CATECHOLAMINE CONTENT AND ELECTROLYTE BALANCE IN THE MYOCARDIUM OF RABBITS POISONED WITH 2,4-DINITROPHENOL

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After intravenous injection of 2,4-dinitrophenol in a dose of 10 mg/kg, destruction of the mitochondria in some myocardial muscle cells was accompanied by hyperfunction of these organelles in others. The noradrenalin content in the heart tissue was increased, but the potassium level was reduced. With a more severe energy deficit (20 and 30-40 mg/kg 2,4-dinitrophenol) signs of destruction predominated in the mitochondria of the myocardial cells, the noradrenalin concentration in the heart tissue fell, but the potassium level in the plasma and myocardium rose. The adrenalin concentration in the heart and adrenal tissue fell. A severe energy deficit gave rise to a syndrome of hyperkaliemia linked with discharge of potassium into the blood stream from the tissue depots.

KEY WORDS: 2,4-dinitrophenol; energy deficit; myocardium; catecholamines; electrolyte metabolism.

When an energy deficit is present, the depletion of the reserves of sympathetic neurohormones [4, 5] and disturbance of the electrolyte balance of the myocardium [6, 7] may play important roles in the changes in functional properties of the heart muscle.

The content of catecholamines and electrolytes in the heart and other organs were determined during energy deficit caused by 2,4-dinitrophenol (DNP).

EXPERIMENTAL METHOD

Rabbits were used. In the experiements of series I (15 rabbits) and II (11) DNP was injected intravenously as a single dose of 10 or 20 mg/kg, respectively, whereas in series III (8 animals) DNP was injected in doses of 20, 10, and 10 mg/kg at intervals of 1-1.5 h.

The body temperature and the blood pressure (in the carotid artery) of the animals were investigated, the ECG was recorded, the concentration of noradrenalin (NA) and adrenalin (A) in the tissues of the cardiac ventricles and adrenals was determined [1], and the concentrations of potassium, sodium, and calcium in the blood plasma, erythrocytes, and tissue of the ventricles were measured by flame photometry (Hitachi spectrophotometer). The ultrastructure of the myocardial muscle cells was investigated with the UÉMV-100 K electron microscope (magnification from 9000 to 21,000 times).

EXPERIMENTAL RESULTS

DNP in a dose of 10 mg/kg caused the body temperature to rise by 1.5°C and the heart rate to quicken 1.5-2 h after injection. Heterogeneity of the myocardial cells was observed on the electromicrograph. In some muscle cells most of the mitochondria were partly or completely homogenized (Fig. 1a), but in other cells in the same part of the myocardium signs of hyperfunction of the mitochondria were present: marked

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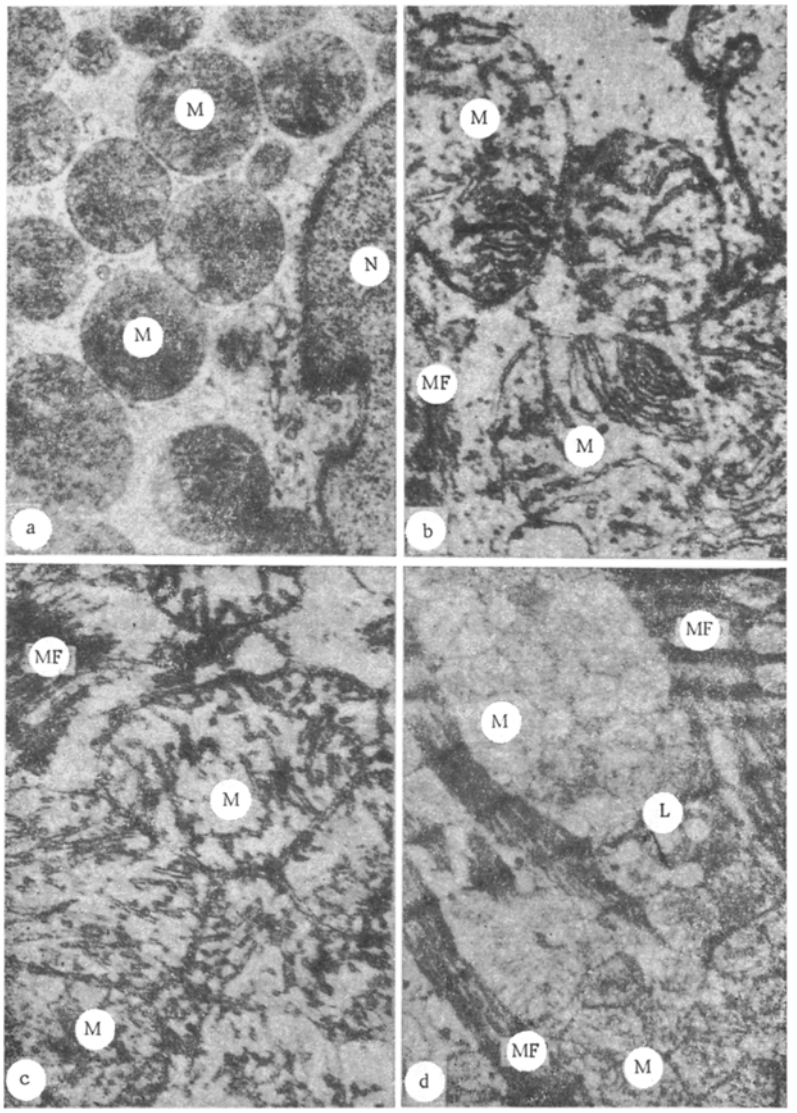

