Effect of Uridine Derivatives on Myocardial Stunning during Postischemic Reperfusion of Rat Heart

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Uridine and uridine-5'-monophosphate prevent myocardial stunning during postischemic reperfusion of isolated rat heart. Uridine-5'-diphosphate does not prevent postischemic myocardial dysfunction, while uridine-5'-triphosphate aggravates it.

Key Words: uridine; uridine nucleotides; myocardial stunning

Myocardial stunning (postischemic dysfunction of the myocardium) is the major manifestation of postischemic reperfusion syndrome. Ischemic myocardium remains hypokinetic or even akinetic after restoring the coronary blood flow [2, 7, 11]. The main causes of stunning is ATP deficiency, LPO activation in cell membranes, calcium overload and contracture of cardiomyocytes, and disturbed excitation-contraction coupling.

Glycolysis activators can be used to prevent reperfusion syndrome. On the one hand, glycolysis is the major energy source during ischemia, and on the other hand, it provides ATP for myocardial contraction and function of the calcium pump [3]. These activators are uridine and uridine nucleotides: uridine-5'-monophosphate (UMP), uridine-5'-diphosphate (UDP), and uridine-5'-triphosphate (UTP). Being precursors of uridine diphosphoglucose (UDPG, a cofactor of glycogen synthesis), these substances play an important role in the maintenance of myocardial contractile activity. During ischemia, glycolysis is the only mechanism of anaerobic ATP synthesis, because glucose transport to the heart is restricted. However, glycogen stores in cardiomyocytes are rapidly depleted. The glycogen content in perfused rat heart after 30-min total ischemia decreased by 60% [12]. The following 30-min reperfusion did not restore the glycogen level. Despite sufficient glucose concentration in the perfusate, the left ventricle developed pressure (LVDP) to the end of the reperfusion period was only 28% of the initial value. Depletion of glycogen stores is accompanied by a decrease in the content of UTP and UDPG in the myocardium [5, 6]. However, addition of 5-50 μmol/liter uridine to the perfusate during postischemic reperfusion markedly increased the content of UTP, UDPG, and glycogen in isolated rat heart against the background of accelerated uridine incorporation into cardiomyocytes. Our aim was to evaluate the effects of uridine, UMP, UDP, and UTP on contractile activity of the left ventricle and coronary blood flow (CBF) during reperfusion of isolated rat heart after a 30-min total ischemia.

MATERIALS AND METHODS

The study was carried out on Langendorff-perfused hearts isolated from albino random-bred male rats weighing 250-280 g. The chest was opened under ether narcosis, the heart was isolated, washed with cold (4°C) Krebs-Henseleit solution, and connected to a perfusion system. Perfusion was performed with Krebs-Henseleit solution containing (in mM): 118.0 NaCl, 4.7 KCl, 2.5 CaCl2, 1.2 KH2PO4, 1.6 MgSO4, 25.0 NaHCO3, 0.5 Na-EGTA, and 5.5 glucose, saturated with 95% O2 and 5% CO2 mixture (37°C; pH 7.4), and delivered at a constant pressure of 97 cm H2O. A small latex balloon connected through a catheter to a EMT-746 semiconductor pressure transducer (Siemens-Elema) was inserted into the left ventricle. LVDP, end-diastolic pressure (EDP), and the maxi-
mum contraction (+dP/dt_{max}) and relaxation (-dP/dt_{max}) rates were determined under isovolumic conditions. The initial EDP was 10 mm Hg. Periodically, coronary blood flow (CBF) was evaluated by measuring the volume of perfusate flowing through the heart during 1 min. After 15-min stabilization perfusion was

![Graphs](image)

**Fig. 1.** Effect of uridine and uridine nucleotides (50 µmol/liter) on left ventricular pressure (a), end-diastolic pressure (b), maximum rates of contraction (c) and relaxation (d), and coronary blood flow (e). 1) control; 2) uridine; 3) uridine-5’-monophosphate; 4) uridine-5’-diphosphate; 5) uridine-5’-triphosphate. *p<0.05 compared to the control.