ASSIMILATORY AND EXCRETORY FUNCTION OF THE ISOLATED PERFUSED DOG LIVER

R. L. Rozental', G. I. Tsimermane,
D. B. Krivulis, A. A. Sondore,
and Yu. A. Sorokin

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In experiments on dogs the assimilatory-excretory function of the liver was studied by means of the bromsulfthalein method in the intact animal and during perfusion of the isolated organ through the portal vein by means of an artificial circulation apparatus. Under perfusion conditions the rate of uptake of the dye was 50-60% of the value of this index in the intact animal. The rate of elimination of bromsulfthalein with the bile and the biliary plasma clearance in the intact animal were five to six times higher. The main cause of the reduction in the assimilatory-excretory function of the isolated liver is evidently hypoxia developing after denervation and removal of the organ from the body, and also during extracorporeal perfusion itself.

KEY WORDS: liver; liver functions; bromsulfthalein method; perfusion.

There is no question that the outlook is good for the study of some aspects of liver physiology and pathology by the use of an isolated organ maintained by extracorporeal perfusion [1, 4, 5]. However, isolation of the liver from the rest of the body, followed by rinsing and artificial perfusion of the organ, reduce its functional powers, with the result that it is difficult to interpret the experimental results correctly.

The state of the liver function was compared in situ and during extracorporeal perfusion.

EXPERIMENTAL METHOD

Twenty experiments were carried out on mongrel dogs weighing 10-17 kg. In 10 of the animals the state of the liver function was studied in situ after premedication with neuroleptics and analgesics and under barbiturate anesthesia, while spontaneous respiration remained intact. For this purpose the peripheral artery and vein, the hepatin veins (through the external jugular vein), and also the common bile duct (after laparotomy and ligation of the cystic duct) were cannulated. In 10 animals the liver function was studied during extracorporeal perfusion of the organ through the portal vein by means of an artificial circulation apparatus (ACA) [2]. The tests began 45-60 min after the beginning of perfusion of the organ or preparation of the animals. Bromsulfthalein (BSP) was introduced into the oxygenator of the ACA or injected into a peripheral vein of the animals in a dose of 5 mg/kg body weight, after which the substance continued to be administered by intravenous drip at a constant rate of 0.2 ml/min/kg body weight. In experiments on the animals, blood samples were taken from the artery and the hepatic veins every 10 min. In the liver perfusion experiments samples were taken at the same times from the oxygenator and the main venous outflow trunk. Bile was collected from a catheter introduced into the common bile duct every 15 min for 2 h. The concentration of bromsulfthalein was determined in the blood and bile [3]. The velocity of the hepatic blood flow, the rate of elimination of the dye by the liver and bile, and the plasma bromsulfthalein clearance were calculated by equations given in [7]. The percentage of BSP excreted into the bile during the experiment also was calculated.

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TABLE 1. State of Function of Dog Liver in situ and during Extracorporeal Perfusion (M ± m)

Experimental conditions	Blood flow through liver (in ml/min/kg weight of organ)	Rate of BSP elimination by liver (in μg/min/kg)	Plasma clearance (in ml/min/kg)	Volume of bile excreted (in ml)	
				1 h	2 h
Liver in situ	1942,3±261,9	5763,9±231,2	255,7±30,1	8,52±0,69	7,7±0,56
Liver during extracorporeal perfusion	999,7±155,1	3005,0±563,3	163,6±27,9	2,6±0,4	2,2±0,4
P	0,02	0,02	0,05	0,001	0,001

TABLE 1 (continued)

Experimental conditions	Rate of BSP elimination by bile (in μg/min/kg)		Biliary clearance (in ml/min/kg)		% of BSP eliminated into bile	
	1 h	2 h	1 h	2 h	1 h	2 h
Liver in situ	1183,9±257,6	1505,9±263,1	59,7±18,2	125,1±33,0	15,2±2,2	20,1±2,7
Liver during extracorporeal perfusion	244,2±90,8	518,8±80,1	9,8±4,2	24,0±7,4	3,0±0,97	6,1±0,97
P	0,01	0,01	0,02	0,02	0,001	0,001

EXPERIMENTAL RESULTS AND DISCUSSION

During the first hour of observation the rate of BSP elimination by the liver in situ was considerably higher than during extracorporeal perfusion of the organ (Table 1). Similar relationships also were observed for the plasma clearance. The rate of uptake of BSP by the liver during perfusion was 50-60% of its uptake in the intact animal. Since the blood flow through the isolated liver was 40-50% less, it can be concluded that the assimilatory function of the liver in fact depends on this factor.

The difference between the indices of the excretory function of the liver was more substantial: During the first hour of perfusion the rate of elimination of the dye by the bile and the plasma clearance effected through the bile were six times higher in the intact animal than during perfusion of the liver. This difference was somewhat diminished after 2 h.

In the course of 2 h the liver in situ excreted 35.3% of the administered dose of the dye with the bile, compared with only 9.1% during perfusion. This marked difference in the preservation of the excretory function of the liver between the two groups of experiments can be attributed primarily to the difference in quantity of bile excreted. Whereas during 2 h the liver in situ excreted 16.2 ml of bile, the perfused liver excreted only 4.8 ml. One cause of the reduced secretion of bile is evidently the deficiency of bile acids in the perfusion fluid. However, this factor cannot be of decisive importance [4].

Bromsulfthalein excretion curves for the experiments in situ and under prefusion conditions differed sharply from each other. In the first case excretion of the dye was completed at the 90th minute of observation, but in the second case the liver excreted bile with a steadily rising concentration of BSP throughout the experiment (2 h). During perfusion, the transfer of BSP from the hepatocytes to the biliary tubules and ducts is evidently delayed. It was shown previously that the primary action of hypoxia is to block the mechanisms of transfer of products of bile formation into the biliary tubules [5, 6]. Isolation and artificial perfusion of the liver undoubtedly produce hypoxia of the organ.

Under the conditions of extracorporeal perfusion of the liver through the portal vein, both the assimilatory and the excretory functions of the organ are thus preserved. However, the level of liver function is reduced by four to five times below that of the intact organ, mainly on account of circulatory hypoxia.

LITERATURE CITED

1. M. S. Margulis, R. L. Rozental', I. K. Krylov, et al., Vestn. Khir., No. 7, 46 (1970).
2. R. L. Rozental', A. A. Sondore, and M. S. Margulis, in: Proceedings of a Conference on Assessment of the Viability of Organs and Tissues [in Russian], Moscow (1970), pp. 46-48.

3. Kienle and Küppers, in: Reference Book of Clinical Function Tests (ed. by A. Gitter and L. Heilmeyer) [Russian translation], Moscow (1966), p. 488.
4. L. Lambotte, J. Physiol. (London), 232, 181 (1973).
5. S. Popov-Cenic, V. Totovic, U. Knüchel, et al., Bibl. Anat., 12, 22 (1973).
6. J. Shorey, S. Schenker, and B. Camhes, Am. J. Physiol., 216, 1441 (1969).
7. K. Winkler, R. Hansen, A. Schmidt, et al., Scand. J. Gastroent., Suppl. 7, 157 (1970).