PROTECTION OF THE ISCHEMIC LIVER BY PERFUSION WITH FLUOROCARBON EMULSION

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One of the most promising trends currently under active development both in the USSR and in the West [4] is the use of fluorocarbon emulsions (FCE) to protect the ischemic liver. There are no data in the literature on determination of the optimal FCE concentration in the solution intended for perfusion in order to protect the ischemic liver. The aim of the present investigation was accordingly to determine the optimal FCE concentration in the perfusion solution on a model of the isolated perfused rabbit liver.

EXPERIMENTAL METHOD

Altogether 47 experiments were carried out with perfusion of the isolated liver of chinchilla rabbits, male and female, weighing 2-2.5 kg. Midline laparotomy was performed under thiopental anesthesia (50 mg/kg). Cannulas were inserted into the portal vein, inferior vena cava, and common bile duct (the cystic duct was ligated). The liver was then isolated from surrounding tissues and removed from the peritoneal cavity. The vascular bed of the liver was washed out to remove blood by perfusion with lactasol containing heparin (5 U/ml). To wash out one liver, 400 ml of lactasol was needed. The animals were withdrawn from the experiment by an overdose of thiopental. The liver was then subjected to ischemia for 90 min at 22-24°C. During ischemia the liver was perfused with the test solution under hypoxic conditions and by an open circuit method. The animals were divided into five groups. Animals of group 1 served as the control: their liver was not perfused during ischemia. In the animals of groups 2-4 the liver was perfused during ischemia with FCE, 12, 24, and 36% by volume, respectively, consisting of a mixture of perfluorodecalin and perfluorotripropylamine (7:3), stabilized by emulsifiers (Proxanol P-268 and egg yolk phospholipids). The total volume of perfusion fluid was inversely proportional to the FCE concentration and was equivalent in the different experimental and control groups: 80 ml in the case of 24% FCE, and 160 and 53.3 ml respectively for 12 and 36% FCE. The 24 and 36% FCE did not contain any additional (except those indicated above) components. The 12% FCE was prepared by diluting 24% FCE with Hanks' solution. To perfuse the liver of the animals of group 5, autologous blood diluted 1:2 with Hanks' solution was used (volume of perfusion fluid 80 ml). In every case the perfusion fluid contained heparin in a dose of 5 U/ml. Liver function was tested in the course of subsequent (after a 90-min period of ischemia) 60-min period of adequate normothermic perfusion (36-38°C) with Hanks' solution (pH 7.4-7.6) according to the following parameters: rate of oxygen consumption (OC), vascular resistance (VR), arteriovenous pH difference of perfusion fluid (A − V pH); rate of release of aspartate and alanine aminotransferase (AsT and AlT, respectively) into the perfusion fluid, rate of bile secretion (BS), and edema of the liver (EL). The liver also was studied by electron microscopy. Normothermic perfusion of the liver was carried out through the portal vein (open circuit).

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TABLE 1. Comparative Study of Several FCE Concentrations on a Model of Isolated Perfused Liver

Parameter	Composition of perfusion fluid				
	control	12% FCE	24% FCE	36% FCE	autologous blood diluted 1:2 with Hanks' solution
Rate of oxygen consumption, $\mu l \cdot min^{-1} \cdot g^{-1}$	3,4±0,1 (7; 35)	10,6±0,7 (10; 50)	9,6±0,6 (10; 50)	5,8±0,3 (10; 50)	8,6±0,6 (10; 50)
Vascular resistance, $N \cdot sec \cdot cm^{-5}$	0,104±0,002 (7; 35)	0,084±0,001 (10; 50)	0,088±0,001 (10; 50)	0,089±0,001 (10; 50)	0,089±0,001 (10; 50)
A—V PH	0,87±0,03 (7; 35)	0,55±0,04 (10; 50)	0,61±0,03 (10; 50)	0,66±0,04 (10; 50)	0,60±0,03 (10; 50)
Rate of release of AsT into perfusion fluid, $ncat \cdot min^{-1} \cdot g^{-1}$	0,111±0,003 (7; 35)	0,036±0,004 (10; 49)	0,040±0,005 (10; 50)	0,028±0,004 (10; 50)	0,075±0,006 (10; 50)
Rate of release of AlT into perfusion fluid, $ncat \cdot min^{-1} \cdot g^{-1}$	0,067±0,004 (7; 35)	0,010±0,002 (10; 49)	0,040±0,004 (10; 50)	0,018±0,002 (10; 50)	0,026±0,001 (10; 50)
Bile secretion, $ml \cdot kg^{-1}$	2,65±0,49 (7; 7)	18,17±1,05 (10; 10)	7,68±1,32 (10; 10)	7,34±1,06 (10; 10)	18,67±1,52 (10; 10)
Edema of liver, in % of initial mass	10,0±1,6 (7; 7)	0 (10; 10)	0 (10; 10)	3,4±1,0 (10; 10)	0,5±0,3 (10; 10)

Legend. Data given in Table 1 differ statistically significantly from control group; first number in parentheses is number of experiments, second number is total number of measurements of that parameter in group.

