CARDIOMONITORING OF THE EFFECT OF PERFTORAN ON ECG PARAMETERS UNDER CONDITIONS OF EXPERIMENTAL HYPOXIC DAMAGE OF THE MYOCARDIUM

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Myocardial damage is a metabolic phenomenon attributed to the lack of oxygen supply. The effect of the blood substitute perftoran on the ECG parameters registered was studied using the model of acute experimental epinephrine-induced hypoxic myocardial damage in rats. The introduction of perftoran prevented the development of changes in the ST segment and violations in the heart rhythm under the model damage conditions.

Modern public health indices present convincing evidence that ischemic cardiopathology is among the main lethal factors [1]. In the basic research in cardiology, myocardial ischemia is most frequently treated as a metabolic phenomenon related to the lack of oxygen supply as compared to the local and/or global demand of myocardial cells [2, 3]. In recent years, clinical cardiology introduced the concepts of “stunning” myocardium and “hibernating” myocardium, which reflect the onset of dysfunction of the left ventricle of the heart in the regions of restored circulation [4, 5]. This situation implies the need for evaluation of the pharmacological effect of drugs from the standpoint of restoration of the characteristics of the myocardium to the normal level after termination of the action of damaging factors upon the organism. It was demonstrated that ECG monitoring not only provides information about the appearance and development of damage in the myocardium, but is also capable of characterizing the onset of violations in the cardiac automatism and the development of ectopic automatism [6].

Among medicinal preparations capable of producing a cardioprotective action, of special interest is perftoran, which is a fluorocarbon compound belonging to the group of blood substitutes and gas-transport agents. Possessing this polyfunctional activity, perftoran is capable of improving the gas exchange and metabolism in tissues, enhancing oxygen transport via the blood, stabilizing membranes, restoring the central hemodynamics, and protecting the myocardium [7, 8]. This study was aimed at characterizing the effect of perftoran as manifested in the dynamics of ECG parameters under conditions of model myocardial damage in rats.

EXPERIMENTAL METHODS

We performed three series of experiments [9] on 140 male mongrel rats weighing 160 – 230 g. The animals were kept under standard vivarium conditions and treated according to the experimental schedule at the Institute for Leprosy Research (Moscow) and the Central Research Laboratory of the Astrakhan State Medical Academy (Astrakhan).

In the first series of tests involving 55 animals, the ECG monitoring was used to determine changes in the main parameters under the conditions of a model acute hypobaric hypoxia. A test rat was narcotized by a 20% hexenal solution (50 mg/kg, i.p.) [10, 11] and placed into a special 2.1-liter chamber, where a model hypoxia regime corresponding to an altitude of 11,000 m was created with the aid of a Kamovskii apparatus. The “elevation” was performed at a rate of 150 – 200 m/sec [12]. The continuous ECG monitoring was performed using a Mingograf 82 system (Siemens Elema, Sweden) after the onset of narcosis, during the elevation process, and for 5 min after attaining the 11,000 m level.

In the second series of tests involving 40 animals, the ECG monitoring was used to determine changes in the main parameters under the conditions of a model acute epinephrine-induced hypoxic myocardial damage. The model myo-

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cardiac damage was reproduced in hexenal-narcotized rats by injections of 0.1% epinephrine hydrochloride solution (15 ml, s.c.), after which the ECG monitoring was performed as in the first series.

In the third series of tests involving 45 animals, the ECG monitoring was used to determine the effect of perftoran on the main ECG parameters under the conditions of a model acute epinephrine-induced hypoxic myocardial damage. In this case, the narcotized rats were pretreated (1 ml/kg, i.p.) with perftoran emulsion (Perftoran Company, Pushchino). In 10 – 15 min after perftoran injection, the model hypoxic myocardial damage was reproduced as described above, and the ECG monitoring was performed as in the first two series of tests.

The effect of perftoran was evaluated in terms of eight experimental parameters (selected from the 14 main ECG characteristics), which are most informative from the standpoint of clinical cardiology: PQ, QT, and RP intervals; P, R, and T waves; ST segment; and heart rate (HR). We have also followed violations in the heart rhythm and the cardial conduction. The experimental data were statistically processed on an Intel Pentium III PC using the corresponding programs for Microsoft Windows 2000XP, Microsoft Word 2000XP, and Microsoft Excel 2000XP.

