COLLATERAL BLOOD CIRCULATION WITH AN ISOLATED LIGATURE OF THE FRONTAL DESCENDING BRANCH OF THE LEFT CORONARY ARTERY AND IN CONJUNCTION WITH STIMULATION OF THE PERIPHERAL SECTION OF THE VAGUS NERVE

EXPERIMENTAL INVESTIGATION IN DOGS

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(Received June 10, 1955. Presented by Acting Member of the Acad. Med. Sci. USSR Prof. V. N. Chernigovsky).

Many experiments by native and foreign investigators show that after ligature of the frontal descending branch of the left coronary artery, in the overwhelming majority of cases there occurs infarct of the myocardium, healed by means of a scar. It is obvious that such an outcome is the result of the insufficiency of collateral blood circulation. However, sometimes under certain conditions, scars do not form. On the basis of our material, we were convinced that scars are not formed if after ligaturing the artery, there appears widespread fusion of the pericardium with the front wall of the left ventricle and left auricle. On histological examination, in place of the scar normally formed, we found muscular tissue, which, it is true, differed somewhat from the normal myocardium, showing weaker color and increased connective tissue.

Thus, apparently, the possibility of preventing infarcts depends on better blood circulation of the ischemic region at the expense of the collaterals forming at the joinings.

Prinzmetal and Bergmann investigated the collateral blood circulation directly after ligature of the descending branch of the left coronary artery in dogs on a beating heart, by introducing radioactive erythrocytes, and came to the conclusion that in the dogs with a ligatured artery, constant active blood circulation occurs. In order to establish the sources of the collateral blood circulation after ligature of the artery, fluorescin was injected into the femoral vein in dogs, and it was detected in the ischemic region. The authors came to the conclusion that the collateral blood circulation in the ischemic region is accomplished through the inter-arterial anastomoses.

Tennant, Grayzel, Sutherland, Stringer et al. [8] observed the histological changes with ligature of the frontal descending branch of the left coronary artery, as established by them in relation to the post-operative period. These changes can be divided into two groups: in the first group, investigated for 24 hours after the ligature, processes of necrosis and exudation predominate; in the second, investigated at later periods, reparative processes predominate. There is no doubt that after ligature of the artery, the reparative processes include the development of re-formed vessels. However, the dynamic of their development has so far been little investigated. Thus, Mallory and White [9] found that growth of re-formed capillaries can be seen, starting from the 4th day. Apart from this paper and the investigations of Donald and Essex, we have not been able to find literature on the question; consequently, we ourselves traced this process in dogs on which we operated.

EXPERIMENTAL METHODS

After ligating the frontal descending branch of the left coronary artery, the dogs were killed at various times after the operation. Their hearts were investigated by means of radiography, after first pouring contrast medium into the vessels, and by study of the histological preparations.

Ligature of the artery was always accomplished at one level, just above the division of the descending branch at the topmost branch, and the branch to the right ventricle.

EXPERIMENTAL RESULTS

After pouring contrast medium into the coronary vessels of the dogs after operation, we ensured that the distal end of the ligated artery was filled with the medium introduced in the left-bending or in the right coronary artery. This indicated the existence of collateral blood circulation through the inter-system or internal-system collaterals.

Fig. 1. Hemorrhagic infarct in region of apex of heart after ligature of artery and stimulation of peripheral segment of vagus nerve, two days after operation.

Fig. 2. Extravasates after ligature of artery and subsequent stimulation of peripheral segment of vagus nerve.

