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EFFECT OF THE MODE OF EXTRAPULMONARY GAS EXCHANGE ON LUNG SURFACTANT FUNCTION AND METABOLISM

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The extensive use of oxygenators of both contact and membrane types for extrapulmonary gas exchange became possible only after a comprehensive study of their action on the body [3, 6, 8]. Until recently, however, little attention had been paid to the study of the relationship between the mode of extrapulmonary gas exchange (the type of oxygenator) and the onset of changes in function and metabolism of the lung surfactant (LS) [1, 6]. However, attention is increasingly being paid at the present time to disturbances in the surfactant system, for it plays an essential role in the development of postoperative pulmonary complications [9, 10].

This paper gives an account of a quantitative and qualitative assessment of changes in LS function and metabolism during the use of a foam-film oxygenator (FFO) and the Sever membrane oxygenator (MO) during venoarterial perfusion.

EXPERIMENTAL METHOD

Two series of experiments were carried out on 28 mongrel dogs of both sexes weighing 21.4 ± 2.1 kg. Changes in LS under the influence of FFO were studied in series I, changes under the influence of the Sever MO in series II. Under conditions of normothermia, trimeperidine–hexobarbital anesthesia, and artificial ventilation of the lungs (AVL), and after intravenous injection of heparin (8–10 mg/kg for the initial dose, and 0.5 mg/kg every 30 min during the experiment), venoarterial perfusion was carried out with extracorporeal blood oxygenation for 120 min according to the following scheme: right atrium–gas exchanger–left femoral artery. The priming volume of the perfusion system was 500–700 ml (Ringer-Locke, 5% glucose, and rheopolyglucin solutions in equal proportions). Blood was returned to the animals by means of the roller pump unit of the ISL-4 apparatus. The average volume velocity of perfusion in the experiments of series I was 47.8 ± 3.7 ml/min•kg and in series II 46.3 ± 5.8 ml/min•kg. The volume velocity of the gas (O_2) flow was 2–6 liters/min. The adequacy of perfusion and oxygenation was monitored by measuring the partial pressure of O_2 and the acid-base balance (ABB) of the blood, by the micro-Astrup method (AME-1 analyzer, from Radiometer, Denmark). During the experiments the arterial pressure (BP) was recorded by the

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TABLE 1. Functional State and Phospholipid Composition of LS during Venoarterial Perfusion and Extrapulmonary Oxygenation, using MO and FFO (M ± m)

Parameter		Initial level		120 min of perfusion		60 min after end of perfusion	
		FFO	MO	FFO	MO	FFO	MO
ST, mN/m		7,6±0,53	8,8±0,58	19,8±0,61*	15,9±1,2*	26,4±1,6*	14,9±0,96*
SI		1,34±0,03	1,13±0,04	0,81±0,03	0,70±0,06	0,59±0,05	0,77±0,03
Phosphatidylcholine	%	69,2±0,78	66,5±0,43	67,4±0,54	65,4±0,45	62,8±0,49*	66,3±0,46
Phosphatidylglycerol	%	12,1±0,74	13,8±1,1	11,9±0,58	14,4±0,46	9,1±0,55	13,4±1,1
Phosphatidylethanolamine	%	6,5±0,55	7,8±0,48	7,2±0,55	7,6±0,29	5,5±0,71	8,1±0,38
Sphingomyelin	%	6,2±0,57	6,8±0,43	8,2±0,47	8,3±0,45	12,2±0,65*	8,2±0,73
Phosphatidylserine	%	3,8±0,33	3,3±0,86	3,1±0,27	2,9±0,25	2,0±0,36	2,5±0,27
Phosphatidylinositol	%	2,2±0,21	1,8±0,31	1,7±0,47	1,4±0,49	1,1±0,50	1,5±0,29
Lysophosphatidylcholine	%	0	0	0,5±0,22	0	7,3±0,61*	0
Phosphatidylcholine/ sphingomyelin		11,8±1,3	10,2±0,7	8,2±0,6	8,1±0,5	5,4±0,3*	8,1±0,06

Legend. *Indicates differences statistically significant compared with initial level ($p < 0.05$).

direct method by means of the Salyut-6 polygraph and the level of hemolysis was determined by the benzidine method. To study the surface-active properties of the lungs and phospholipid metabolism of LS the method of segmental bronchoalveolar washings (BAW) as described in [7] was used. The surface tension (ST) of BAW was determined on Wilhelmy scales, and the stability index (SI) of the alveoli was then calculated as in [4]. Phospholipids of BAW were analyzed by two-dimensional microthin-layer chromatography on "Silica Woelm" silica-gel (Woelm Pharma, West Germany). The relative percentages of the phospholipids were determined as in [12] and the phosphatidylcholine/sphingomyelin ratio was calculated. The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

When FFO was used a considerable and statistically significant increase in ST_{min} of BAW was observed (Table 1), which was most marked after the end of perfusion and return of the blood from the extracorporeal system to the animal, evidence of depression of LS function [9, 10]. Because of the increase in ST_{min}, SI of the alveoli also regularly decreased. In the experiments of series II the increase in ST_{min} was smaller and it remained stable throughout perfusion and the immediate postperfusion period. The decrease in SI of the alveoli was correspondingly smaller.

