Effect of Extracorporeal Blood Treatment with an Ozone-Oxygen Mixture on Pulmonary Functions in Healthy Dogs and Dogs with Shock Lungs

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Extracorporeal blood treatment with an ozone-oxygen mixture increased the efficacy of pulmonary ventilation and improved gas exchange, blood oxygenation in the pulmonary circulation, and the microcirculation in peripheral tissues in intact dogs and dogs with experimentally produced shock lung. This procedure activated glycogenolysis, glycolysis, and metabolic processes in the lung tissue (in particular, the uptake of palmitate from the blood by the lungs was increased in intact dogs, as was the uptake of lactate and pyruvate in dogs with shock lung), and it also raised blood levels of molecular lipid peroxidation products in dogs of both groups.

Key Words: *ozone; pulmonary functions; shock lung*

Extracorporeal blood treatment (ECBT) with an ozone-oxygen mixture containing ozone in a concentration of 48 μg/liter has been shown to promote a better supply of the body with oxygen and to raise the metabolic activity of biological systems [7]. However, parenteral administration of ozone is severely limited because of its extremely strong oxidizing action on biomembrane phospholipids. The purpose of this work was to study the gas-exchanging and metabolic functions of the lungs after ECBT in intact dogs and dogs with experimentally produced shock lung.

MATERIALS AND METHODS

A total of 36 adult mongrel dogs of both sexes weighing 12.3±4.7 kg were used. They were divided into four groups. Group 1 (n=10) consisted of intact control dogs. Group 2 (n=10) comprised intact dogs whose blood had been treated for 30 min in an arteriovenous shunt (femoral artery -

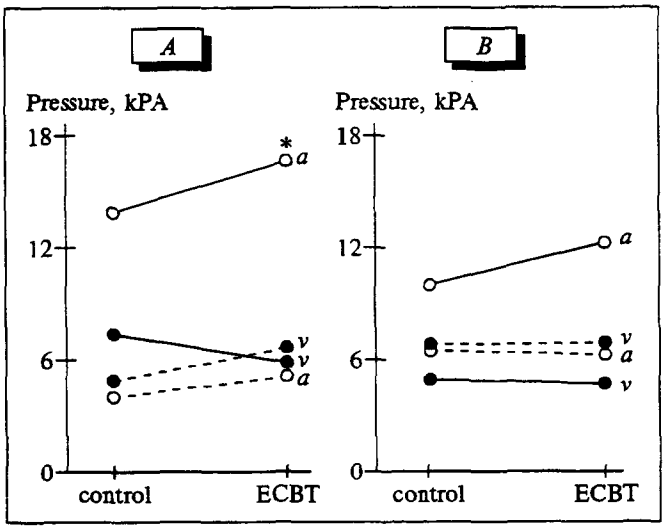

Fig. 1. Pressure of blood gases after extracorporeal blood treatment (*ECBT*) in intact dogs (*A*) and dogs with shock lung (*B*). Solid line: pO_2; dashed line: pCO_2. Here and in Figs. 2 and 3: a = arterial blood; v = venous blood; $^*p<0.05$ in comparison with baseline.

