EFFECT OF CARDIAC GLUCOSIDES ON THE CORONARY CIRCULATION AND THE OXYGEN ABSORPTION BY THE HEART IN EXPERIMENTAL MYOCARDIAL INFARCTION

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One of the criteria used to evaluate drugs given for the treatment and prophylaxis of myocardial infarction is their effect on the blood supply to the heart. The cardiac glucosides are often used in the treatment of myocardial infarction, but no information could be found in the literature regarding their effect on the volume velocity of the coronary blood flow in coronary insufficiency. Most research in this field has been concerned with the study of the effect of these drugs on the changes in the ECG and in the hemodynamics [3, 4, 10, 11].

Because of the urgency of this problem, we have made a comparative study of the effect of strophanthin, erysimin, and digitoxin on the coronary circulation and on the absorption of oxygen by the heart in experimental myocardial infarction.

EXPERIMENTAL METHOD

Experiments were carried out on cats anesthetized with urethane and chloralose. The volume velocity of the blood flow from the coronary sinus was measured [6]. The oxygen absorption by the heart was determined by the accepted formula from measurement of the oxyhemoglobin concentration in the blood by Krebs's method [7]. The cardiac activity was recorded by a Hurthle's manometer and electrocardiographically. The arterial pressure was recorded in the carotid artery by means of a mercury manometer. Experimental insufficiency of the coronary circulation was produced by ligation of the left descending coronary artery in its upper third through a thoracotomy with the aid of artificial respiration. The cardiac glucosides were injected intravenously in therapeutic doses of 0.1-0.3 cat units/kg (c.u./kg).

EXPERIMENTAL RESULTS

After ligation of the left anterior descending artery in its upper third, in the majority of experiments bradycardia developed, and in some experiments – arrhythmia. The volume velocity of the coronary blood flow fell by 33% and the oxygen absorption by the heart fell by 30%. These indices did not recover in the course of the experiment (30-40 min). Usually the glucosides were injected intravenously 15 min after ligation.

In the healthy animals strophanthin and erysimin in a dose of 0.1 c.u./kg and digitoxin in a dose of 0.05 c.u./kg had little effect on the coronary blood flow and the oxygen absorption by the heart. In larger doses, strophanthin (0.3 c.u./kg), erysimin (0.2 c.u./kg), and digitoxin (0.1 c.u./kg) increased the volume velocity of the coronary blood flow and the oxygen absorption by the heart, while under these circumstances the pressure usually rose by 10-15 mm and the heart rate increased, except in a few experiments in which it was slowed for a short time.

In experimental coronary insufficiency the reaction to the cardiac glucosides was considerably modified. Erysimin in a dose of 0.1 c.u./kg, for instance, increased the volume velocity of the coronary blood flow by 53% and the oxygen absorption by the heart by 55%, quickened the heart rate, and caused a transient increase in the arterial pressure. In a dose of 0.2 c.u./kg, erysimin lowered the coronary blood flow by 20% and the oxygen absorption by 17%, lowered the arterial pressure, and caused bradycardia and arrhythmia (Fig. 1). A similar effect was produced by digitoxin in a dose of 0.05-1.0 c.u./kg and strophanthin in a dose of 0.1-0.2 c.u./kg (Fig. 2). After a preliminary

