma; shock; pulmonary complications; acetylcholine–cholinesterase; histophysiology of the lung.

There is no dispute nowadays that acute pulmonary failure is a dangerous complication of trauma. According to some statistics [10, 13], it is found in 20-50% of patients with multiple injuries complicated by shock. Despite many investigations of the pulmonary complications developing in the posttraumatic period, as well as of the "shock lung" syndrome itself, the pathogenesis and morphogenesis of these states are still subjects for lively discussion. The probability of appearance of a syndrome of pulmonary insufficiency in traumatic shock may be determined by many factors and, above all, by a disturbance of neurohumoral regulation of the functional systems of the body [2, 5, 11, 14].

The objects of the present investigation were, accordingly, to study the activity of the acetycholine–cholinesterase system in the medulla, peripheral blood, and lung tissue and to compare the values obtained with the activity of the surfactant system and with the histological structure of the lung.

EXPERIMENTAL METHOD

Experiments were carried out on 106 noninbred male albino rats weighing 220-240 g. Traumatic shock was produced by Cannon's method. The acetylcholine (ACh) level was determined by biological and chemical methods previously checked against each other [8, 9, 12], and cholinesterase (ChE) activity was determined as in [13]. The state of the surfactant system of the lung (SSL) was assessed from the surface tension of the tissue extracts [7] and the frequency and amplitude of the respiratory excursions were determined with the ST-19 resistor element. The combined study of the histological structure of the lung was based on morphometric analysis [1, 15] of serial histotopographical sections stained with hematoxylin–eosin and by Van Gieson's method. Statistical analysis of the numerical results in all series was carried out by the method of indirect differences [6].

EXPERIMENTAL RESULTS

On the first day after shock two types of changes in ACh metabolism were found in the surviving animals. In some rats (group 1) there was a very small increase in ACh concentration and ChE activity in the medulla and peripheral blood, whereas in the lungs the ACh concentration was reduced almost to one-third of that in the intact animals, and ChE activity was halved (Table 1). Deep and rapid respiration was noted in the experimental rats of this group. The lung index (the ratio of the weight of the lung to the body weight) was 60% higher than in intact animals. Synthesis of surfactant was preserved (Table 2).

In the rats of group 2 the ACh content and ChE activity in the medulla and peripheral blood were reduced by almost three-quarters. The ACh concentration in lung tissue was trebled, although ChE activity was unchanged (Table 1). Respiration was fast and superficial. The lung index was almost doubled, and the surface tension of the lung tissue extracts was increased, evidence of reduced activity of alveolar surfactant (Table 2).

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TABLE 1. State of the Cholinergic System of the Medulla, Lungs, and Peripheral Blood in Rats 24 h After Shock and During Experimental Treatment with Propionylcholinesterase (16 mg/kg) (M ± m)

Type of experiment and times of taking material	Number of experiments	Medulla		Lung		Peripheral blood		
		ACh	AChE	ACh	ChE	ACh	AChE	BChE
Intact	10	16,62±0,06	24,96±0,067	2,326±0,007	46,67±0,29	12,44±0,05	27,04±0,05	277,36±1,04
Traumatic shock, decapitation after 24 h	14	18,26±0,08†	28,39±0,08†	0,75±0,09†	21,84±0,04†	19,65±0,64†	280,64±1,15	289,04±0,67†
	11	3,56±0,06†	13,39±0,04†	2,19±0,03	21,9±0,34†	2,73±0,09†	84,92±0,011†	89,59±0,39†
Propionylcholinesterase:								
before trauma	20	11,74±0,18†	19,39±0,202†	1,89±0,056†	10,03±0,103†	8,429±0,104†	162,24±1,328†	148,91±2,092†
after trauma	20	13,146±0,26†	19,49±0,32†	1,88±0,08†	27,55±0,34†	18,57±0,15†	267,3±4,42†	189,87±4,32†

†P < 0.05.

Legend. ACh) In homogenates, in nanomoles/kg tissue, in blood in nanomoles/liter; AChE (acetylcholinesterase), BChE (butyrylcholinesterase), and ChE, in millimoles ACh/h/kg body weight or/liter (for blood).

TABLE 2. State of the Surfactant System of the Lung, Lung Coefficient, and Results of Morphometry of the Lung in Rats 24 h After the Onset of Shock and During Experimental Treatment with Propionylcholinesterase (16 mg/kg) (M ± m)

Type of experiment and times of taking material	Number of experiments	LI	ST, N/m^2	Morphometry				
				unchanged tissue	emphysema	hemorrhage	atelectasis	edema
Intact	10	5,99±0,30	61,90±0,17	94,31±2,03	1,16±0,40	2,24±0,96	2,29±0,62	0,12±0,10
Traumatic shock, decapitation after 24 h	14	9,63±0,22*	68,09±0,27*	—	—	—	—	—
	11	11,75±0,23†	71,02±0,26†	63,85±5,82	11,12±2,11	6,91±0,91	9,63±1,27	8,27±1,29
Propionylcholinesterase:								
before trauma	20	8,14±0,17†	68,05±0,27†	90,97±2,49	1,91±0,51	3,18±0,88	3,10±1,06	0,36±0,09
after trauma	20	7,58±0,11†	64,91±0,25†	89,59±2,82	2,54±0,71	3,63±1,07	3,21±0,94	0,89±0,23

*P < 0.1.

