OXYGEN CONSUMPTION IN THE LUNGS OF DOGS AFTER EXTERNAL BLOOD LOSS AND REINFUSION

V. I. Kulitskaya, T. V. Feduchkina, T. V. Sevast'yanova, and N. S. Kuz'mina

UDC 616-005.1-085.38-092.9-07:616.24-008.7-074

KEY WORDS: blood loss; respiratory failure; lipids; oxygen consumption.

In surgical practice in the treatment of emergency states associated with acute surgical diseases and traumatic injury to the thoracic and abdominal organs, massive blood loss is often the cause of postoperative complications and unsuccessful treatment, and even death [5, 10]. In this connection problems relating to the correction of posthemorrhagic states demand urgent solution. Recent investigations have shown the efficacy of reinfusion of the victims' own blood for this purpose, and some of the mechanisms of its effect on the state of the basic parameters of homeostasis have been assessed [8-10]. However, data on changes in the intensity of metabolic activity of the lungs during massive blood loss and in the postresuscitation period could not be found in the accessible literature. Since these data are directly related to our understanding of the mechanisms of the pathogenesis of posthemorrhagic respiratory failure, we undertook an experimental investigation with the aim of determining oxygen consumption in the lungs of dogs during external blood loss of increasing volume, during the first hours and day after reinfusion, and their relationship to the entry of energy-yielding substrates, total lipids in particular, into the lungs.

EXPERIMENTAL METHOD

Experiments were carried out on 10 dogs weighing form 12 to 21 kg, into whose jugular vein, and carotid and femoral arteries catheters were implanted under general anesthesia (1% hexobarbital solution, intravenously). Using a "floating microcatheter," the right chambers of the heart and the pulmonary artery were catheterized through the jugular vein. A thermodilution transducer was introduced through a catheter in the carotid artery into the aorta to determine the cardiac output and cardiac index (CI). Bleeding was then carried out from the femoral artery in volumes of 10, 20, 30, and 40 ml/kg, at intervals of 30-40 min, in the course of 10-15 min each time. The blood was then returned to the animal via the jugular vein. No anticoagulants were added to the blood. The animals were investigated 5-10 min after each blood loss, and 1 h and 24 h after reinfusion. The respiration rate (RR), and respiratory volume (RV) were recorded in all the animals, the respiratory minute volume (RMV) and oxygen consumption per minute ($\dot{V}_{O_2}$) (on an SG-2M spirograph) were calculated, and CI (by the thermodilution method), and P_{O_2} of arterial and mixed venous blood (from the pulmonary artery) were recorded on a Corning gas analyzer (England). The oxygen concentration in arterial and mixed venous blood [7] and oxygen consumption in the systemic ($V_{O_2}SC$) and pulmonary ($V_{O_2}PC$) circulation [4] were calculated. The relative serum total lipid concentrations in arterial (SLa) and mixed venous blood (SLv) were determined by multiplying lipid concentrations in arterial blood (CLa) or mixed venous blood (CLv) by CI. Total lipids were extracted from blood serum by the method in [13]. Spontaneous very weak fluorescence of total lipids of arterial (VWFa) and mixed venous blood (VWFv) was measured on a "Radiometer-20 046" apparatus (East Germany) together with FÉU-85 photoelectric multiplier at 37°C.

Laboratory of Experimental Pathology, N. V. Sklifosovskii Emergency Aid Research Institute, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. K. Permyakov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 110, No. 7, pp. 22-24, July, 1990. Original article submitted September 25, 1989.

 0007-4888/90/0007-0864$12.50

TABLE 1. Effect of Blood Loss on Pulmonary Ventilation, Blood Flow, and Intensity of Metabolism in Dogs