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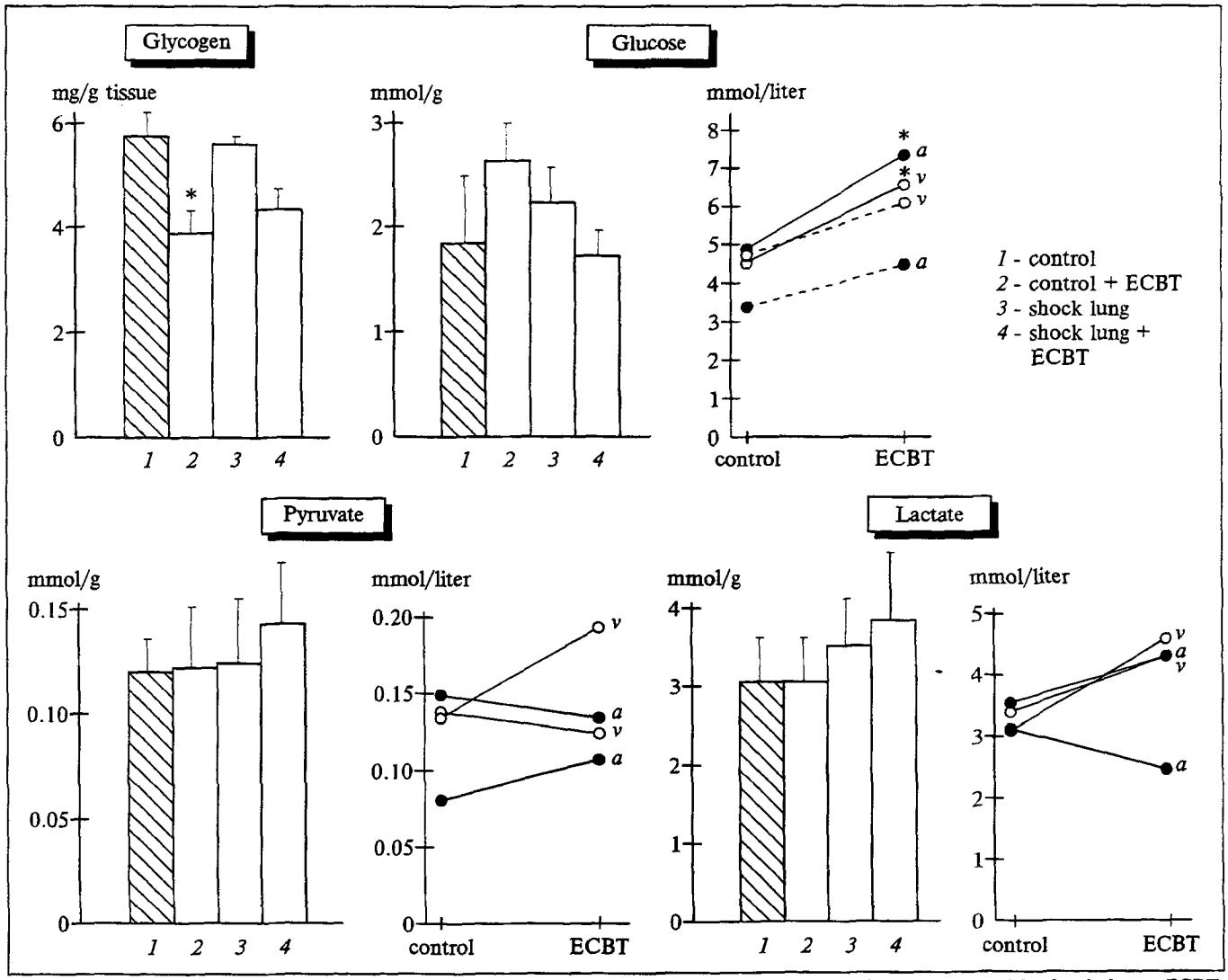

Fig. 2. Lung tissue and blood levels of carbohydrates. Solid line: intact dogs; dashed line: dogs with shock lung. ECBT: extracorporeal blood treatment.

femoral vein) with an oxygen-ozone mixture containing ozone (obtained in an ozonizer) in a concentration of 48 μg/liter [7]. In group 3 (n=10) and group 4 (n=6), ECBT was carried out, respectively, 48 h before and some time after shock lung was induced by the method we had developed [10]. All tests were done with Nembutal-anesthetized (30 mg/kg intravenously) and heparinized (0.1 mg/kg intravenously) dogs. Blood samples were taken via catheters from the right heart (venous blood) and from the aortal orifice (arterial blood) at the baseline, 60 min after the ECBT, and 48 h after the onset of shock lung. Lung tissue samples were also taken at the indicated times - at thoracotomy under deep Nembutal anesthesia - and kept frozen in liquid nitrogen. External respiration was evaluated spirographically and by measurement of blood gases in a gas analyzer. Nucleotides, carbohydrates, and molecular products of lipid peroxidation (LPO) were measured in both tissue and blood samples [4-6,11,12]. The fatty acids were analyzed by gas-liquid chromatography [2]. The results were subjected to statistical treatment using Wilcoxon's and Student's tests.

RESULTS

ECBT raised the efficiency of external respiration in intact dogs (as evidenced by the 47% increase in the oxygen utilization coefficient - Table 1) and improved gas exchange in the lungs, blood oxygenation in the pulmonary vessels, and the microcirculation in peripheral tissues in both intact dogs and dogs with shock lung (Fig. 1).