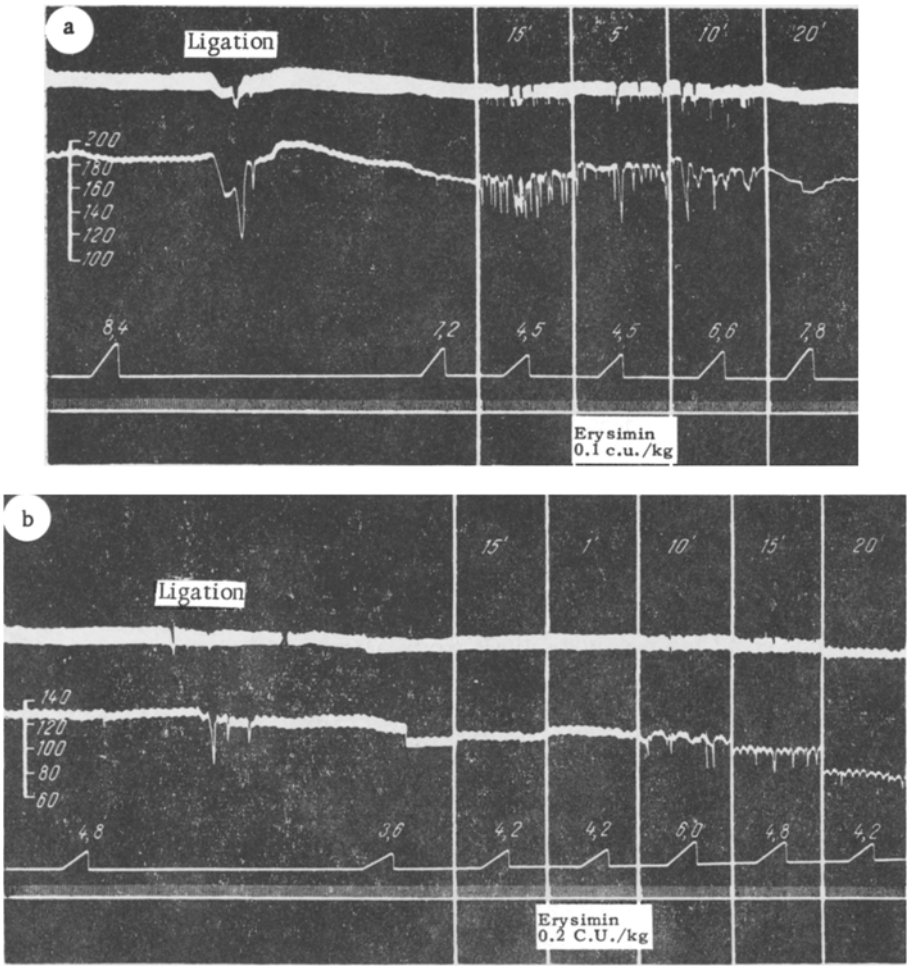

Fig. 1. Changes in the volume velocity of the coronary blood flow following injection of erysimin in doses of 0.1 c.u./kg (a) and 0.2 c.u./kg (b) in experimental myocardial infarction. Significance of the curves (from above down): cardiac activity; arterial pressure; volume velocity of the coronary blood flow (the numbers above the columns correspond to the volume velocity of the blood outflow per minute); time marker (1 sec).

injection of atropine in a dose of 1 mg/kg, erysimin and strophanthin, in a dose of 0.2 c.u./kg, did not lower the volume velocity of the coronary blood flow and the absorption of oxygen by the heart.

In some experiments, besides recording the coronary blood flow, simultaneous recordings were made of the ECG, usually in standard lead 2. After ligation of the left descending coronary artery considerable changes were observed in the ECG – displacement of the S-T interval, enlargement of inversion of the T wave, and a reduction in the voltage of the R wave. In some experiments arrhythmia developed 10-15 min after ligation as a result of disturbance of the pacemaker function, the excitability, or the conductivity of the heart.

After injection of strophanthin and erysimin in a dose of 0.1 c.u./kg and digitoxin in a dose of 0.05 c.u./kg normalization of the ECG was observed – the T wave was diminished, the S-T interval was depressed to the isoelectric line, and the arrhythmia disappeared. The characteristic shortening of the Q-T interval produced by glucosides was observed as a result of intensification of systole; no slowing of atrioventicular conduction was seen with these doses. The anti-arrhythmic action of the cardiac glucosides in experimental myocardial infarction is illustrated in Fig. 3. With an increase in the doses of the cardiac glucosides (erysimin and strophanthin 0.2 c.u./kg, digitoxin 0.1 c.u./kg) the normal ECG was not restored, and in some experiments ventricular extrasystoles appeared.

