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LITERATURE CITED


ENERGY METABOLISM AND CONTRACTILE ACTIVITY OF THE MYOCARDIUM AFTER CARDIOCYTOTOXIC INJURY


Experiments on anesthetized dogs with a closed chest showed that injection of anticardiac cytotoxic serum into one of the main branches of the left coronary artery was followed by zonal disturbances of energy metabolism (a decrease in the ATP, ADP, AMP, and glycogen concentrations and contractility of the affected area of the left ventricle). Compensatory hyperfunction of the left and right ventricles and an increase in their noradrenalin concentration were found. The indices of energy metabolism in the unaffected area of the heart showed no significant change.

KEY WORDS: cardiodynamics; myocardial metabolism; injury to the heart.

It was shown previously that injection of anticardiac cytotoxic serum (ACS) into one branch of the left coronary artery led to sharp and prolonged disturbances of the hemodynamics similar to the picture of cardiogenic shock [1] and to disturbances of the contractile activity of the myocardium [3] and to deposition of blood [5]. Focal injury of the heart muscle developed in the region of direct action of ACS [7].

To shed light on the mechanisms of disturbance of cardiac activity after cytotoxic injury, it was considered important to compare changes in energy metabolism in different parts of the heart with zonal changes in contractile activity of the myocardium.

Fig. 1. Changes in contractile activity (1) and noradrenalin concentration (2) in injured (A) and uninjured (B) areas of left ventricle after injection of ACS. Abscissa, zonal changes in contractile activity of myocardium and in noradrenalin concentration in myocardium (in % of initial level); ordinate, time after injection of ACS (O), in min.

EXPERIMENTAL METHOD

The systemic arterial pressure (SAT), the cardiac output (by the thermodilution method), the pressure in the left ventricle, and its first derivative were recorded in acute experiments on dogs weighing 16–21 kg under morphine-chloralose anesthesia (0.0025 and 0.07 g/kg body weight respectively) without thoracotomy. ACS (titer in the complement fixation test - CFT - 1:400) was injected in a dose of 1–1.5 ml into the circumflex or descending branch of the left coronary artery through a specially made "coronary" catheter, and after indices of the cardiodynamics had been recorded at various times after injection of ACS (5–7 and 60 min) thoracotomy was performed and samples of myocardial tissue taken. In the affected (corresponding to the site of injection of ACS) and undamaged areas of the left ventricle and also in the right ventricle the concentrations of adenine nucleotides (ATP, ADP, AMP) [13], of inorganic phosphorus [2], of oxidized (NAD + NADP) and reduced forms of nicotinamide coenzymes [10], and glycogen [8], activity of cytochrome c-oxidase (CCO) [14] and succinate dehydrogenase [12], and the concentrations of catecholamines [4] were determined.

Zonal changes in contractile activity of the myocardium in the area of direct action of ACS (injured area) and in the uninjured area of the left ventricle were investigated in a special series of experiments on thoracotomized animals by means of strain gauge transducers fixed to the heart (14 experiments). Details of the method were described previously [3]. In control experiments normal rabbit serum was injected into the coronary circulation.

The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The most marked disturbances of the circulation were found during the first minutes of intracoronary injection of ACS. SAP fell by 43.3%, the cardiac output by 32.5%, the pressure in the left ventricle by 44.3%, and its first derivative (dp/dt max) by 29.3%. All these indices except the cardiac output showed a tendency to recover 40–60 min later, but the total peripheral resistance (TPR) was a little higher than initially. In the area of direct action of ACS definite weakening of contractile activity was observed (Fig. 1), and it continued throughout the period of observation (1 h). Meanwhile, in an area of myocardium from the left ventricle some distance from the site of injury, no regular changes in the force of contractions as a rule were observed. In most experiments (10 of 14) an increase in the force of contractions was observed in this part: On average by 13±4.3% (n=10, P< 0.05) after 15 min. No significant changes in the indices of energy metabolism of the myocardium were detected in the first 5 min.

Significant zonal disturbances of energy metabolism were found in the myocardium 1 h after injection of ACS. The level of adenine nucleotides fell considerably in the injured part of the left ventricle: ATP by 36.7%, ADP by 41.1%, and AMP by 35.5%. The concentrations of glycogen and noradrenalin (by 37.6 and 55% respectively) showed significant decreases at the same time. In the injured part of the myocardium of the left ventricle and in the right ventricle no such changes were observed (except a decrease in CCO activity). Meanwhile in the uninjured part, 1 h later there was an increase in the total nicotinamide coenzymes (by 34.8%), mainly on account of oxidized forms. The noradrenalin concentration was increased in the early period of the reaction, but 60 min later in the uninjured part of the left ventricle it was virtually unchanged and showed a definite tendency to rise in the right ventricle.