†P < 0.05.

Legend. LI) weight of lung/body weight; ST) reciprocal of surfactant content (surface tension)

Comparison of these results with changes in the histological structure of the lung showed that in the animals of group 1 congestion of the lung tissue, thickening of the alveolar septa, and the presence of subpleural pinpoint hemorrhages and small areas of collapsed parenchyma, located usually in the paravertebral and peripheral zones of the lobes, were observed. Morphometric investigation of the lungs in the rats of group 2 revealed marked changes of histological structure, manifested as the development of areas of incomplete expansion of the lung and atelectasis, massive hemorrhages, emphysema, and edema of the parenchyma.

In animals on the first day after the development of shock, activity of the cholinergic system thus changed both in intensity and in localization in two distinct ways, correlating with the disturbance of external respiration and the histophysiology of the lung tissue.

These observations enable further development of the writers' concept expressed previously [2] on the relationship between disturbance of respiration and the state of the neurotransmitters in shock and hemorrhage. The work of Kulagin [4] has demonstrated the important role of ACh in the pathogenesis of shock and possibility of pathogenetic treatment of this state by means of substances which activate or inhibit the mediator system. These considerations justified a search for methods of treatment of lung complications by means of substances acting directly on the cholinergic system, for which purpose exogenous ChE was used (Table 2).

In one series of experiments propionylcholinesterase was injected intraperitoneally in a dose of 16 mg/kg for 7 days before the production of experimental traumatic shock, and all the parameters were subsequently studied at the same times as in series I (control). Analysis of the results showed that preliminary administration of the enzyme increased the activity of the cholinergic system in the medulla and peripheral blood and, at the same time, lowered the ACh concentration in the lung tissue. The lung index in these rats was lower than in the control animals of group 2. The surface tension was reduced, evidence of preservation of the surfactant system. Quantitative analysis of the morphological changes in the lung showed an increase in the area of unchanged functioning structural components. The amplitude of respiration in these rats was increased and its frequency reduced.

In the next series of experiments, propionylcholinesterase was injected in the same dose 10 min after trauma. Under these circumstances the rhythm and depth of respiration were normalized. The SSL was preserved and the lung index was lower than in the rats of group 2 of the control series. Areas of atelectasis, emphysema, hemorrhages, and edema which were found were very slightly smaller than after pure trauma, but they were a little larger than the corresponding areas in rats receiving the enzyme previously, and still larger than those in intact animals.

Analysis of the length of survival and the mortality showed that as a result of the use of propionylcholinesterase prophylactically and therapeutically the length of survival of the animals was increased to 498.00 ± 2.34 min (compared with 183.0 ± 1.2 min in the control) and mortality was reduced by 15%.

The results are evidence that functional characteristics of the lung correlate with the state of ACh metabolism in the body in general. Administration of propionylcholinesterase had a beneficial effect both on acetylcholine metabolism and on external respiration and the histophysiology of the lung, and as a result, this enzyme can be recommended for use in the treatment of lung complications of traumatic shock.

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ULTRASTRUCTURAL CHANGES IN ERYTHROCYTES AFTER IMPLANTATION OF AN ARTIFICIAL HEART

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Whether or not satisfactory results are obtained with implantation of an artificial heart is largely determined by the adequacy of the artificial circulation. Under unsatisfactory conditions of artificial circulation, serious injury may take place to the erythrocytes, leading to massive hemolysis. These changes may be observed to a lesser degree even if perfusion is adequate [2, 3, 6-8]. Data have recently been published on changes in erythrocytes in animals with an implanted artificial heart, which can also be regarded to some extent as an intracorporeal artificial circulation apparatus [5, 6, 9]. However, no information could be found in the current literature on the sequence of development of ultrastructural changes in the blood cells after implantation of an artificial heart. This paper is devoted to a study of this problem.

EXPERIMENTAL METHOD

Ten experiments were carried out (Professor V. I. Shumakov) on calves of the Kholmogorok breed weighing 80-120 kg and aged 3-4 months. In the course of the experiments an artificial circulation apparatus (ACA) was connected and continued to function until an artificial heart (AH) of the "Poisk" type was connected to the blood flow.

Blood samples were taken 5 min and 1 and 2 h after the ACA began to work, at the time of its disconnection, and also 1, 3, 6, 9, and 12 h after the beginning of functioning of the AH. A cell count was carried out on the blood samples: Blood films were fixed with methanol, stained by the Romanovsky–Giemsa method, and examined under the microscope in the usual way to determine structural changes in the erythrocytes. For electron-microscopic examination, the blood cells were fixed with glutaraldehyde, postfixed with osmium

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