EFFECT OF NITROGLYCERIN ON THE SIZE OF AN EXPERIMENTAL MYOCARDIAL INFARCT

N. I. Afonskaya, Yu. M. Ostrogorskii,
N. M. Cherpachenko, Yu. B. Rozonov,
N. V. Kaverina, and M. Ya. Ruda

UDC 616.127-005.8-092.9-085.224.547

KEY WORDS: experimental myocardial infarction; limitation of size; nitroglycerin.

Experimental and clinical studies in recent years have shown that certain measures taken in the early stages after coronary occlusion can lead to a reduction in size of the zone of myocardial necrosis [3, 6]. This can be achieved by reperfusion [5], aortic counterpulsation [11], administration of β-adrenoblockers [9], of hyaluronidase [1, 12], of steroid hormones [14], and of certain other preparations. Among pharmacological agents, special attention is currently being paid to nitroglycerin. The efficacy of this substance with respect to protection of the zone around the infarct from ischemia is associated with the peripheral (chiefly venous) vasodilatation, the positive effect on the blood supply to the zone surrounding the infarct, and to the cardiostimulant properties of the compound [4, 10, 15]. It is the latter which distinguish nitroglycerin from β-adrenoblockers and widen the scope for its use. Meanwhile the question of possible limitation of the zone of infarction by means of nitroglycerin has not been finally settled.

The object of this investigation was to study the effect of nitroglycerin on the size of an experimental myocardial infarct following intravenous injection of the drug in the early stages after coronary occlusion.

EXPERIMENTAL METHOD

Experiments were carried out on male chinchilla rabbits weighing 2.5-3 kg. A myocardial infarct was induced by ligation of the descending branch of the left coronary artery of a spontaneously breathing animal anesthetized with pentobarbital (25 mg/kg body weight, intravenously). The ECG was recorded in 18 precordial leads on a Mingograph-82 multichannel recorder (Elema, Sweden). The integral rise of the ST segment in 18 precordial leads (ΣST) and the cardiac frequency (CF) were calculated from the ECG. Cardiography was carried out 30, 120, 180, and 360 min after the operation. A new presentation of nitroglycerin for intravenous injection (1% alcoholic solution in ampuls), developed and studied at the Research Institute of Pharmacology, Academy of Medical Sciences of the USSR, was used. Two main groups of animals were studied: control (25 rabbits) and experimental (25 rabbits), into which nitroglycerin was injected intravenously at the rate of 100 μg/min for 1 h, between 120 and 180 min after the operation. The size of the infarct was measured planimetrically by Roberts' method [13] on the 7th day after the operation. An example of the record of such a determination is shown in Fig. 1. During data processing the size of the infarct was expressed as a percentage of the weight of the left ventricle. The numerical results were subjected to statistical analysis by Student's t-test.

EXPERIMENTAL RESULTS

The dynamics of ΣST, both spontaneous and under the influence of nitroglycerin, is shown in Fig. 2. A spontaneous decrease in ΣST in the control group began from the 120th minute

Department of Emergency Cardiology, A. L. Myasnikov Research Institute of Cardiology. All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR. Laboratory of Pharmacology of the Cardiovascular System, Research Institute of Pharmacology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 91, No. 2, pp. 175-177, February, 1981. Original article submitted June 20, 1980.

 0007-4888/81/9102-0158$07.50

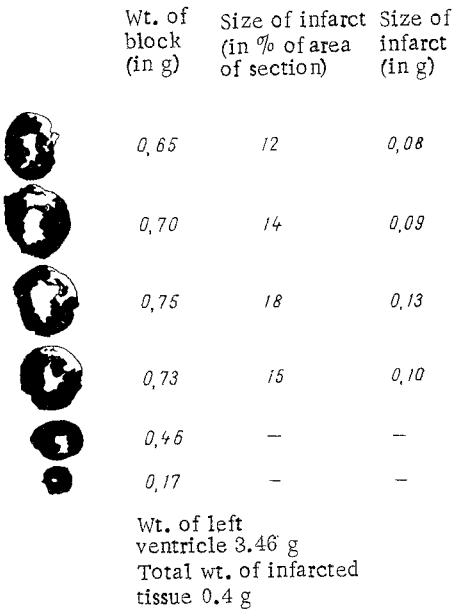

Fig. 1. Planimetric determination of size of infarct.

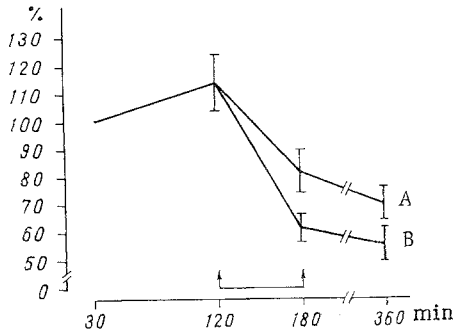

Fig. 2. Changes in ΣST in control (A) and experimental (B) groups (in % of ΣST 30 min after operation). Here and in Fig. 3 values of M ± m given. Arrows indicate time of injection of nitroglycerin in experimental group.

after the operation, so that by the 180th minute it was 81% of its initial value (at the 30th minute, $P < 0.02$). No significant changes in the value of ΣST were found during the next 180 min.

