EFFECT OF NITROGLYCERIN ON SIZE OF AN EXPERIMENTAL MYOCARDIAL INFARCT

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Recent experimental and clinical studies have shown that some procedures used in the early stages after coronary occlusion lead to a decrease in size of the myocardial infarct [3, 6]. Such a reduction can be achieved by reperfusion [5], aortic counterpulsation [11], and administration of β-adrenoblockers [9], hyaluronidase [1, 12], steroid hormones [14], and certain other preparations.

Among pharmacological agents, special attention has been paid recently to nitroglycerin. The efficacy of this substance in relation to protection of the zone surrounding the infarct against ischemia is associated with the peripheral, predominantly venous, vasodilatation, its positive effect on the blood supply to the zone surrounding the infarct, and also its cardiostimulant properties [4, 10, 15]. It is the latter which distinguishes nitroglycerin from the β-adrenoblockers and broadens the scope for its use.

Meanwhile the problem of whether the size of an infarct can be reduced with the aid of nitroglycerin has not yet been finally solved. The object of this investigation was to study the effect of nitroglycerin on the dimensions of a myocardial infarct when the drug was injected in the early stages after occlusion of the coronary artery.

EXPERIMENTAL METHOD

Male Chinchilla rabbits weighing 2.5-3 kg were used. A myocardial infarct was induced by ligation of the anterior descending branch of the left coronary artery during spontaneous respiration and under pentobarbital anesthesia (25 mg/kg body weight, intravenously). The ECG was recorded in 18 precordial leads, on a Mingograph-82 multichannel recorder (from Elema, Sweden). The total height of the ST segment in 18 precordial leads (ΣST) and the heart rate (HR) were determined from the ECG. Electrocardiography was carried out 30, 120, 180, and 360 min after the operation. A new therapeutic form of nitroglycerin for intravenous injection (1% alcoholic solution in ampuls), developed at the Institute of Pharmacology, Academy of Medical Sciences of the USSR, was used. Two main groups of animals were studied: control and experimental (25 rabbits in each group). Nitroglycerin was injected intravenously into the experimental animals at the rate of 100 μg/min for 1 h from the 120th to the 180th minutes after the operation. Planimetric determination of the size of the infarct was carried out by the method in [13] on the 7th day after the operation. An example of one such determination is given in Fig. 1. During analysis of the data the size of the infarct was expressed as a percentage of the weight of the left ventricle. The significance of differences was determined by Student's t-test.

EXPERIMENTAL RESULTS

Data showing the trend of changes in ΣST, both spontaneous and under the influence of nitroglycerin, are illustrated in Fig. 2. A spontaneous decrease in ΣST in rabbits of the control group began 120 min after the operation and by the 180th minute ΣST had fallen to 81% of its initial (after 30 min) level ($P < 0.02$). During the next 3 h no changes in ΣST were found.

In the experimental animals a significant decrease in ΣST was found compared with the control ($P < 0.05$), and after 180 min it was down to 60.5% of the initial value. During the next 3 h ΣST remained at the level reached toward the end of treatment with nitroglycerin.

It can thus be concluded that, first, spontaneous changes in ΣST begin with effect from 2 h after the operation, second, that under the influence of nitroglycerin the decrease in ΣST takes place more rapidly and reaches a lower level than

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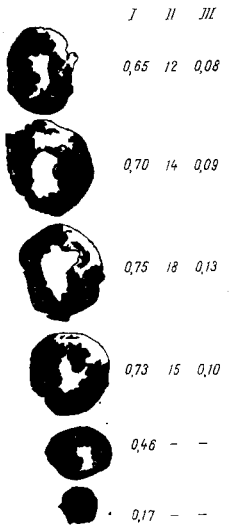

Fig. 1. Planimetric determination of size of infarct: I) weight of block (in g), II) size of infarct (in % of area of section), III) the same (in g). Weight of left ventricle 3.46 g, total weight of infarcted tissue 0.4 g.

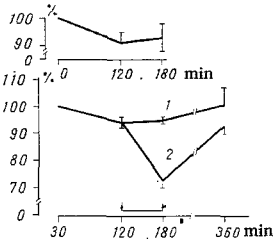

Fig. 2

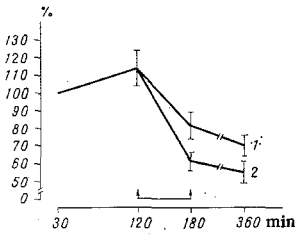

Fig. 3

Fig. 2. Dynamics of changes in ΣST in animals of control (1) and experimental (2) groups (in % of ΣST 30 min after operation). Here and in Fig. 3, arrows indicate time of injection of nitrolgycerin in experimental group.

Fig. 3. Dynamics of changes in HR in animals of control (1) and experimental (2) groups (in % of HR 30 min after operation). Top graph shows trend of changes in HR in animals of additional group (in % of initial level before injection of pentobarbital).

in the control, and third, that 3 h after the operation the lowering of the ST segments follows a parallel course in the animals of both groups, and that the level of this parameter after 6 h is determined by its actual level observed after 3 h.

During analysis of the ECG attention was drawn to slowing of the heart following injection of nitroglycerin. Data on the effect of treatment on HR are shown in Fig. 3. In the control animals a small decrease in HR was observed after the operation, but by the 6th hour the heart rate was significantly higher than that observed during the first 3 h. Nitroglycerin slowed HR by comparison with the control ($P < 0.001$); this ratio was maintained 3 h after the end of treatment. No correlation could be found between the initial HR and the degree of its reduction.

Nitroglycerin is known to cause some increase in HR, but these observations do not apply to patients with acute myocardial infarction. At the same time, some workers have noted the development of bradycardia when nitroglycerin is given in the acute stage of the disease [8]. To shed more light on this question an additional series of experiments was carried out on intact animals, into which nitroglycerin was injected, 2 h after intravenous injection of pentobarbital (25 mg/kg) for 1 h at the rate of 100 μg/min. A decrease in HR under the influence of anesthesia was observed in the animals of this group, just as in animals of the control group undergoing operation, but administration of nitroglycerin had virtually

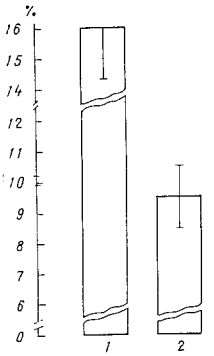

Fig. 4. Weight of infarct (in % of weight of left ventricle) in animals of control (1) and experimental (2) groups.

no effect on HR (Fig. 3). It can accordingly be concluded that nitroglycerin in fact slows the heart of animals with experimental myocardial infarction.

To judge from observations of Kaverina et al. [2], besides its indirect sympathomimetic effect, nitroglycerin also causes partial blockage of β-adrenergic structures. This mechanism may perhaps be dominant in the acute phase of myocardial infarction and may be responsible for the development of bradycardia under the influence of nitroglycerin.

A comparative study of the size of myocardial infarct 7 days after the operation showed a significant difference in the size of the infarct (Fig. 4): In treated animals the infarct was 41% smaller than in the control ($P < 0.01$).

The results thus confirm that the size of an experimental myocardial infarct can be limited by treatment with nitroglycerin.

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