Examination of lung tissue bioenergetics in the intact dogs after ECBT (group 2) showed little change in the guanyl nucleotides (p>0.05) but a

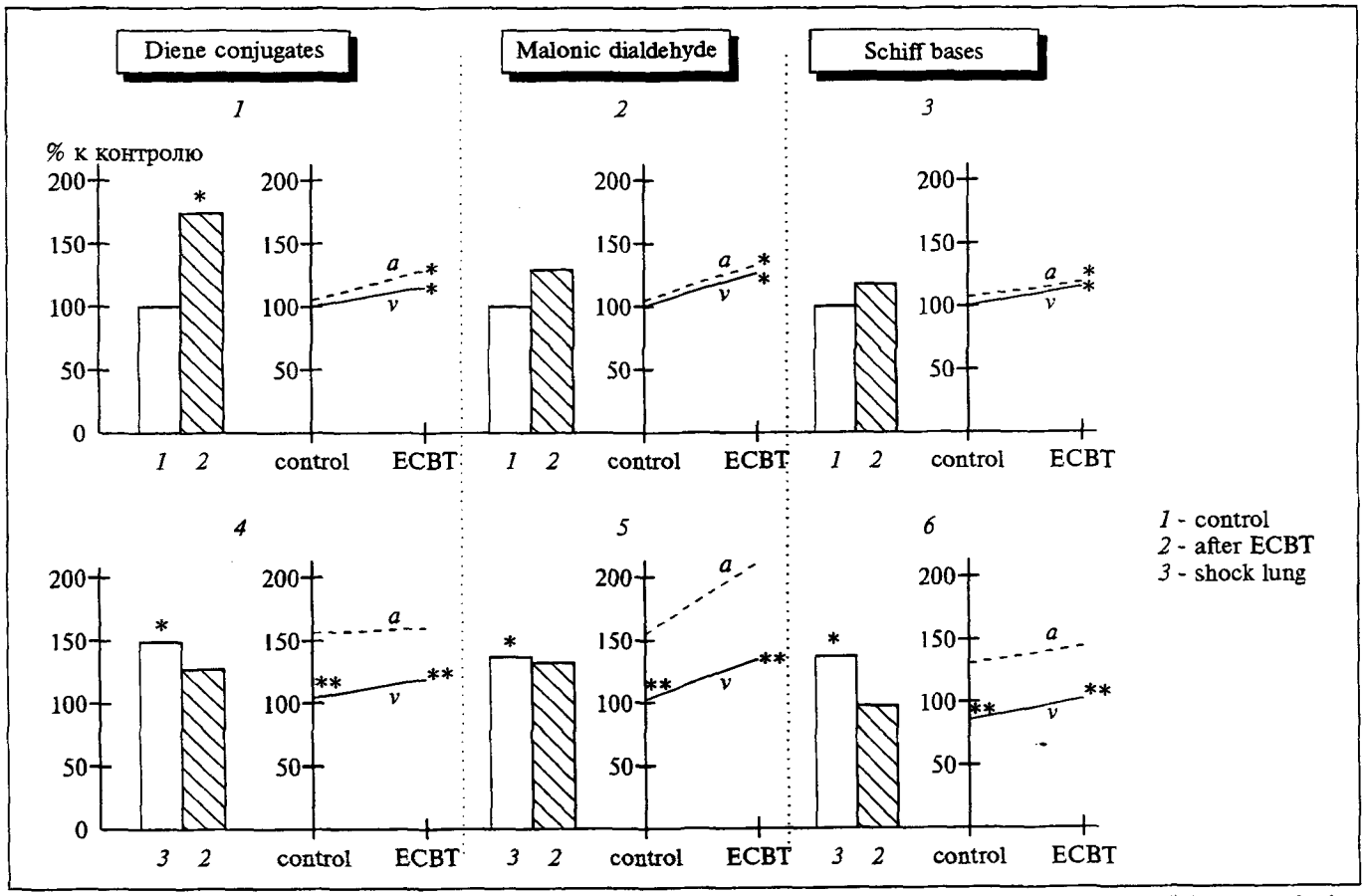

Fig. 3. Lung tissue and blood levels of LPO products in intact dogs (*1–3*) and those with shock lung (*4–6*) before and after extracorporeal blood treatment (ECBT). *Significant change in the difference between *v* and *a* at $p<0.05$.

significant rise in ADP ($p<0.05$) and a tendency toward a decrease in ATP (Table 2).

By 48 h after shock lung induction, the total guanyl nucleotides in the lung tissue had decreased by more than 1.5-fold (group 3, Table 2). After ECBT, intensified ATP breakdown to AMP ($p<0.002$) (the ATP/AMP ratio was only half that before ECBT) and GTP ($p<0.05$) occurred (group 4, Table 2).

