MECHANISMS OF BLOOD DEPOSITION IN DOGS WITH CYTOTOXIC INJURTY TO THE HEART

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Reactions of capacitive vessels of the abdominal and pelvic organs of vagotomized dogs to cytotoxic injury to the heart were studied. The same reactions were investigated under crossed circulation conditions in recipient dogs following injury to the heart of the donor dogs. Nervous reflex and humoral cardiogenic factors were shown to play a definite role in the development of blood deposition.

KEY WORDS: cardiovascular failure; hemodynamics; blood deposition.

Previous investigations [7] showed that the development of cytotoxic injury to the myocardium (CIM) is accompanied by retention of a considerable quantity of blood in the venous part of the blood stream in the abdominal and pelvic organs, and together with weakening of myocardial contractility [5], this causes a decrease in cardiac output and a fall of the systemic arterial pressure (cardiocytotoxic shock).

The possible participation of nervous and humoral mechanisms in the deposition of blood in CIM was studied in the present investigation.

EXPERIMENTAL METHOD

In two series of acute experiments on dogs weighing 14-21 kg, anesthetized with morphine and chloralose (0.0025 and 0.07 g/kg respectively) the systemic arterial pressure (SAP), the central venous pressure (CVP), the pressure in the left ventricle, its first derivative (dp/dt), and the end-diastolic component (EDP_{lv}), the resistance to the blood flow in the vessels of the abdominal and pelvic organs, and changes in the capacity of this vascular region (by means of the extracorporeal reservoir method, modified by the authors [9]), were recorded. The nature of the modification was that the abdominal and pelvic organs were perfused through the femoral arteries (1) and veins (2), and hemodynamic isolation of the test region was achieved by occlusion of the aorta and posterior vena cava at the level of the diaphragm by means of catheters with balloons (3) at their ends (the recipient dog in Fig. 1). The catheters (4) with balloons were introduced through the left brachial artery and external jugular vein. The effectiveness of hemodynamic isolation was verified by the absence of changes in arterial and venous pressure in the isolated region when sudden changes of pressure were artificially induced in the unisolated part of the dog's vascular system. By means of this modification tests could be carried out on animals without the need for thoracotomy and laparotomy, and during natural breathing. CIM was produced by injecting 1-1.5 ml of anticardiac cytotoxic serum (ACS) into one branch of the left coronary artery through a special metal catheter. Serum was obtained from rabbits immunized with a saline extract of dog myocardium. The titer of the serum used in the complement fixation test was 1:320-1:640.

The animals of the experiments of series I (14 experiments) received an injection of ACS after bilateral vagotomy in the neck region. In series II (10 experiments) the role of humoral factors in blood deposition was studied by the crossed circulation method (Fig. 1). Arterial blood of the donor into whose coronary artery ACS was injected passed at constant volume velocity into the hemodynamically isolated posterior half of the body of the recipient dog, in which the resistance to the blood flow in the vessels and changes in their capacity were recorded. Blood flowing from the posterior vena cava of the recipient dog was returned at the same velocity into the donor's vascular system.

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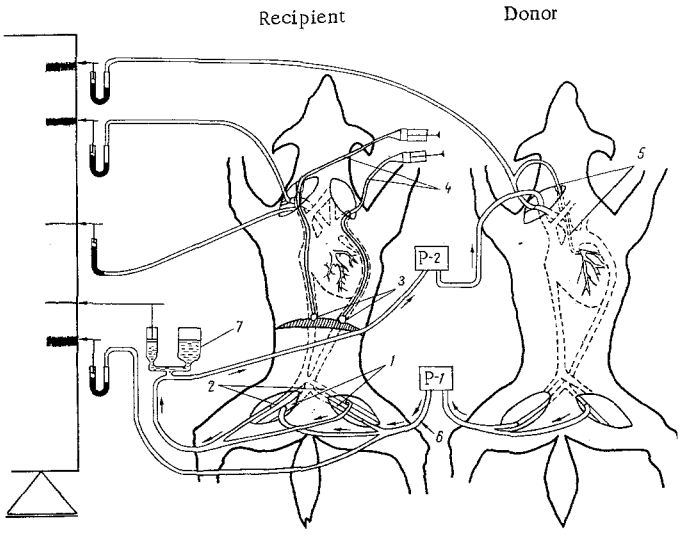

Fig. 1. Scheme of investigation of role of humoral factors in blood deposition during cytotoxic injury to the heart. 1) Femoral arteries; 2) femoral veins; 3) balloons; 4) catheters; 5) "coronary" catheter; 6) site of injection of ACS in control experiments; 7) extracorporeal reservoir; P-1) "arterial" perfusion pump; P-2) "venous" perfusion pump.

