FUNCTIONAL-BIOCHEMICAL PARALLELS DURING TWO-STAGE DEVASCULARIZATION OF THE LIVER

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After reproduction of acute hepatic failure in dogs by two-stage devascularization of the liver (Eck's fistula followed by ligation of the hepatic artery) the dynamics of the blood biochemistry and liver function was studied. The results indicate that disturbances of intermediate metabolism precede the encephalopathy and severe circulatory changes in the body and also accompany them.

KEY WORDS: hepatic failure; experimental simulation; biochemical changes; functional disturbances.

Despite many investigations of hepatic coma, there is no universally accepted view on the role of biochemical disturbances in its pathogenesis. Besides experimental evidence of a connection between lesions in certain organs and systems in coma and changes in intermediate metabolism [1, 4, 6], there are other observations pointing to the absence of any such connection [5, 7, 9].

The object of this investigation was to determine the degree of biochemical changes in the blood and their correlation with functional disturbances in animals with experimental hepatic coma.

EXPERIMENTAL METHOD

Hepatic coma was produced in dogs (15-25 kg) by two-stage devascularization of the liver [8, 10] under general anesthesia [3]. As a first step a midline laparotomy was performed, a side to side portocaval anastomosis was formed, and the portal vein was ligated at the hilus of the liver (Eck's fistula). The second stage of the operation was to ligate the hepatic and gastro-duodenal arteries, and this was performed 48 h later. A continuous intravenous infusion of 25% glucose solution at the rate of 0.25-0.5 g/kg/h was given to the animals in the postoperative period until death. The systematic arterial pressure, central venous pressure, EDG, and EEG were recorded (four-channel ink-writing encephalograph). The concentrations of ammonia, bilirubin, potassium, and lactic and pyruvic acids in the blood, the pH of the blood, and activity of the enzymes alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT) were determined [2].

The determinations were made before and after formation of the Eck's fistula and every 6 h after the second stage of the operation.

EXPERIMENTAL RESULTS AND DISCUSSION

Significant changes in the biochemical picture of the blood were observed 48 h after formation of the Eck's fistula: The ammonia and lactic and pyruvic acid concentrations and the serum transaminase activity in the blood were all increased (Table 1). Meanwhile no significant changes were found in the clinical and functional indices characterizing the general state of the animals; the dogs remained active and walked confidently, and their arterial pressure remained stable. Mixed activity was recorded on the EEG with an amplitude of the α-waves of 20 μV and of the Q-waves of 30 μV (Fig. 1A). The biochemical changes in the

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TABLE 1. Changes in Blood Biochemical Indices after Two-Stage Devascularization of the Liver (M±m)

Index studied	Before operation	48 h after formation of Eck's fistula	After ligation of hepatic artery	
			12 h	24 h
Bilirubin (in mg %)	0,53±0,04	0,58±0,1	1,48±0,25	2,47±0,06
P		>0,05		<0,01
Ammonia (in mg %)	0,09±0,004	0,21±0,05	1,91±0,25	2,41±0,11
P		<0,05	<0,001	<0,001
Lactic acid (in mg %)	23,0±1,9	46,0±4,7	40,2±3,1	64,2±12,7
P		<0,01	<0,001	<0,01
Pyruvic acid (in mg %)	3,3±0,05	4,96±0,6	5,1±0,61	5,9±1,05
P		<0,02	<0,01	<0,05
ASAT (in units)	24,0±1,9	40,3±7,1	212,6±9,5	271±44,1
P		<0,05	<0,001	<0,001
ALAT (in units)	29,7±2,05	85,0±8,0	367±12,8	316,0±11,0
P		<0,001	<0,001	<0,001
Potassium (in meq/liter)	4,4±0,36	3,8±0,46	2,6±0,7	2,66±0,3
P		>0,5	<0,05	<0,01