Fig. 1. Changes in ultrastructure of contractile myocardium in DNP poisoning: a) DNP given in a dose of 10 mg/kg. Swelling and homogenization of mitochondria, reduced number of cristae. 15,000 ×. b) Same dose of DNP. Marked swelling of mitochondria, blurring of their matrix, decrease in number and fragmentation of cristae. Residual cristae arcuate in shape; 21,000 ×; c) DNP given in dose of 20 mg/kg. More marked changes in mitochondria, marked fragmentation of their cristae. 21,000 ×. d) DNP given in dose of 30 mg/kg. Destruction of mitochondria; dilation of tubules of sarcoplasmic reticulum, appearance of lipid inclusions, overcontraction of myofibrils. 9000 ×. M) mitochondria, N) nucleus, MF) myofibrils, SR) sarcoplasmic reticulum, L) lipids.

swelling, circular shape, clear matrix, reduced number of highly fragmented, arcuate cristae with anastomoses (Fig. 1b). The NA content in the heart tissue of these animals (Fig. 2) was increased ($P < 0.05$), most probably because of the increased extracardiac sympathetic influences and not an increase in the uptake of NA from the blood. In fact, in the isolated heart DNP reduces the NA level in the myocardium and inhibits its uptake from the perfusion fluid [5]. The potassium concentration in the plasma and heart tissue of the animals of this series fell (Fig. 3), and the sodium concentration was indistinguishable from the control.

After administration of DNP in a dose of 20 mg/kg the body temperature rose on the average by 2.5-

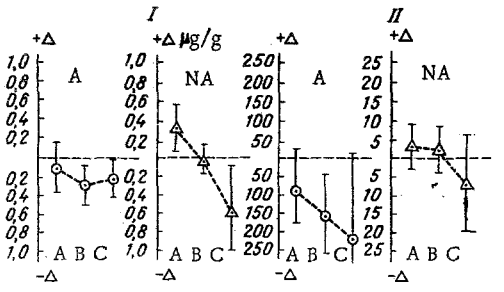

Fig. 2

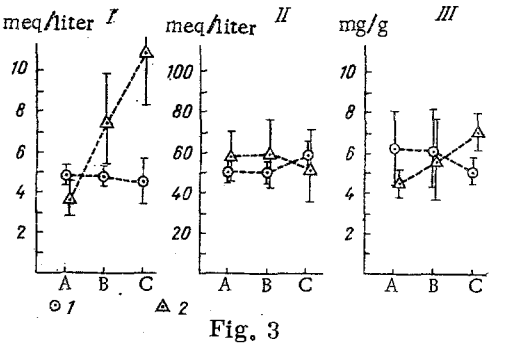

Fig. 3

Fig. 2. Changes in A and NA concentrations in rabbit heart and adrenal tissues in DNP poisoning. Ordinate, difference (delta) between values in experimental and control series (in μg/g); A) 10 mg/kg, B) 20 mg/kg, C) 30-40 mg/kg DNP. I) Heart, II) adrenals.

Fig. 3. Potassium concentration in plasma (I), erythrocytes (II), and heart tissues (III) of rabbits with DNP poisoning. Ordinate, potassium concentration (in meq/liter or mg/g dry weight): 1) control, 2) experiment. Remainder of legend as in Fig. 2.

3°C, and death of 45% of the animals was imminent. On the electron micrographs damage to the mitochondria was more severe (Fig. 1c). The NA and electrolyte concentrations in the heart tissues of the surviving and dying rabbits differed. In the survivors the NA concentration remained high (0.54 μg/g); the potassium concentration in the myocardium was low, but the sodium concentration was raised ($P < 0.05$). In the dying animals (at the moment of death) an idioventricular rhythm was observed, the NA concentration in the heart tissue was reduced (to 0.34 μg/g), but the potassium concentration was raised. The plasma potassium concentration of these rabbits was higher than in the survivors and much higher than in the control ($P < 0.05$).

In a dose of 30-40 mg/kg DNP caused general convulsions and fibrillary muscular spasms, hypotension, and the appearance of an idioventricular cardiac rhythm. The body temperature rose on the average by 3.7° and death of all the animals was imminent. Heterogeneity of the muscle cells was ill-defined on the electron micrographs of the contractile myocardium, most of the mitochondria were swollen, generally fragmented, with a blurred matrix, and the number of cristae was sharply reduced (Fig. 1d). The NA concentration in the heart tissue of these animals was lower than in rabbits dying after receiving DNP in a dose of 20 mg/kg. The adrenalin concentration in the heart and adrenals was reduced in all series of experiments, but most of all after injection of DNP in a dose of 30-40 mg/kg. Potassium accumulation in the plasma of these rabbits and the simultaneous increase in its concentration in the myocardium, accompanied by the fibrillary muscular twitches, were evidently connected with an increase in the plasma K/Ca ratio (3.93 compared with 1.58 in the control, $P < 0.05$), and the elevation of the T_2 wave on the ECG is characteristic of a syndrome of hyperkaliemia. The fall of the potassium concentration in the femoral muscles ($P < 0.05$) observed after administration of DNP in a dose of 30-40 mg/kg suggests that this syndrome was due to the discharge of potassium into the blood stream from its depots as a result of tissue changes arising during the energy deficit.

In the initial stages of changes in energy metabolism, cardiac activity thus was not significantly disturbed because of compensatory hyperfunction of the mitochondria. The development of tachycardia under those conditions was accompanied by elevation of the NA concentration in the heart tissue, lowering of the potassium level, and an increase in the sodium concentration. Sodium cations play a direct part in the preservation of the NA reserves in the heart [2, 3]. If the energy deficit is severe, the disturbances of cardiac activity are accompanied by exhaustion of the NA reserves in the heart, which may be linked with the accumulation of potassium in the plasma and heart tissue, blocking neuronal uptake of NA.

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