In the experimental group a significant decrease in ΣST compared with the control ($P < 0.05$) was observed, down to 60.5% of the initial level after 180 min. Later, during the next 180 min, ΣST remained at the level reached by the end of nitroglycerin therapy.

The observations can thus be summarized as follows: a) A spontaneous dynamics of ΣST begins 120 min after the operation, b) under the influence of nitroglycerin ΣST falls more rapidly and by a greater degree than in the control group, c) the lowering of the ST segments 180 min after the operation follows a parallel course in the two groups, and by the 360th minute the value of this parameter was to all intents and purposes the same as that observed after 180 min.

Analysis of the ECGs revealed slowing of CF after injection of nitroglycerin. The effect of treatment on CF is shown in Fig. 3. In the control group a small decrease in CF was observed after the operation, but by the 360th minute CF was significantly faster than the rate observed during the first 180 min. Nitroglycerin caused a significant decrease in CF compared with the control ($P < 0.001$); this relationship continued to hold good 180 min after the end of treatment. No correlation was found between the initial CF and the degree of slowing of the rhythm.

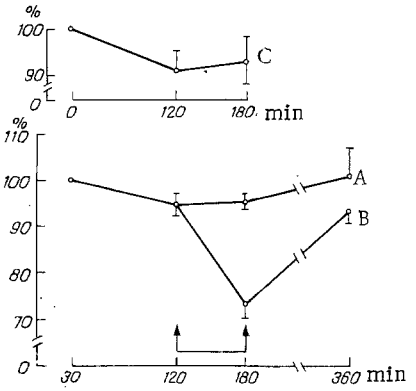

Fig. 3. Changes in CF in control (A), experimental (B) and supplementary (C) groups in % of CF 30 min after operation. A and B) in % of CF 30 min after operation; C) in % of initial value of CF (before pentobarbital).

Nitroglycerin is known to increase CF somewhat, but this does not apply to patients with acute myocardial infarction. Meanwhile, some workers have observed the development of bradycardia when nitroglycerin is given in the acute period of infarction [8]. To clear up this problem a supplementary series of experiments was carried out on intact animals, into which nitroglycerin was injected at the rate of 100 μg/min over a period of 1 h, 2 h after intravenous injection of pentobarbital (25 mg/kg). It will be clear from Fig. 3C that CF decreased under the influence of anesthesia in this group, just as in the control group of animals with experimental infarction, but injection of nitroglycerin had virtually no effect on this parameter. It can thus be concluded that nitroglycerin does in fact reduce CF in experimental myocardial infarction.

To judge from the observations of Kaverina et al. [2], a combination of nitroglycerin with indirect sympathomimetic measures also gives rise to a partial blockage of β-adrenergic structures. This effect may perhaps be dominant in the acute phase of infarction and may be responsible for the development of bradycardia under the influence of nitroglycerin.

A comparative study of the size of the myocardial infarct 7 days after the operation showed a significant difference in the area of necrosis: In the treated group the size of the lesion was 40% less than in the control group ($P < 0.01$).

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

LITERATURE CITED

1. N. I. Afonskaya, N. M. Cherpachenko, and V. S. Zhdanov, Kardiologiya, No. 1, 103 (1979).
2. N. V. Kaverina and V. B. Chemburidze, Pharmacol. Ther., 4, 109 (1979).
3. E. I. Chazov, Ter. Arkh., No. 4, 3 (1974).
4. J. Abrams, Patient Care, 9, 95 (1975).
5. C. M. Bloor and F. C. White, Am. J. Cardiol., 31, 121 (1973).
6. E. Braunwald and P. R. Maroko, Circulation, 50, 206 (1974).
7. W. D. Bussmann, T. Bartmann, E. Berghof, et al., Circulation, 55-56, Suppl. 3, 111 (1977).
8. P. C. Come and B. Pitt, Circulation, 54, 624 (1976).
9. G. J. Jesmok, D. C. Warltier, G. J. Cross, et al., Basic Res. Cardiol., 73, 559 (1978).
10. B. Jugdutt, G. Hutching, B. H. Bulkley, et al., Circulation, 58, Suppl. 2, 11 (1978).
11. R. C. Leinbach, H. K. Gold, M. J. Buckley, et al., Circulation, 48, Suppl. 4, pp. IV-100 (1973).
12. P. R. Maroko, R. Libby, C. M. Bloor, et al., Circulation, 46, 430 (1972).
13. A. G. Roberts, P. R. Cirpiano, and D. R. Alonso, Circulation, 57, 35 (1978).
14. J. A. Spath, D. L. Lane, and A. M. Lefer, Am. J. Cardiol., 33, 171 (1974).
15. T. Fukuyama and R. Roberts, Circulation, 48, Suppl. 4, pp. IV-100 (1973).