TABLE 1. Changes in Indices of Cardiodynamics and Hemodynamics during Cytotoxic Injury to Donor Dog's Heart in Crossed Circulation Experiments (M ± m)

Index	Control	Time after injection of anticardiac serum, min			
		5	15	30	60
Recipient dog					
Volume of blood deposited, ml	0	46±7,2	42±8,3	34±8,1	62±19,1
*P**		<0,01	<0,01	<0,01	<0,01
Perfusion pressure in resistive vessels of abdominal organs, mm Hg	96±6,4	93±6,9	96±5,6	89±5,2	87±7,2
P		>0,05	>0,05	>0,05	>0,05
Donor dog					
SAP, mm Hg	109±4,7	83±5,1	103±3,1	99±4,4	103±4,9
*P**		<0,01	<0,05	<0,01	<0,05
CVP, mm Hg	18,3±4,3	20,6±4,2	18,0±4	18,2±5	18±4,9
P		>0,05	>0,05	>0,05	>0,05
Pressure in left ventricle, mm Hg	136±8,3	107±7,3	121±5,3	123±7,7	121±8,9
P		<0,02	>0,05	>0,05	>0,05
dp/dt_{max} of left ventricle, mm, Hg	3197±233	2466±322	2647±207	2616±180	2792±50
*P**		<0,05	<0,01	<0,05	<0,05
EDP_{lv}, mm Hg	3,8±0,3	4,2±0,6	5,2±0,6	5,8±1,4	7,5±1,9
P		>0,05	>0,05	>0,05	>0,05

* P calculated by the difference method.

In control experiments the same dose of ACS was injected intravenously into the donor and into the recipient's abdominal aorta (Fig. 1: 6).

EXPERIMENTAL RESULTS AND DISCUSSION

In animals undergoing preliminary vagotomy, blood deposition in the abdominal and pelvic organs was preserved. Just as in the experiments without vagotomy, its intensity differed in each separate experiment. Blood deposition began 1.5-3 min after intracoronary injection of ACS, and in some experiments reached 100-200 ml in the course of a few minutes. The quantity of blood stored in the depots 5 min after injection of ACS averaged 35 ± 15 ml, rising to 123 ± 41 ml after 15 min and 242 ± 59 ml after 60 min. Compared with the intensity of blood deposition in intact animals [7], the volume of blood retained in the depots of the vagotomized dogs at various times after injection of ACS was 21-54% less. This difference was evidently due to the exclu-

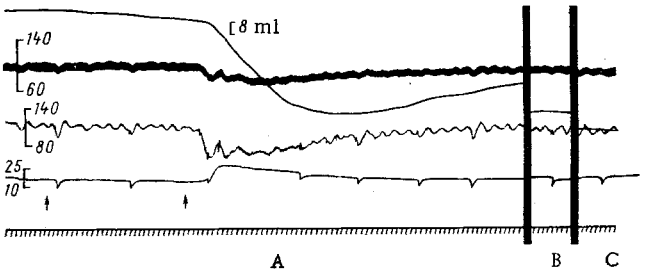

Fig. 2. Changes in hemodynamics of dogs after cytotoxic injury to heart of donor dog. From top to bottom: changes in blood volume in extracorporeal reservoir (in ml), perfusion pressure in vessels of abdominal and pelvic organs of recipient dog (in mm Hg), SAP (in mm Hg) and CVP (in mm water) of donor dog, time marker (10 sec). Successive arrows indicate: injection of ACS into blood flowing toward recipient dog and intracoronary injection of ACS into donor dog. A) Time of injection of serum, B) 30 min, and C) 60 min after injection of anticardiac serum.

sion of reflex effects from the injured heart. There is evidence [2, 6, 9] to confirm reflex dilatation of the capacitive vessels during stimulation of the receptor zone of the heart and also the presence of a reflex component in the development of changes in the cardiodynamics and hemodynamics accompanying CIM [8].

