CIRCULATORY DISTURBANCES IN ACUTE EXPERIMENTAL PANCREATITIS

O. S. Kochnev

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Hypotension associated with acute pancreatitis in experiments on dogs is accompanied by portal hypertension and by a decrease in the central venous pressure. Trasylol, a drug with antikinin action, did not abolish these circulatory disturbances. After administration of ε-aminocaproic acid, neutralizing trypsin, the hypotension induced by trypsin was not so marked as in the control and it was shorter in duration. It is concluded that the direct action of activated trypsin on the vessel wall plays an important role in the development of the circulatory disturbances in acute pancreatitis.

Circulatory disturbances are found in two-thirds of patients with acute pancreatitis. Views differ as regards not only the character of these changes, but also their causes. Some workers explain pancreatic hypotension by the liberation of vasoactive kinins [7, 8]. The suggestion has been made that the vascular disturbances in acute pancreatitis are attributable to the ability of trypsin to act on the vessel wall and on its neural elements [1-3].

In the investigation described below the hemodynamic changes during the course of acute pancreatitis and the possible causes of the vascular disturbances were studied.

EXPERIMENTAL METHOD

Three series of experiments were carried out on 29 dogs. In series I, on 15 dogs, the arterial, portal, and central venous pressures were determined initially in the intact animals, and later from the 1st until the 10th day of acute pancreatitis. The arterial pressure was determined manometrically in the femoral artery, the portal pressure with a Waldman's apparatus by puncture of the portal vein and the central venous pressure by introducing a catheter into the posterior vena cava [5]. Acute pancreatitis was produced

TABLE 1. Arterial Pressure and Pressure in Portal Vein and Inferior Vena Cava of Dogs with Acute Pancreatitis (M ± m; n = 15)

Index	Normal	Day of disease				
		1	2	3	4	6—10
Maximal arterial pressure (in mm Hg)	95±2,53	115±6,48 $P<0,01$	63±10,9 $P<0,01$	70±5,76 $P<0,001$	80±2,89 $P<0,001$	97,5±7,77 $P<0,5$
Portal pressure (in mm water)	130±2,57	175±8,78 $P<0,001$	160±2,74 $P<0,01$	197±21,2 $P<0,01$	174±6,01 $P<0,01$	152±7,81 $P<0,01$
Pressure in posterior vena cava (in mm water)	50±1,46	80±3,88 $P<0,001$	20±4,67 $P<0,001$	15±2,57 $P<0,001$	40±2,91 $P<0,001$	65±6,34 $P<0,05$

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TABLE 2. Arterial Pressure and Pressure in Portal Vein and Posterior Vena Cava of Dogs with Acute Hypotension Induced by Trypsin and after Prophylactic Administration of Trasylol and EACA (M ± m)

Index	Normal	After injection of		
		trypsin (2-3 mg/kg)	trasylol (2000-3000 units) + trypsin	EACA (0.2-0.3 g/kg) + trypsin
Maximal arterial pressure (in mm Hg)	95±2,53	26±4,6 $P<0,001$	30±5,76 $P<0,5$	55±6,45 $P<0,01$
Portal pressure (in mm water)	130±2,57	260±15,6 $P<0,001$	245±6,45 $P<0,5$	150±4,09 $P<0,001$
Pressure in posterior vena cava (in mm water)	50±1,46	10±1,9 $P<0,001$	15±2,87 $P<0,5$	35±5,4 $P<0,02$
Duration of acute hypotension (in mm)	—	27,5±1,41	20±2,06 $P<0,05$	0,4±0,05 $P<0,001$

by injecting bile (0.25 ml/kg body weight) under pressure into the chief pancreatic duct. The diagnosis was confirmed by histopathological study of the pancrease and by blood tests for amylase and lipase. In the experiments of series II (6 dogs), in order to produce hypotension analogous to the pancreatic type, crystalline trypsin (2-3 mg/kg) was introduced into the portal system which drained blood from the pancreas. In the experiments of series III (8 dogs), before injection of the trypsin, either trasylol (2000-3000 units/kg), which possesses antikinin properties, or ε-aminocaproic acid (EACA, 0.2-0.3 g/kg), which neutralizes trypsin [4, 6, 9], was injected intravenously.

EXPERIMENTAL RESULTS

In the first 24 h of acute pancreatitis, when the predominant feature in the gland was edema, the arterial pressure was raised (Table 1). From the 2nd to the 4th day, in the period of development of hemorrhagic necrosis in the gland, marked hypotension accompanied by a hemorrhagic effusion into the peritoneal cavity (100-800 ml), took place. The portal hypertension was particularly marked in the first 4 days of acute pancreatitis, while the central venous pressure was raised during the first 24 h of the disease, but fell significantly below its initial value on the 2nd-4th day of acute pancreatitis.

In the experiments of series II, the same indices were studied in an artificial model of pancreatic collapse. It was assumed that since blood from the pancreas drains directly into the portal venous system, activated pancreatic enzymes, notably trypsin, must act on the vessels of the portal system, inducing stasis and accumulation of blood in them. The experiments showed that intraportal injection of trypsin led to a critical drop of arterial pressure lasting on the average 27.5 ± 1.4 min. The pressure in the portal vein rose sharply and the central venous pressure fell (Table 2), indicating a decrease in the circulating blood volume. Hence, both in natural and in artificially induced pancreatic hypotension, similar changes were observed in a number of hemodynamic indices.

The prophylactic administration of trasylol did not prevent the critical drop of arterial pressure, the development of portal hypertension, or the decrease in the central venous pressure. A small yet constant decrease in the duration of the hypotension was observed. After injection of EACA, the trypsin-induced hypotension was less marked and of very short duration. The portal and central venous pressures showed little change (Table 2). Stabilization of all the hemodynamic indices occurred rapidly.

These results suggest that in pancreatic hypotension blood accumulates in the peritoneal cavity because of the direct action of trypsin on the blood vessels. Since trasylol, which has an antikinin action, does not prevent the development of pancreatic hypotension, the role of kinins in its genesis is doubtful [4, 9]. The effectiveness of EACA in pancreatic collapse, considering the antitrypsin effect of this compound [6], confirms the important role of the direct action of this proteolytic enzyme on the blood vessels in the development of pancreatic collapse.

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