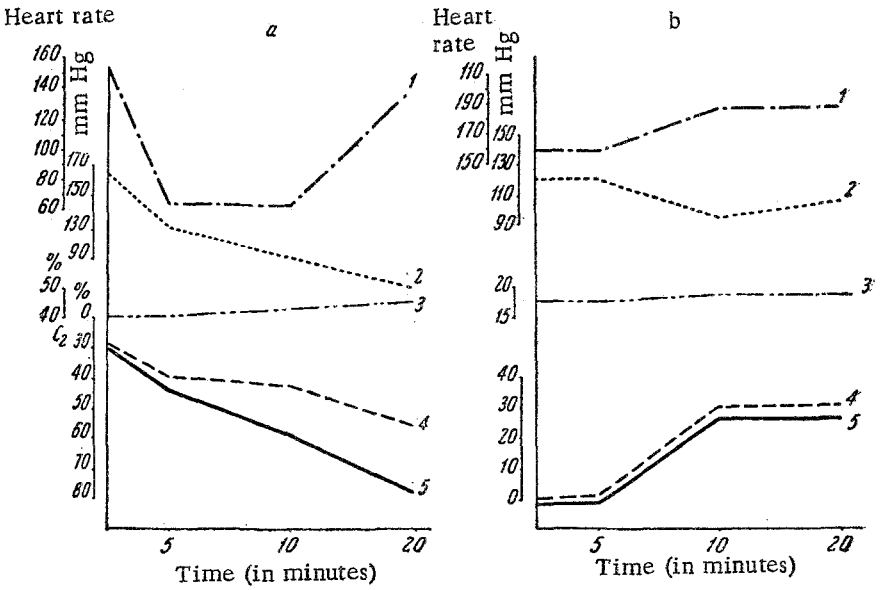

Fig. 2. Changes in volume velocity of coronary blood flow and in oxygen absorption by the heart in experimental myocardial infarction (a) and after administration of strophanthin (0.1 c.u./kg) to cats with this condition (b). 1) Heart rate; 2) arterial pressure; 3) oxyhemoglobin in blood from sinus venosus (C_2); 4) volume velocity of coronary blood flow (V); 5) oxygen absorption by the heart (A).

The effect of the cardiac glucosides on the transmission of excitation from the vagus nerves to the heart muscle was studied in cats with experimental myocardial infarction. The peripheral segment of the left vagus nerve, divided in the neck before the experiment, was stimulated by means of rectangular pulses with a frequency of 30 cps and a duration of 0.5 millisec, supplied by an electronic stimulator. In most of the experiments on animals with myocardial infarction the transmission of excitation from the vagus nerves to the heart muscle was impaired, and only in individual cases was transmission unaffected or promoted. After injection of strophanthin (0.2 c.u./kg) and erysimin (0.1 c.u./kg) the transmission of excitation was greatly facilitated; an increase in the doses of the glucosides was accompanied by impairment of the transmission of impulses.

The toxicity of strophanthin was also studied in these experiments by Vanhaarden's method in healthy cats and in cats with experimental myocardial infarction. The mean dose of strophanthin causing cardiac arrest in healthy cats was 104 mg/kg (0.095-0.111 mg/kg); in experimental myocardial infarction this dose fell to 0.048 mg/kg (0.032-0.059 mg/kg); the difference is statistically significant.

These experiments showed that in experimental myocardial infarction the volume velocity of the coronary blood flow and the oxygen absorption by the heart were considerably reduced. Similar findings were obtained by other authors [9, 12-15].

Strophanthin and erysimin in a dose of 0.1 c.u./kg, and digitoxin in a dose of 0.05 c.u./kg, which do not cause changes in the coronary blood flow and oxygen absorption by the heart in healthy animals, caused a considerable increase in these indices in experimental myocardial infarction and restored the normal ECG.

When cardiac glucosides were given in doses increasing the coronary blood flow and oxygen absorption by the heart (strophanthin 0.3 c.u./kg, erysimin 0.2 c.u./kg, digitoxin 0.1 c.u./kg) in healthy animals, both these indices were lowered in animals with experimental myocardial infarction, the heart rate was slowed, arrhythmia developed, and the arterial pressure fell. The normal ECG was not restored. Similar results were obtained by other workers [15].

In experimental myocardial infarction the transmission of excitation from the vagus nerves to the heart muscle was significantly depressed, but after administration of cardiac glucosides (0.1-0.2 c.u./kg) it was facilitated. Similar results were obtained in experimental myocarditis [2, 5]. A. M. Blinova and G. N. Aronova [1] also report depression of the reaction to stimulation of the vagus nerve after ligation of the left descending artery, except in a few experiments in which the reaction was enhanced. The toxicity of the cardiac glucosides increased considerably in experimental myocardial infarction, a fact also reported by V. V. Gatsura, P. P. Provotorova, and others.

