MEDIATOR SYSTEMS AND RESPIRATORY FUNCTION AFTER ACUTE LETHAL BLOOD LOSS

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The manner in which disturbances of respiratory function after acute blood loss are determined by the character of neurohumoral relations was studied in experiments on 54 dogs. The concentration of adrenalin-like substances in the blood shows consistent changes in response to blood loss. The cholinergic activity and the serotonin level, on the other hand, change in two different ways: they may either increase or decrease. Depending on the type of change in cholinergic activity of the blood and in the serotonin level, changes in respiration may follow a different pattern. In the first case deep respiration develops, accompanied by respiratory alkalosis; in the second case fast shallow breathing develops, accompanied by respiratory acidosis.

The important role of the cholinergic and adrenergic systems and also of serotonin in the regulation of respiratory function and the rhythmic activity of the respiratory center has been demonstrated [1, 2, 4, 7].

In the investigation described below the way in which disturbances of respiratory function after acute lethal blood loss are determined by the character of changes in the mediator system of the blood was studied.

EXPERIMENTAL METHOD

In experiments on 54 dogs weighing 14-16 kg, under hexobarbital anesthesia (60 mg/kg body weight) a massive blood loss (4.8 ± 0.26% of the body weight) of lethal proportions was produced by bleeding from the femoral artery.

Catecholamines in the blood were determined by Shaw's method in Matlina's modification [5], acetylcholine by Shutskii's method [10] on the SF-4 spectrophotometer, cholinesterase activity by a chemical method [13], and serotonin by a biological method on the ileum of the albino rat [9]. Shutskii's method of determining acetylcholine in the blood was first verified by comparison with a modified biological method of determination of acetylcholine on the frog's lung [8, 13].

Respiration was recorded pneumographically and at the same time with the AOOZ-M Soviet closed-type spirograph (Kazan' Medfizpribor Technical Design Bureau). The EEG, ECG, and electrical activity of the inspiratory (external intercostal) and expiratory (external oblique abdominal) muscles were recorded simultaneously on two type ÉÉChS-1 electroencephalographs. It has been said that electromyography enables the most complete estimate to be made of the state of the respiratory center and of the neuromuscular apparatus of respiration [6, 12].

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TABLE 1. Dynamics of Cholinergic Activity and Serotonin Concentration in the Blood during Acute Lethal Blood Loss (Variant 1)

Stages of terminal process	Statistical index	AC (in μg %)	PCE (in mg/ml per hour)	ACE (in mg/ml per hour)	Serotonin (in μg/ml)
Initial data	*M*	4,1	6,7	16,1	0,74
	±*m*	0,121	0,134	0,289	0,018
	P	—	—	—	—
Beginning of blood loss	*M*	4,3	6,9	16,4	0,75
	±*m*	0,124	0,107	0,315	0,018
	P	>0,1	>0,1	>0,1	>0,1
Phase of increased respiration rate	*M*	8,0	12,08	21,84	1,4
	±*m*	0,120	0,155	0,296	0,033
	P	<0,001	<0,001	<0,001	<0,001
Terminal pause	*M*	1,4	4,3	10,75	0,39
	±*m*	0,066	0,121	0,324	0,014
	P	<0,001	<0,001	<0,001	<0,001
Agony	*M*	4,2	7,1	16,0	0,76
	±*m*	0,109	0,151	0,208	0,019
	P	>0,1	>0,05	>0,1	>0,1
Clinical death	*M*	0,28	6,9	2,26	0,29
	±*m*	0,019	0,148	0,164	0,14
	P	<0,001	>0,1	<0,001	<0,001

Legend. Here and in Fig. 2: AC (acetylcholine), PCE (pseudocholinesterase); ACE (acetylcholinesterase); P) significance of difference relative to initial values.