These changes in the functional activity of LS correlated closely within certain limits with disturbances of its metabolism. Quantitative relations were established between these parameters. For instance, during perfusion with MO, ST_{min} of BAW was 15-19 mN/m and this was not accompanied by any change in the composition or relative percentages of the individual fractions of phospholipids in LS (Table 1). This was demonstrated by chromatographic analysis of the phospholipids of BAW from the animals after perfusion with the Sever MO (Fig. 1a). The increase of ST_{min} of BAW within these limits is evidence of the physiological response of this system to a change in ventilation-perfusion relations during venoarterial perfusion, and was not connected at this stage with significant disturbances of phospholipid metabolism of the alveolar lining.

Different relationships were established during working with FFO: after perfusion for 120 min and in the immediate postperfusion period, ST_{min} of BAW reached 25 mN/m, and this was accompanied by disturbances of LS metabolism. These took the form of a decrease in the content of phosphatidylcholine, the principal component of LS which determines its physiological role, by 7% and the appearance of a lysophosphatidylcholine (the end product of hydrolysis of PC under the influence of phospholipase A_2 [9]) fraction in BAW (Fig. 1b). At the same time, the sphingomyelin content was increased by 6% and the phosphatidylcholine/sphingomyelin ratio was reduced: according to data in the literature [5], this is characteristic of the state of LS in adult patients with the respiratory distress syndrome.

Criteria of adequacy of perfusion (blood gases, ABB, BP) generally accepted in clinical practice did not differ significantly in the experiments of series I and II from the original data (except p_aO_2) and they lay within optimal limits (in series I and II respectively,

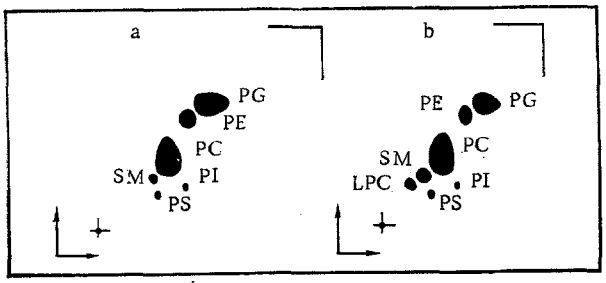

Fig. 1. Diagram of two-dimensional microchromatogram of BAW phospholipids when the Sever MO (a) and FFO (b) were used. PC) Phosphatidylcholine, PG) phosphatidylglycerol, PE) phosphatidylethanolamine, SM) sphingomyelin, PS) phosphatidylserine, PI) phosphatidylinositol, LPC) lysophosphatidylcholine.

toward the end of perfusion p_aO_2 was 245.9 ± 22.7 and 245.8 ± 11.6 mm Hg, p_aCO_2 was 40.6 ± 2.7 and 27.2 ± 1.9 mm Hg, pH 7.35 ± 0.02 and 7.42 ± 0.02, BE −1.7 ± 1.70 and −5.5 ± 1.40 mM, and BP 101 ± 4.4/64.0 ± 4.5 and 94.6 ± 11.5/77.0 ± 4.8 mm Hg). Only trauma of the blood was significantly greater after perfusion with FFO than with MO (the free plasma hemoglobin of blood reached 0.252 ± 0.012 and 0.054 ± 0.006 g/liter respectively).

The writer's previous investigations showed that the Sever MO has no adverse effect likewise on the blood plasma protein during long-term operation (3 h) [2], whereas the short-term use of oxygenators of contact type, including FFO, leads to denaturation, to a change in the fractional composition of the plasma proteins, and to the appearance of the so-called "extracorporeal circulation protein" [11]. It can be tentatively suggested that disturbances of LS metabolism during the use of FFO in the present experiments were connected with precisely these changes.

It is being reported increasingly more often in the recent literature that the membrane method of extrapulmonary gas exchange has advantages over oxygenators of contact type. Data on the effect of FFO and MO on LS function provide further confirmation of the good prospects ahead for the use of MO in a wide field of clinical practice.

Thus the method of extrapulmonary gas exchange (the type of oxygenator) has a significant effect on the function and metabolism of LS during long-term (2 h) venoarterial perfusion: membrane oxygenation is more physiological than gas exchange of the contact type. The use of the Sever MO under the above conditions was accompanied by some increase in ST_{min} of BAW (15-19 mN/m), but this was not associated with any significant changes in phospholipid metabolism of LS, and this level of ST_{min} of BAW can be taken as the criterion of adequacy of perfusion. The increase in ST_{min} of BAW (when FFO was used) to 25 mN/m or more was due to disturbances of phospholipid metabolism of LS: the phosphatidylcholine content was reduced but the sphingomyelin level was raised, a lysophosphatidylcholine fraction appeared, and the phosphatidylcholine/sphingomyelin ratio decreased.

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