Period of observation	RR, cycles/min	RV, ml/kg	RMV, ml/kg·min	CI, ml/kg·min	$\dot{V}_{O_2}$, ml/min·kg	$\dot{V}_{O_2}$ SC, ml/min·kg	$\dot{V}_{O_2}$ PC, ml/min·kg
Initial							
Hemorrhage							
Blood loss							
10 ml/kg	21,2±3,05	10,23±1,15	191±20,46	221,8±29,64	11,5±1,23	6,81±0,99	4,69±1,64
20	25,0±8,68	12,9±1,93	285±58,39	127,1±16,40*	10,7±1,08	5,62±1,71	5,08±1,22
30	24,1±6,93	11,4±2,03	250±45,01	110,5±8,22*	9,6±1,68	7,10±0,18	2,50±0,62
40	31,6±6,08	12,6±1,41	380±53,99*	84,8±6,88*	8,0±1,15	6,87±1,04	1,13±0,46
Posthemorrhagic							
Time after reinfusion	22,6±2,16	9,4±4,01	201±74,89	62,9±6,22*	6,5±1,94	4,56±1,43	1,94±0,54
1 h	30,6±4,94	16,2±2,25	393,3±57,18*	268,1±43,22	14,2±2,45	7,71±3,30	6,49±1,96
1 day	21,4±3,34	22,4±2,73*	486±122,33*	254,2±48,33	19,5±2,51*	8,65±1,40	10,65±2,81

Legend. Asterisk indicates values differing statistically significantly from initial level.

The numerical results were subjected to statistical analysis by Student's test and are given in Table 1 and Fig. 1.

EXPERIMENTAL RESULTS

After the preliminary operation on the dogs about 40% of the value of $\dot{V}_{O_2}$ was accounted for by $\dot{V}_{O_2}$ PC. Under these circumstances CLv was statistically significantly lower than CLa ($p < 0.05$), but VWFv was statistically higher than VWFa ($p < 0.05$), evidence of the release of lipids from the lungs into arterial blood (Fig. 1a, c).

External blood loss in a volume of 10 to 40 ml/kg evoked a gradual fall of $\dot{V}_{O_2}$ in the dogs, which amounted on average to 56.6% of the initial value after loss of 40 ml/kg blood. The decrease in $\dot{V}_{O_2}$ during the period of blood loss was mainly due to a decrease in $\dot{V}_{O_2}$ PC, which began after blood loss of 20 ml/kg, and after blood loss of 30 ml/kg it amounted to about 24% of the initial value. The $\dot{V}_{O_2}$ SC level in the period of increasing blood loss did not change significantly, and even after blood loss of 40 ml/kg it had only slight tendency to fall compared with the initial level (Table 1). The increase in the volume of blood loss was accompanied by a decrease of CI, an increase of RMV, and preservation of or an increase of p_aO_2 compared with the corresponding initial values (Table 1; Fig. 1d, 2). Under these circumstances an increase in CLv was observed, with a tendency for SLv to fall, VWFv, CLa, and SLa decreased, but VWFa increased compared with the corresponding initial data (Fig. 1a-c). At the beginning of blood loss (10 ml/kg) the release of lipids from the lungs, which occurred before blood loss, was replaced by retention of lipids in the lungs: CLv became statistically significantly higher than CLa ($p < 0.05$). Later, however, with an increase in the volume of blood loss, this difference ceased to be observed.

Reinfusion led to rapid delivery of $\dot{V}_{O_2}$ to its initial level (1 h), and after 1 day $\dot{V}_{O_2}$ was already twice as high as initially. Changes in $\dot{V}_{O_2}$ in the posthemorrhagic period, just as in the hemorrhagic period, were mainly determined by changes in $\dot{V}_{O_2}$ PC, which after 1 h was almost 1.5 times higher, and after 1 day almost 2.5 times higher than initially (Fig. 1d). $\dot{V}_{O_2}$ SC in this period developed a slight tendency to increase above the initial value. Reinfusion led to rapid normalization of CI, RMV rose sharply, but it was accompanied by some decrease in p_aO_2 (compared with the corresponding initial data, see Fig. 1). Under these circumstances CLv showed a tendency to return to normal, but there was a sharp increase in the SLv, a decrease in VWFv, incomplete restoration of CLa and SLa, and an increase in VWFa compared with the corresponding initial data (Table 1). In the first hour after reinfusion a tendency was observed for lipids to be released from the lungs (SLa was higher than SLv), but after 1 day, on the contrary, there was a tendency for lipids to be retained (SLa was lower than SLv and VWFa was higher than VWFv, $p < 0.05$).