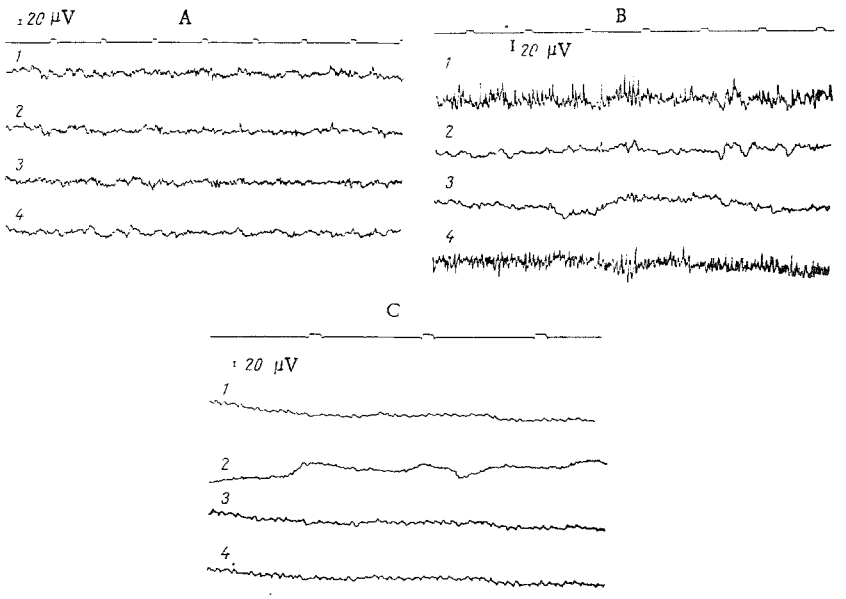

Fig. 1. EEG of dog during simulation ot acute hepatic failure by two-stage devascularization of the liver: A) EEG of dog 48 h after formation of Eck's fistula (first stage of operation); B) EEG of dog 6 h after ligation of hepatic artery (second stage of operation); C) EEG of dog 18 h after ligation of hepatic artery.

blood 12 h after ligation of the hepatic and gastro-duodenal arteries indicated an increased degree of acute hepatic failure. The ammonia and lactic acid concentrations in the blood were sharply increased and the blood bilirubin level (including indirect) was raised. Serum transaminase activity also was increased. The potassium ion concentration was lowered. At this stage clinical signs of acute hepatic failure appeared: the dogs became apathetic and drowsy and at times they exhibited motor excitation. The arterial pressure fell to 85-90 mm. Signs of interhemispheric asymmetry and desynchronization of rhythms appeared on the EEG. Fast spike-like β-waves (16-18 and 20-22 waves/sec) with high amplitude (80 μV), superposed on slower waves, were observed (Fig. 1B).

Even more severe changes in intermediate metabolism were found at the end of 24 h of observation on the animals. A further increase in the lactic and pyruvic acid concentrations in the blood was accompanied by a fall of pH. The ammonia and bilirubin concentrations were increased. Enzyme activity continued high. The animals fell into coma 16-20 h after the second stage of the operation: They ceased to communicate, they lost consciousness, and no longer responded to external stimulation. Marked arterial hypotension was observed at this stage (50-60 mm Hg). Another 2-3 h later the terminal phase of acute hepatic failure ensued. The arterial pressure fell to 30-40 mm Hg. Evidence of encephalopathy on the

EEG became stronger: The fast rhythm was replaced by a slower rhythm, features of interhemispheric asymmetry were reduced, and the amplitude of the waves decreased (Fig. 1C). Later, i.e., 22-24 h after ligation of the hepatic artery, as a rule the animals died.

After two-stage devascularization of the liver, which reproduces hepatic coma better than other methods [8, 10], severe changes were observed in the biochemical picture of the blood and in the functional state of the animals. Changes in intermediate metabolism preceded functional disturbances of the organs and systems and, consequently, they were an essential part of the pathogenetic mechanism of hepatic coma. The results suggest that an important role in the mechanism of development of irreversible changes in the body in hepatic coma is played by the pathochemical consequences of the developing ischemia of the liver and the associated circulatory disturbances.

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