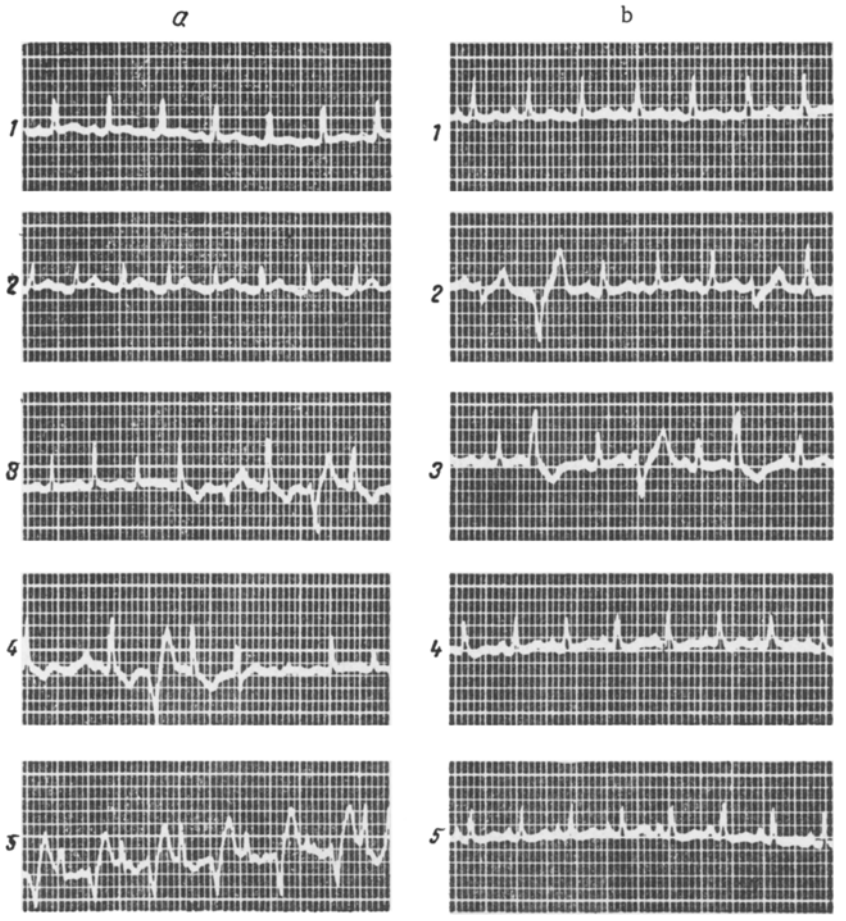

Fig. 3. Changes in the ECG of the cat after ligation of the left descending artery (a) and after this procedure and injection of strophanthin (0.1 c.u./kg) (b). a: 1) normal; 2) 5th min after ligation; 3) 10th min; 4) 15th min; 5) 20th min; b: 1) normal; 2) 10th min after ligation; 3) 10th min after injection of strophanthin; 4) 15th min; 5) 20th min.

It may be concluded from these results that the qualitative difference in the reaction to injection of cardiac glucosides in acute coronary insufficiency is due to an increase in their toxicity in this pathological state. A strengthening of the vagus influence on the heart is also concerned here, because blocking the muscarine-like cholinergic structures with atropine abolished the reduction in the volume velocity of the coronary blood flow and absorption of oxygen by the heart caused by the subsequent injection of strophanthin and erysimin in a dose of 0.2 c.u./kg in the absence of the preliminary injection of atropine. The importance of excitation of the vagus nerves in myocardial infarction has been stressed by other authors [4, 8].

SUMMARY

A study was made of the effect produced by strophanthin, erysimin and digitoxin on the coronary circulation, cardiac oxygen absorption, ECG and toxicity in experimental myocardial infarction. Cardiac glucosides, given in therapeutic doses (0.05-0.1 c.u./kg), in conditions of coronary insufficiency induced by ligation of the left descending coronary artery, increased the volume velocity of the coronary circulations and cardiac oxygen absorption, normalized the EEG and possessed an anti-arrhythmic action. Erysmin and digitoxin produced a more marked effect on the coronary circulation than strophanthin. The toxicity of cardiac glucosides increased considerably in experimental myocardial infarction; during the action of these preparations the transmission of excitation from the vagus nerves to the cardiac muscle is facilitated.

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