The results thus showed that fluctuations in basal metabolism observed after blood loss [3] are due primarily to fluctuations in the intensity of basal metabolism in the system of the pulmonary circulation. Administration of a general anesthetic (hexobarbital), and the beginning of blood loss and, in particular, reinfusion of the lost blood lead to marked activation of the nongas-exchange functions of the lungs, which utilize O_2. Massive blood loss, on the other hand, inhibits them. Activation or inhibition of oxidation-reduction processes in the lungs in the hemorrhagic and posthemorrhagic periods could be connected to some degrees with lipid metabolism in the lungs [6, 9]. Evidence in support of this is given also by our data showing retention of lipids in the lungs, or their release from them, accompanied by a high level of $\dot{V}_{O_2}$ PC. The negative correlation between $\dot{V}_{O_2}$ PC and VWFa ($r = -0.57, n = 21, p < 0.01$) suggests that conversion of lipids in the lungs may affect the concentration of free radicals and lipid peroxides in arterial blood. The fact that free radicals and lipid peroxides can be

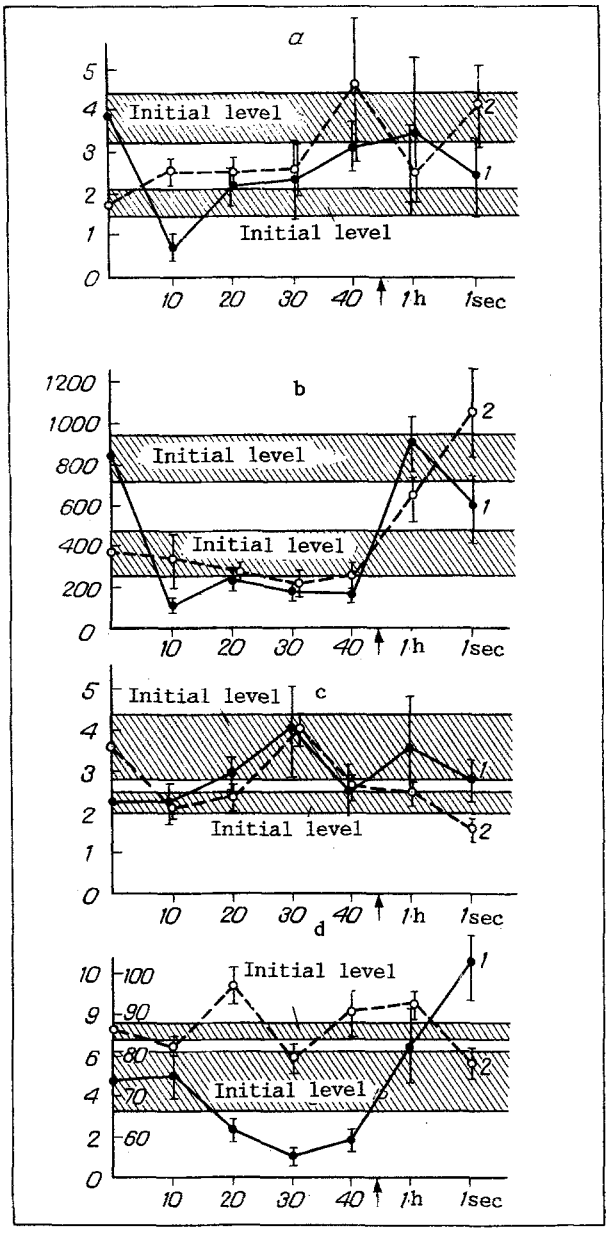

Fig. 1. Concentration (*a*, mg/ml), content (b, mg/min · kg), and very weak fluorescence (c, relative units) of total lipids in serum from arterial (1) and mixed venous blood (2), and gas exchange in lungs (d), $\dot{V}_{O_2}$ (1, ml/min · kg) and p_aO_2 (2, mm Hg) in dogs after external blood loss and reinfusion. Abscissa, volume of blood loss (in ml/kg) and time after reinfusion (1 h and 1 day). Arrow indicates reinfusion.