TABLE 2. Dynamics of Cholinergic Activity and Serotonin Concentration in the Blood during Acute Lethal Blood Loss (Variant 2)

Stages of terminal process	Statistical index	AC (in μg%)	PCE (in mg/ml per hours)	ACE (in mg/ml per hour)	Serotonin (in μg/ml)
Initial data	*M*	3,8	7,0	15,5	0,69
	±*m*	0,122	0,138	0,379	0,027
	P	—	—	—	—
Beginning of blood loss	*M*	3,6	6,8	15,1	0,67
	±*m*	0,129	0,141	0,923	0,028
	P	>0,1	>0,1	>0,1	>0,1
Phase of increased respiration rate	*M*	2,0	4,1	10,6	0,36
	±*m*	0,127	0,141	0,292	0,014
	P	<0,001	<0,001	<0,001	<0,001
Terminal pause	*M*	1,0	3,4	7,5	0,24
	±*m*	0,083	0,142	0,215	0,010
	P	<0,001	<0,001	<0,001	<0,001
Agony	*M*	3,7	5,3	15,1	0,63
	±*m*	0,184	0,127	0,274	0,020
	P	>0,1	<0,001	>0,1	0,05
Clinical death	*M*	0,2	5,1	2,3	0,17
	±*m*	0,017	0,129	0,174	0,014
	P	<0,001	<0,001	<0,001	<0,001

The excitability and lability of the respiratory center were recorded by the method described by Garanina [3]. The gas composition of the arterial blood at the various stages of blood loss was determined on the AZIV-1 apparatus with attachment (Kazan' Medfizpribor Technical Design Bureau) by Astrup's method. The times of taking the blood samples (stages of lethal blood loss) were obtained from the pneumographic curve.

EXPERIMENTAL RESULTS

The blood catecholamine level was shown to change consistently in response to acute blood loss, rising immediately after the beginning of bleeding to 19.3 ± 0.306 μg% (normal value 2.8 ± 0.116 μg%), thereafter falling to 1.53 ± 0.108 μg% in the terminal pause, and rising again to 9.9 ± 0.174 μg% during agony and then falling sharply in the period of clinical death (to 0.54 ± 0.042 μg%).

The cholinergic activity of the blood and the blood serotonin level changed in two ways during acute blood loss. In the first way the cholinergic activity of the blood and the serotonin level rose in response to blood loss, fell gradually in the terminal pause, returned to their original level during agony, and then fell sharply again during clinical death (Table 1). In the second way the cholinergic activity and serotonin level of the blood began to fall immediately in response to bleeding, returning to their initial level during the period of agony and then falling sharply during clinical death (Table 2).

Changes in the blood mediator level during acute blood loss occurred much before the changes in pH, PCO_2, and PO_2.

In variant 1 of the changes in cholinergic activity and serotonin concentration in the blood, from the initial phases and almost until the terminal pause, respiration was rapid and deep (the respiration rate rose by 125 ± 3.245% and the respiratory volume by 77 ± 4.025%) and the excitability of the respiratory center and the electrical activity of the inspiratory and expiratory muscles increased (whereas normally the threshold of stimulation of the central end of the vagus nerve was 0.3 ± 0.7 mA, in this series of experiments it fell to 0.1 ± 0.016 mA); the electrical activity of the inspiratory and expiratory muscles increased from 42 and 32 to 52-56 and 42-44 spikes/sec respectively.

The minute pulmonary ventilation increased and the oxygen consumption of the animal rose by 62.3 ± 2.678%, while the elimination of carbon dioxide was increased by 53.4 ± 1.543%, as a result of which respiratory alkalosis began to develop (pH 7.42, PCO_2 21 mm Hg).

In variant 2 of the changes in cholinergic activity and serotonin concentration in the blood, against the background of a decrease in the acetylcholine level and cholinesterase activity and a fall in the serotonin concentration in the blood, respiration was rapid and shallow (the respiration rate was increased by 132 ± 5.432%, the respiratory volume was reduced by 44 ± 3.421%), and the excitability of the respiratory center and electrical activity of the inspiratory and expiratory muscles fell (the threshold of stimulation of the vagus nerve was increased to 2.6 ± 0.228 mA) and the electrical activity of the inspiratory and expiratory muscles fell to 28-30 and 20-22 spikes/sec respectively. The pulmonary ventilation was reduced, the oxygen consumption of the animal fell by 32 ± 2.345%, the carbon dioxide elimination fell by 47.8 ± 2.1%, and respiratory acidosis developed (pH 7.08, PCO_2 56 mm Hg).

These experiments thus showed that the increase in the concentration of the cholinergic complex and of serotonin in the blood after blood loss is accompanied by rapid and deep respiration with the development of respiratory alkalosis. Conversely, with a decrease in the level of cholinergic activity and of the serotonin concentration in the blood rapid but shallow respiration is observed, with the development of respiratory acidosis.

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