TOPOLOGY OF DNA SYNTHESIS IN THE LEFT VENTRICULAR WALL DURING REPAIR OF THE HEART AFTER MYOCARDIAL INFARCTION

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KEY WORDS: myocardial infarct; repair processes; DNA synthesis

An important role in the outcome of myocardial infarction (MI) is played by the speed of resuscitation processes [3]. Their intensity rises as the disease develops, and this is reflected in activation of DNA synthesis in the heart [4, 5].

The aim of this investigation was to study the distribution of DNA synthesis in different parts of the heart wall after infarction.

EXPERIMENTAL METHOD

Experiments were carried out on 18 adult mongrel dogs weighing 6-18 kg. A model of MI was created under anesthesia by ligation of the anterior interventricular artery at two places along its length. The animals were taken from the experiment under intravenous thiopental anesthesia 1, 2, 4, 7, 10, and 15 days after the operation. DNA synthesis in tissue in the central, intermediate, and peripheral areas of the zone of infarction (ZI), the peri-infarct zone, and the intact myocardium was studied with the aid of ^{3}H-thymidine by the method in [1]. Activity of DNA synthesis was judged from the intensity of β-decay in cpm, measured on a "Beta-I" radioimmunoassay instrument. Activity of the ^{3}H-thymidine was 1 mCi. The error of the measurements did not exceed ±1%. Indices of synthetic activity in different parts of the heart wall during the development of MI were normalized relative to values established on the first day of the experiments. The arithmetic mean, its standard deviation, the error of the mean, and values of coefficients of correlation for the measured values of β-decay per minute in different parts of the heart wall were calculated on the "Iskra-226" computer.

EXPERIMENTAL RESULTS

Under normal conditions synthetic activity in the left ventricular myocardium, as shown by levels of β-decay was 2326 ± 381 cpm. The normal level is shown in Figs. 1 and 2 by oblique shading and it reflects the ratio of these values of DNA synthesis to that established on the first day of the experiment.

During repair of the myocardial infarct after an initial fall on the first day the intensity of synthesis increased in all areas of the heart wall, to reach peak values by the 7th day of the experiment (Figs. 1 and 2). It then began to fall, and by the 15th day it reached values characteristic of the initial level. Although the picture was qualitatively similar, the quantitative laws of the dynamics of DNA synthesis differed in different areas of the myocardium.

The decrease in the intensity of synthetic processes observed on the first day in different areas of the heart wall was unequal. It was most marked (by 3.2 times) in ZI, and in areas, moreover, which were farthest the site of occlusion, and weakest (by 1.3 times) in the intact myocardium. These data can be explained by the ischemic and necrotic changes developing at this time in the myocardium of ZI [6, 8, 9].

The increase in the values of the index of DNA synthesis was observed earliest of all (at the end of the first day) in the peri-infarct zone. In ZI it was observed 1-3 days later, and even there it was earlier (on the 2nd day) in the peripheral and later (on the 4th day) in the intermediate and central areas of ZI, which must be explained by oriented migration of

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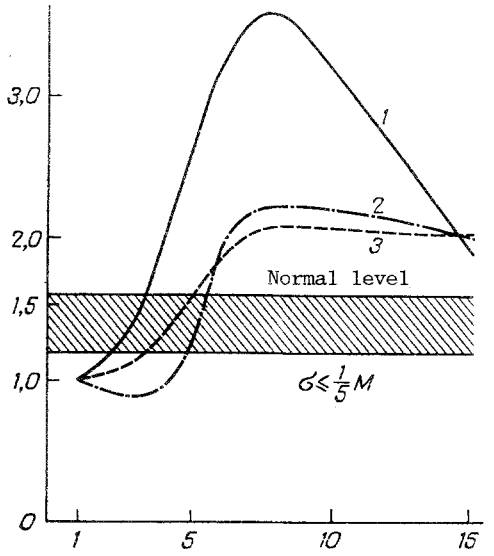

Fig. 1. Activity of DNA synthesis in intact myocardium and peri-infarct zone in experimental MI. Here and in Fig. 2: maximal value of σ indicated here and in Fig. 2 for all times of observation of the animals. Areas of ZI: 1) peripheral; 2) intermediate; 3) central. Abscissa, duration of experiment (in days); ordinate, activity of DNA synthesis (normalized relative to values established on 1st day).

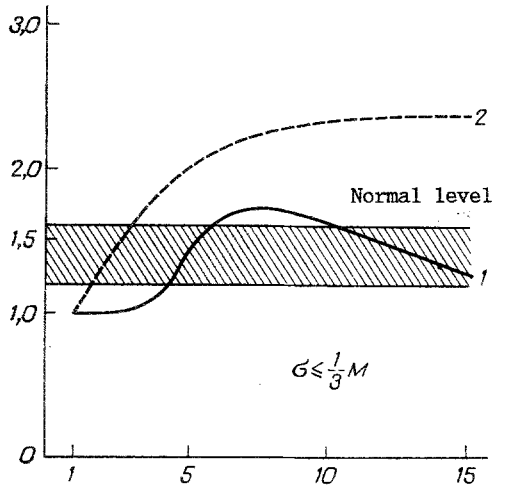

Fig. 2. Activity of DNA synthesis in different regions of ZI in experimental MI. 1) Intact myocardium; 2) peri-infarct zone.

cells forming the proliferative pool for granulation tissue, from the peri-infarct zone [2]. The results are in agreement with data obtained in [4], whose authors found that the first thymidine-labeled nuclei of connective tissue cells in ZI were found on the 3rd day of the experiment.

The high rate and earlier increase in the intensity of synthetic processes at the periphery of ZI ensured that on the 7th day it reached higher values than those in all other areas of ZI. The results can be explained by the greater density of cell forms at the stage of granulation tissue formation along the periphery of ZI [2]. Synthetic processes in different areas of ZI were equalized 2 weeks after experimental MI. According to data described in [8], by this time the formation of young granulation tissue of ZI is basically complete, with transition to scar tissue formation.

Although the beginning of activation of DNA synthesis in ZI was delayed by 1-3 days after that established for synthesis in the peri-infarct zone, nevertheless the two correlated

($r = 0.67$). These findings can be explained by the results of investigations [2, 3] which showed that the formation of the proliferative pool of granulation tissue cells in ZI takes place through the peri-infarct zone. The equalization of the intensities of synthetic processes over the whole area of ZI during the period of maturation of granulation tissue must be noted, for this is evidently one condition for the formation of a structurally perfect post-infarct scar.

The increased activation of DNA synthesis, to reach peak values by the end of the first week, also was observed in the intact myocardium. There, however, it was weaker (by 1.4 times) and shorter in duration (of 3-5 days). Later the intensity of synthetic processes in the intact myocardium fell to the normal level. Correlation between changes in the parameters of DNA synthesis in the intact myocardium and ZI was weak, possibly due to differences in the mechanisms lying at their basis. According to one study [7], processes of intracellular regeneration predominate in the intact myocardium, whereas in ZI the necrotic myocardium is replaced by granulation tissue, going on to scar formation.

Thus the intensity of DNA synthesis falls in the tissues of the left ventricle of the dog's heart at the beginning of development of MI, and the fall is most marked in the central areas of ZI. Later synthesis is activated: earlier in the peri-infarct zone and around the periphery of ZI, and later in the intermediate and central areas of ZI. In the period of maturation of the granulation tissue the intensity of synthetic processes in different areas of ZI falls gradually and is equalized. Activation of DNA synthesis in the intact myocardium toward the end of the first week was less marked and shorter in duration, and was followed ultimately by restoration of the initial levels.

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