RESULTS AND DISCUSSION

Based on the results of the first experimental series, it was found that a certain fraction of the animals is characterized by the individual resistance to the action of acute hypobaric hypoxia on the organism. In other animals, the ECG monitor revealed manifestations of the myocardial damage, which could be subdivided into three main types: (i) changes in the terminal part of the ventricular complex, as manifested by an increase in the ST segment or the T wave; (ii) violations in the heart rhythm and/or conduction (arrhythmia); (iii) a combination of the above changes in the terminal part of the ventricular complex and the heart rhythm and/or conduction disorders.

Thus, the experimental male rats exhibited four different types of response of myocardium to the model acute hypobaric hypoxia. In order to consistently describe the drug action upon the myocardium as evaluated from the ECG monitor data, it was necessary to find or develop a model characterized by analogous manifestations in the ECG pattern. We have attempted to model the observed changes (i) by ligation of the coronary artery and (ii) by introducing epinephrine in histotoxic doses for the myocardium.

In the case of a model myocardial damage induced by ligation of the coronary artery, the ECG of all the experimental animals exhibited a single-phase increase (Pardee’s arc) in the ST segment and the T wave. However, it was established that the ligation-induced myocardial damage is always characterized by the progressive development of necrosis in the myocardium. The degree of necrosis was dependent on the diameter of the ligated blood vessel. For this reason, the administration of cardiotropic drugs did not influence the development of necrosis in the myocardium.

The parenteral introduction of epinephrine in histotoxic doses for the myocardium (0.5 – 1.0 ml of 0.1% solution) was recommended as a means of modeling acute ischemic damage in the myocardium [13]. However, the introduction of epinephrine in the indicated doses hindered the ECG monitoring as a result of the development of side reactions, which distorted the experimental results. A decrease in the epinephrine dose to 0.1 – 0.2 ml did not provide for a required myocardial damage reliably manifested on the ECG monitor.

In order to develop an appropriate experimental model for the myocardial damage, we used the well-known approach based on the use of a combination of several factors. An example is the administration of epinephrine in combination with physical loading by means of a treadmill or forced swim [12]. Unfortunately, such models offer no technical possibilities of monitoring the myocardial damage by means of ECG. Further experiments led us to a new model of the acute myocardial damage, which included the subcutaneous introduction of 0.1% epinephrine solution (0.15 ml) followed by the induction of acute hypobaric hypoxia. In this case, the ECG monitor showed a decrease in the ST segment by 1 mm

### TABLE 1. Effect of Perftoran on ECG Parameters (X ± x) under Conditions of Experimental Acute Hypoxic Damage of Myocardium

<table>
<thead>
<tr>
<th>Test conditions</th>
<th>ECG intervals, mm/sec</th>
<th>ECG waves, mm</th>
<th>ST segment, mm</th>
<th>HR, cpm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PQ</td>
<td>QT</td>
<td>RR</td>
<td>P</td>
</tr>
<tr>
<td>Control (intact)</td>
<td>0.05 ± 0.02</td>
<td>0.08 ± 0.001</td>
<td>0.2 ± 0.01</td>
<td>1.4 ± 0.5</td>
</tr>
<tr>
<td>Perftoran (1 ml/kg)</td>
<td>0.04 ± 0.001</td>
<td>0.08 ± 0.01</td>
<td>0.3 ± 0.04</td>
<td>2.0 ± 0.1*</td>
</tr>
<tr>
<td>Acute hypoxic myocardial damage</td>
<td>0.05 ± 0.001</td>
<td>0.08 ± 0.01</td>
<td>0.24 ± 0.01</td>
<td>1.3 ± 0.1</td>
</tr>
<tr>
<td>Acute hypoxic myocardial damage on background of perftoran (1 ml/kg)</td>
<td>0.07 ± 0.01*</td>
<td>0.08 ± 0.01</td>
<td>0.33 ± 0.05</td>
<td>1.3 ± 0.1*</td>
</tr>
</tbody>
</table>

**Notes:** Difference are reliable for \( p < 0.05 \), * between control and perftoran treatment and ** between model damage with and without perftoran pretreatment.