In the intact dogs (Fig. 2), ECBT lowered glycogen in the lung tissue ($p<0.05$) while raising glucose in both the lung tissue and blood ($p<0.05$) and increasing 2-fold the arteriovenous (a-v) difference; in the blood, a tendency toward lowered pyruvate and elevated lactate levels was noted, with a rise of the lactate/pyruvate ratio from 24.56 to 34.68 in the venous blood and from 23.76 to 32.09 in the arterial blood. These changes may occur due to lactic acid being washed out from peripheral tissues under conditions of improved microcirculation [7].

In the dogs with shock lung, ECBT activated glycogenolysis and glycolysis in the lung tissue, leading to a rise of both pyruvate and lactate (Fig. 2), apparently as a result, in particular, of their increased uptake from the circulation given that

TABLE 1. Parameters of Pulmonary Ventilation

Parameter	Intact dogs		Dogs with shock lung	
	before ECBT (n=10)	after ECBT (n=10)	before ECBT (n=10)	after ECBT (n=6)
Respiratory rate, No. of breaths/min	51.0±8.6	35.0±7.5	37.3±8.1	63.0±13.17*
Respiratory volume, ml/kg	19.0±1.87	14.8±2.7	20.0±4.46	21.0±9.67
Minute volume, ml/kg/min	1252±331	670±181	655±103	841±138
Oxygen consumption, ml/kg/min	9.3±1.6	7.3±0.65	5.5±0.85	8.35±2.17
Oxygen utilization coefficient, %	100	147	100	108

Note. *$p<0.05$ in comparison with values before ECBT.

TABLE 2. Nucleotide Levels in Lung Tissues, μmol/g tissue

Group	Total nucleotides	AMP	ADP	ATP	GDP	GTP	Adenine/gyanyl nucleotides
1	2.773±0.222	0.621±0.081	0.425±0.037	1.051±0.135	0.349±0.150	0.342±0.037	3.03
2	2.779±0.212	0.551±0.067	0.713±0.120*	0.789±0.061	0.372±0.044	0.355±0.112	2.89
3	2.328±0.255	0.689±0.134	0.301±0.098	0.953±0.062	0.179±0.060	0.205±0.074	5.05
4	2.290±0.253	0.820±0.062	0.442±0.134	0.604±0.087**	0.253±0.134	0.172±0.058	4.39

Note. *$p<0.05$ in comparison with group 1; **$p<0.02$ in comparison with group 3. Group 1: intact dogs; group 2: intact dogs after ECBT; group 3: dogs with shock lung; group 4: dogs with shock lung after ECBT.

the lungs can utilize them as energy substrates [3]. The lactate/pyruvate ratio before ECBT was 23.06 in the venous blood and 38.52 in the arterial blood (indicating a predominance of glycolytic processes in the latter) but decreased to 23.8 in both after this procedure.

In the intact dogs, ECBT initiated LPO processes in the lungs, as attested by a 70% rise in diene conjugates ($p<0.05$) and elevated (by 20% on average) levels of secondary and final molecular LPO products; it also raised significantly the levels of all LPO products in the blood ($p<0.05$) and increased the *a-v* difference (Fig. 3, *1-3*) (the concentration of diene conjugates rose from 12.4 to 23.6 mmol/liter, that of malonic dialdehyde from 0.25 to 0.88 mmol/liter, and that of Schiff bases from 3.0 to 4.73 rel. units).

In the dogs with shock lung before ECBT, LPO activation in the lung tissue ($p<0.05$) and elevated levels of diene conjugates, malonic dialdehyde, and Schiff bases were recorded in the blood, with a significant increase ($p<0.05$) in the *a-v* difference. After ECBT, the levels of LPO products tended to decrease in the lung tissue and increase in the blood, particularly that of malonic dialdehyde (the change in the *a-v* difference was significant at $p<0.05$) (Fig. 3, *4-6*).

Finally, as demonstrated by chromatography, ECBT led to a 2-fold increase in the utilization of palmitic and stearic acids in the intact dogs (palmitic acid is used by the lungs for the synthesis of surfactant precursor [1]).

The results of this study show that the 30-minute extracorporeal blood treatment with the ozone-oxygen mixture containing 48 μg of ozone per liter improved gas exchange in the lungs and blood oxygenation in the pulmonary vessels and activated metabolic functions of the lungs. This procedure may therefore be considered as an effective tool for efferent therapy of hypoxic states. The changes brought about by the ozone-oxygen mixture in the lungs (as manifested, *inter alia*, in the activation of glycolysis producing a hyperglycemic effect), are, in our view, a reflection of nonspecific adaptation of the lungs [9], since ozone exhibits glucocorticoid activity [13], and this adaptation, like any other [8], requires the expenditure of energy.

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