ABSORPTION AND RELEASE OF BIOGENIC AMINES BY THE LUNGS DURING RECOVERY AFTER HYPOVOLEMIC HYPOTENSION

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The active role of the lungs in the maintenance of homeostasis of the blood under normal and pathological conditions is now accepted [4, 10]. In terminal and postresuscitation states a combination of hypoxic damage to lung tissue with an increase in the load on its metabolic function is frequently found, because of sudden changes in the composition and properties of the blood [3]. Under these conditions lung function, especially in the regulation of blood levels of biologically active substances, including interconnected stages of their assimilation, metabolism, and excretion, may be weakened, and the lungs may become the object of their aggression. Serotonin and histamine, for instance, which play an important role in the humoral control of the pulmonary circulation, may at the same time be involved in the development of certain forms of lung pathology [2, 6, 7, 9, 11, 13].

The aim of this investigation was to evaluate the metabolic function of the lungs in relation to biogenic amines and to compare it with the state of respiration and the circulation during hypovolemic hypotension and in the postresuscitation period.

EXPERIMENTAL METHOD

Experiments were carried out on 14 anesthetized (trimeperidine 8 mg/kg, pentobarbital 5-10 mg/kg), heparinized (500 U/kg) male and female dogs weighing 17-34 kg. In nine experiments (group 1) the animals were subjected for 2-3.5 h to hypovolemic hypotension (arterial pressure BP = 45 mm Hg, total blood loss 33.2 ± 3.9 ml/kg), followed by reinfusion of the blood. In five other animals (group 2), subjected to hypovolemic hypotension for 1 h (BP = 41 mm Hg, total blood loss 35.0 ± 5.0 mg/kg), a model of lung damage of the fat embolism type was created in the post-terminal period. For this purpose, during replacement of the lost blood, oleic acid was injected into the pulmonary artery in a dose of 0.1 ml/kg [5]. Before blood loss, at the end of hypotension (before the beginning of reinfusion of the blood), and at different stages of the recovery period (30 min, 3, 5, and 24 h) the histamine and serotonin concentrations in mixed venous blood were determined by a fluorometric method [12, 14]. Parameters of the central hemodynamics (BP, pulmonary arterial pressure, cardiac output by the thermodilution method), of external respiration, and of the acid-base balance were measured. Serotonin and histamine transport from the blood to the lungs, their assimilation and release by the lungs, and the total peripheral and pulmonary resistance were calculated. In the animals of group 2, the tests were confined to 3 h after reinfusion of the blood. The results were subjected to statistical analysis by Student's *t* test.

EXPERIMENTAL RESULTS

Against the background of a fall in the volume velocity of the blood flow to 40% of its initial value, during hypovolemic hypotension, a significant and progressive increase in the venous concentration of biogenic amines was observed after 1 ± 2-3.5 h: serotonin by 18 and 63%, histamine by 3 and 19% compared with the initial level of 317.2 and 47.7 and 298.3 ± 42.6 nmoles/liter, respectively. Under these circumstances the frequency of cases of absorption of serotonin and histamine by the lungs up to 93 and 72%, respectively, compared with the initial relative frequency of 56 and 33%, was increased. Despite the decrease

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TABLE 1. Parameters of Metabolic Function of Lungs, Central Hemodynamics, and Gas Exchange in Animals Exposed to Hypovalent Hypotension, during Recovery Period ($M \pm m$

Parameter	Initial state	Recovery period 30 min-24 h	
		animals surviving	animals dying
Serotonin concentration in arterial blood, %	100	114,8±5,2* (8)	85,7±5,9*** (15)
concentration in venous blood, %	100	131,6±6,4* (9)	94,8±3,5** (14)
transport to lungs, %	100	168,1±12,0* (9)	68,3±6,6*** (14)
absorption by lungs, nmoles·min^{-1}·kg^{-1}	1,87±0,68 (5)	2,34±0,69 (6)	5,19±0,69*** (9)
release from lungs, nmoles·min^{-1}·kg^{-1}	5,94±1,64 (4)	4,6 (2)	8,6±3,4 (5)
Histamine, concentrate in arterial blood	100	140,3±27,3 (9)	100,4±4,5 (15)
concentration in arterial blood, %	100	128,8±16,0 (9)	100,4±4,9 (14)
transport to lungs, %	100	161,2±10,2* (9)	75,1±6,2** (14)
absorption by lungs, nmoles·min^{-1}·kg^{-1}	3,55±1,77 (3)	5,5±2,2 (3)	3,86±1,65 (4)
release from lungs, nmoles·min^{-1}·kg^{-1}	6,37±0,84 (6)	29,0±11,5* (4)	5,76±1,0 (9)
cardiac output, ml·kg^{-1}·min^{-1}	124,7±15,4 (9)	161,0±17,5 (9)	8,4±10,6*** (15)
BP, mm Hg	103±2 (9)	115±3 (9)	100±5** (15)
Total pulmonary resistance, dynes·sec·cm^{-5}·kg^{-1}	21,6±2,8 (9)	20,1±3,4 (7)	32,5±3,5*** (13)
Total peripheral resistance, dynes·sec·cm^{-5}·kg^{-1}	157,0±18,6 (9)	145,6±19,8 (9)	224,4±19,4*** (15)
PO_2 in arterial blood, mm Hg	94±2 (9)	100±5 (8)	110±4* (15)