EXPERIMENTAL RESULTS

The lowest rate of OC was observed in animals of the control group (Table 1). The groups were arranged in the following order of an increase in this parameter: control, 36% FCE, autologous blood, 24% FCE, and 12% FCE. OC in the last three groups did not differ statistically significantly. Thus the highest value of OC was observed during the use of a perfusion fluid containing 12 and 24% FCE and autologous blood.

Another very important parameter characterizing the degree of preservation of liver function is VR, which increases with an increase in the degree of ischemic liver damage [2]. A high VR and, consequently, the severest damage, were observed in the control group; a low VR and the minimal degree of damage were recorded in the liver perfused with 12% FCE.

A similar distribution by groups also was found for another parameter of liver function, namely A — V pH. With an increase in the degree of ischemic liver damage, the numerical value of this parameter increased [1]. The lowest value of A — V pH was found with the liver perfused with 12% FCE, the highest, with the liver in the control group.

The highest rate of release of AsT into the perfusion fluid was shown by the liver in the control group, lower and approximately equal values were given by the livers protected with 12, 24, and 36% FCE. A similar distribution by groups also was found with the rate of release of AlT by the liver. Considering that release of enzymes into the perfusion fluid can take place only through the damaged cell membrane and, in particular, the hepatocyte membrane, it can be tentatively suggested that one of the incidental components of the antihypoxic action of FCE is that they possess membrane-stabilizing properties.

The rate of bile production is known to be directly dependent on the degree of preservation of the liver function [3]. The highest rate of bile secretion was found in the livers perfused with 12% FCE and with autologous blood, diluted 1:2 with Hanks' solution. Reduction of bile production by more than half was observed in groups with perfusion of the liver with 24% and 326% FCE. In the control group the rate of bile secretion was lowest of all, evidence of marked liver damage. Considerable EL was observed in this group, although it was absent or very mild in degree in the liver perfused with 12% and 24% FCE and with autologous blood. Considerable EL was present during perfusion of the liver with 36% FCE.

Electron microscopy showed that the hepatocyte ultrastructure after perfusion of the liver with 12% FCE was virtually identical with the hepatocyte ultrastructure of the intact liver. The nuclei of the hepatocytes and their cytoplasm, with their numerous organelles, remained unchanged. The mitochondria had a matrix of average density and the cristae were in a satisfactory state. Vacuolation of the cytoplasm was observed in the hepatocytes due to their uptake of FCE.

The most promising perfusion medium for anti-ischemic protection of the liver is thus that containing 12% FCE.

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CHARACTER OF THE PULMONARY CIRCULATION IN EXPERIMENTAL PULMONARY EDEMA DATED BY ARTIFICIAL VENTILATION

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Data have been published on the efficacy of artificial ventilation of the lungs (AVL), using various schedules, during the development of pulmonary edema [7, 9, 11]. An important step in the pathogenesis of pulmonary edema is considered to be a disturbance of the circulation in the lungs [1, 7]. However, the problem of the effect of various schedules of AVL on the pulmonary hemodynamics in this form of pathology has received only little study.

The aim of this investigation was to study the parameters of the pulmonary hemodynamics during the development of acute experimental pulmonary edema, accompanied by an increase in the frequency of volume of AVL.

EXPERIMENTAL METHOD

Experiments were carried out on 20 cats weighing 2.5-4 kg, anesthetized with pentobarbital (30-40 mg/kg, intraperitoneally), immobilized with tubocurarine (0.25-0.5 mg/kg, intravenously), with a closed chest. AVL was applied by means of a "VITA-1" respirator. Pulmonary edema was produced by intravenous injection of a mixture of fatty acids with olive oil in a dose of 0.04 ml/kg [10]. The pulmonary circulation during the development of pulmonary edema was studied during application of AVL with increased frequency (threefold) or volume (twofold) and compared with that recorded with the initial parameters of ventilation, namely frequency 19 ± 2 min^{-1} and volume 40 ± 3 cm^3, which corresponded to the frequency and volume of the animal's natural respiration. A catheter was introduced through the superior lobar artery of the lung into the lumen of the left pulmonary artery and pressure in it was recorded by means of an electromanometer [4]. The blood flow in the left lower lobar artery and vein was studied by means of ultrasonic transducers, applied to the corresponding vessels [5]. Values of blood flow and pressure in the lobar artery of the lung were led to an analog computer, which calculated the vascular resistance in the test lobe of the lung in the course of the process. The initial values were: pressure in the pulmonary artery 14 ± 2 mm Hg, blood flow 51 ± 4 ml · min^{-1}, vascular resistance of the lung 0.27 ± 0.05 mm Hg · ml^{-1} · min^{-1}. The degree of pulmonary edema was estimated

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