formed in the lungs as intermediate products of lipid conversion is shown by changes in the VWF level of lipids after they have passed through the lungs. However, an excess of these same products in the cell can cause damage to it and can lead to a disturbance of the gas-exchange function of the lungs [12, 14]. The high coefficient of positive correlation between VWFa and RR ($r = +0.29$, $n = 51$, $p < 0.05$), which we found, suggests that free radicals and lipid peroxides in the arterial blood may affect the lability of the respiratory center, i.e., they are among the intrapulmonary metabolites which control the character of pulmonary ventilation. These results serve to unify our ideas on changes in the lungs in the hemorrhagic and posthemorrhagic periods, arising at different levels from submolecular to functional, and they show how closely metabolic processes in the pulmonary circulation under extremal conditions depend, on the one hand, on gas exchange processes and, on the other hand, on metabolic processes in the tissues of the systemic circulation. Preservation of the $\dot{V}_{O_2}$ SC level, which we found during blood

loss of increasing volume, is in agreement with data in the literature [3], and may be due to the fact that during blood loss, parallel with inhibition of mitochondrial oxidation [15], even in the perfused tissues processes of free-radical oxidation, utilizing cellular O_2 [1], are activated [2]. Under these circumstances, however, despite the sufficiently high $\dot{V}_{O_2}$ SC level, incompletely oxidized products begin to accumulate in the body under conditions of blood loss and the degree of circulatory-anemic hypoxia increases [3].

Activation of oxidation-reduction processes in the lungs is evidently one of the mechanisms influencing the formation of p_aO_2. Since a fall in the value of p_aO_2 after reinfusion took place against the background of intensive hyperventilation, it can be tentatively suggested that respiratory failure of metabolic genesis cannot be completely abolished by stimulation of pulmonary ventilation.

Our results show that, first, in the posthemorrhagic period the O_2 demand of the body is determined not only, as is generally considered, by the O_2 demand of the tissues of the systemic circulation [7], but also to a large degree by the O_2 demand of the system of the pulmonary circulation. Second, a definite role in the pathogenesis of posthemorrhagic respiratory failure may be played by processes of activation of the nongas-exchange functions of the lungs, including reactions of lipid conversion.

LITERATURE CITED

1. A. I. Archakov, Microsomal Oxidation [in Russian], Moscow (1975).
2. V. T. Dolgikh, A. M. Kochetov, S. I. Eremeev, and P. T. Mal'kov, Anest. Reanimatol., No. 1, 24 (1988).
3. N. I. Kochetygov, Blood Substitutes in Blood Loss and Shock [in Russian], Moscow (1984).
4. V. I. Kulitskaya and G. G. Rogatskii, Byull. Éksp. Biol. Med., No. 3, 287 (1986).
5. N. V. Lebedev, M. M. Abakumov, and V. B. Khvatov, Khirurgiya, No. 8, 67 (1988).
6. M. Ya. Livchak, Metabolism of the Lungs in Nonspecific Diseases of the Respiratory Organs [in Russian], Leningrad (1979), pp. 55-61.
7. M. Navratil, K. Kadlec, and S. Daum, Pathophysiology of Respiration [in Russian], Moscow (1967).
8. A. V. Serkina and V. A. Vlasenko, Khirurgiya, No. 9, 88 (1979).
9. N. V. Syromyatnikova, V. A. Goncharova, and T. V. Kotenko, Metabolic Activity of the Lungs [in Russian], Leningrad (1987).
10. D. V. Usov, Vestn. Khir., No. 4, 76 (1983).
11. M. I. Shalaev, I. I. Kalugin, V. V. Kuznetsov, and A. K. Svin'in, Klin. Khir., No. 3, 61 (1979).
12. S. M. Deneke and B. Z. Fanburg, Brit. J. Anaesth., **54**, No. 7, 737 (1982).
13. J. Folch, J. Ascoli, M. Lees, et al., J. Biol. Chem., **191**, 833 (1951).
14. F. F. Slatter, in: Free Radicals and Tissue Damage, J. G. Strawitz et al. (eds.), New York (1979), pp. 143-177.
15. J. G. Strawitz, H. Hift, R. L. Temple, A. Ehrhardt, and N. Kazansky, Am. J. Physiol., **200**, No. 2, 257 (1961).