Legend. Number of experiments shown in parentheses; *$p < 0.05$ compared with initial value; **) compared with corresponding parameter in subgroup with which compared.

in serotonin (to 55%) and histamine (to 45% of initially) transport to the lungs the absolute value of serotonin uptake by the lungs was increased more than fourfold. Uptake of histamine by the lungs was unchanged but its release from the lungs was reduced by more than 3 times compared with initially. Meanwhile, the serotonin and histamine concentrations in the arterial blood remained stable.

In the course of the 1st day of the recovery period the main values of most of the parameters studied according to the results of the experiments of group 1 as a whole gradually returned to the initial level. However, some of them differed significantly depending on whether the outcome of resuscitation was favorable or not, i.e., the long survivors (33.3%) and those dying in the first 1-3 days (66.7% of the animals).

In the animals which survived, a moderate increase in the serotonin and histamine concentrations in arterial and venous blood compared with initially was observed in the recovery period. Conversely, in the animals which died this reaction was not found or the blood level of biogenic amines actually fell (Table 1). Differences discovered in the time course of the biogenic amines are in agreement with data obtained by other investigators [1, 8], who described the negative consequences of their relative deficiency in the blood in critical states. The mechanisms of onset of the differences thus observed were as follows. In the surviving animals serotonin and histamine transport in the lungs during the first day of the recovery period exceeded the initial level on average by 65%. In the animals which died it remained low (down to 70%), due in part to the lower negative volume of the circulation. The ratio between reactions of uptake and release of biogenic amines by the lungs did not differ significantly in the subgroups. In the dying animals, increased uptake of serotonin by the lungs was preserved, whereas in the surviving animals its uptake was close to the initial level. This explained the relative decrease of the arterial serotonin level in the former and its increase in the latter.

Release of histamine by the lungs into the blood, which was reduced in all the animals during hypovolemic hypotension, increased more than threefold after resuscitation in the subgroup of surviving animals, but only reached the initial level in those which died. One result of this was evidently the relative increase in the arterial histamine concentration in the former animals and the absence of any such increase in the latter (Table 1).

Analysis of data characterizing the state of external respiration and gas exchange in the lungs of animals surviving hypovolemic hypotension revealed no evidence of respiratory failure or hypoxia in the blood of the two subgroups. Meanwhile in the animals which died the cardiac ejection and BP were 1.8 and 1.2 times lower than in the surviving animals, whereas the total peripheral and pulmonary resistance was 1.5 and 1.6 times higher, respectively (Table 1).

In the experiments of group 2, in animals with a complicated course of the early postresuscitation period, as a result of damage to the lungs by oleic acid, the trend of the parameters of the circulation, the blood levels of serotonin and histamine, and their uptake and release by the lungs, were similar in the character and depth of the changes to those observed in the animals of group 1, which were subjected to more severe hypoxia and subsequently died. In some experiments of group 2 with early development of disturbances of external respiration and gas exchange ($PaO_2 = 66 \pm 6$ mm Hg) in the lungs and which died during the first day, moreover, these changes were more marked and were distinguished by an increase in the frequency of the reaction of serotonin and histamine uptake by the lungs (to 83 and 100% of cases, respectively).

The increase in the uptake of biogenic amines by the lungs in all the experiments with hypovolemic hypotension (in the compensation phase), and in the uptake of serotonin in the postresuscitation period also, when its course and outcome were unfavorable, is thus evidence of intensification of the nonrespiratory function of the lungs, whereas the decrease in their histamine production and replacement, in individual cases, of the extraction of serotonin by its release, is evidence of its weakening. The increased serotonin consumption by the lungs is usually matched by an increase of resistance in the pulmonary circulation, which is useful during hypovolemic hypotension, but after reinfusion of blood it is converted into a factor leading to gradual disturbance of ventilation-perfusion ratios in the lungs. In turn, the shift of the reaction of the lungs toward histamine uptake (instead of its secretion) in the presence of fat embolism in the lungs is usually accompanied by the development of interstitial edema. Under these conditions the role of the lungs in the maintenance of processes of production and exchange clearance of biogenic amines at optimal levels for restoration becomes less important. On the whole, if the course of the postresuscitation process is complicated and its outcome unfavorable, by contrast with the situation in which the outcome is favorable a combination of a more marked increase in the pulmonary assimilation of serotonin and a lower pulmonary histamine production is observed. One of the conditions for the appearance of these changes in postresuscitation states is evidently a hypokinetic type of circulation.

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