Meanwhile, persistence of the blood deposition effect in the vagotomized animals suggested that a role in the development of blood deposition was played by humoral factors, the concentration of which in the circulating blood may probably vary in animals with different injuries to the heart [3, 4].

The results obtained in the experiments of series II (with a crossed circulation) confirmed this suggestion (Table 1, Fig. 2).

In all these experiments deposition of blood in the abdominal and pelvic organs of the recipient dog began 1-3 min after intracoronary injection of ACS into the donor dog (Fig. 2). The intensity of blood deposition differed in different experiments. The mean volume of blood deposited after 5 min was 45.7 ± 7.2 ml, and toward the end of the first hour it was 61.8 ± 19.1 ml. When ACS was injected in the same doses into the arterial blood flow toward the abdominal organs of the recipient dog (bypassing the heart of the donor dog), no blood deposition was observed in the recipient (Fig. 2).

Consequently, retention of blood in the depots after intracoronary injection of ACS is not the result of the direct action of anticardiac serum or of the products of its interaction with blood on the vessels. The essential condition for blood deposition to take place is realization of the antigen–antibody reaction in the organ, in this case the heart, and also, evidently, the subsequent secretion of biologically active substances of tissue origin. The possibility that vasoactive substances may be secreted from the heart during experimental procedures, such as those producing acute ischemia, has been demonstrated [10-13]. However, the physiological significance of this phenomenon has not been established.

The results are evidence of the role of cardiogenic humoral factors in the mechanism of blood deposition.

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EFFECT OF THE DURATION OF PRECEDING ISCHEMIA AND THE MASS OF ISCHEMIZED TISSUE ON THE STATE OF THE CLOTTING AND ANTICLOTTING SYSTEMS OF THE BLOOD IN TOURNIQUET SHOCK

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Experiments on 80 rabbits showed that inclusion of previously ischemized limbs in the circulation is accompanied by an increase in the clotting potential of the blood and by inhibition of fibrinolysis in the early stages after removal of the tourniquets, followed by hypocoagulation and activation of fibrinolysis. These changes depend on the duration and mass of the previously ischemized tissues. The authors consider that these disturbances in tourniquet shock lead either to the risk of intravascular thrombosis or to hypocoagulation followed by secondary fibrinolysis.

KEY WORDS: ischemia; tourniquet shock; coagulation; fibrinolysis; blood clotting system.

Tourniquet shock is a serious pathological condition which frequently causes death of patients. The severity of its course is directly dependent on the duration of ischemia and the mass of ischemized tissue. Tourniquet shock, like other forms of shock, is based on disturbances of the microcirculation that are closely linked with changes in the state of the blood clotting system and fibrinolysis [12, 14]. The role of disturbance of the state of these systems in the development of tourniquet shock has not been adequately studied, and data on the problem are contradictory [1, 5, 8].

The object of this investigation was to study the state of the clotting and anticlotting systems of the blood in the early period of tourniquet shock and its dependence on the duration of previous ischemia and the mass of ischemized tissue.

EXPERIMENTAL METHOD

Experiments were carried out on 80 rabbits weighing 2.5-3 kg. Tourniquets were applied to the limbs 30 min after subcutaneous injection of morphine hydrochloride (0.3 ml of the 1% solution/kg body weight). The degree of ischemia was monitored by determining the electrical excitability of the muscles. Blood was taken in all experiments from the marginal vein of the ear before and 1, 2, 3, and 5 h after removal of the tourniquets. To study the effect of the duration of previous ischemia on the state of the systems to be tested three series of experiments were carried out in which tourniquets were applied to the fore- and hindlimbs on one side for periods of 1, 6, and 9 h. To determine the effect of the mass of ischemized tissue, two series of experiments were carried out in which tourniquets were applied to one hind limb or to the fore- and hindlimbs on one side for identical periods of ischemia, namely 6 h. Three series of experiments acted as controls: 1) intact animals, 2) animals with tourniquets applied to the fore- and hindlimbs on one side for 6 h and not subsequently removed, 3) animals with tourniquets applied to the fore- and hindlimbs on one side for 6 h but with preservation of the blood flow along the main trunk vessels (the tourniquets were applied beneath previously exteriorized vascular bundles). The clotting and anticlotting systems of the blood were studied in rela-

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