On investigation of the histological preparations, foci of necrobiosis were found in the first 24 hours after ligaturing the artery. The proliferation of the connective tissue elements was well pronounced, even on the third day. It was possible to observe both amitotic division of the cells and mitosis. The reaction on the part of the myocardium was expressed in an enlargement of the size of the nuclei of the muscular cells, with the presence of necrobiosis. On the sixth day, we noted differentiation of the cells and re-formation of the capillaries with young epithelial cells, the nuclei of which were porous and succulent. In the myocardium, homogenization and fragmentation of the muscular fibers with continued transverse striations at places were detected in them, and growth of connective tissue in the foci of necrosis. On the ninth day, connective tissue with a small number of arterioles and veins was seen. Apart from large foci of necrosis, the presence of microinfarcts (micromyomalacia, according to Vail). The initial stages of albumin dystrophy of the muscular fibers, preceding necrosis, were expressed in uneven staining and homogenization of the sarcoplasm. In the same preparation, it was possible to see a manifestation of myoblasts — an indication of regeneration of the muscular fibers. The question of the regeneration of the myocardium is still contentious, and up to the present, unsolved.

Fig. 3. Initial stages of albumin dystrophy of muscular fibers 2 hours after ligature of artery and stimulation of peripheral segment of vagus nerve.

On the 12 and 15th day after the operations, we discovered ripe connective tissue, with an abundant quantity of larger cells, the structure of which sometimes prevented identification. Despite the large number of these re-formed vessels, filling of them with contrast medium did not take place. As with the earlier preparations, a considerably larger number of microinfarcts were noted.

Subsequently, we observed growth of ripe connective tissue at the site of the dying muscular fibers, and formation of the scars and re-formation of vessels, the number of which was much higher at the periphery of the scar. It should be noted that the round cell infiltration and presence of erythrocytes among the muscular fibers did not disappear even 45 days after ligaturing of the artery.

It is clear from what has been described that degeneration of the myocardium occurred before the development of the collateral blood circulation.

The essential factor in the restoration of the collateral blood circulation is an adequate level of blood pressure. With ligature of the artery in its distal section, blood pressure falls, promoting a retrograde blood flow. However, as the experiments of Ekshtein et al. showed, the retrograde flow of blood is almost constant within limits of 0.5 to 5.8 cc a minute, and then together with the peripheral diastolic pressure, grows very slowly, being dependent on the increase in the difference of pressure; contributing to the opening of the collaterals.

Proceeding from the findings of A. I. Smirnov [4] on the favorable effect of tonic influences of the vagus nerve on the cardiac muscle in pathological conditions, it could be assumed that stimulation of the peripheral segment of the vagus, imitating to a certain degree the tonic excitation of its center, and leading to strengthening of the cardiac contractions, should contribute to the creation of more favorable conditions for collateral blood circulation. Therefore, at the suggestion of A. I. Smirnov, working in his laboratory, we ligatured the descending branch of the left coronary artery in the dogs, with subsequent stimulation of the peripheral segment of the vagus nerve with an induction current. The stimulation took place directly after ligaturing the artery, or 2-3 days after ligature. In all the experiments, stimulation of the peripheral segment of the vagus produced pronounced contractions of the ventricles of the heart.

One dog, in which the peripheral segment of the vagus nerve was stimulated two hours after ligaturing the artery, died 27 minutes after the start of stimulation. The other dogs were killed on the second and third days after the operation.

The changes on the part of the heart of these dogs were glaringly apparent. The heart was almost spherical, the coronary vessels were greatly enlarged. Heavy hemorrhage just below the ligature was found in a dog which died 2 1/2 hours after the operation. Macroscopically, visible hemorrhagic infarcts were found in the dogs on the second and third day after operation, a phenomenon which had not been observed in the cases with an isolated ligature (Fig. 1).

Upon infusion of the heart of the given series with the medium, we noted an increase in the amount of the infused medium, and its free penetration in the cavity of the ventricles (particularly the left one), which suggested enlargement of Viensens-Thebesian vessels. On the roentgenograms of the heart, we found extensive extravasates, which had not been seen in dogs not subjected to stimulation of the vagus (Fig. 2). The presence of extravasates shows the easy permeability of the vascular wall. Initial stages of albumin dystrophy of the muscular fibers preceding necrosis and expressed in uneven staining of the sarcoplasm, were found in dogs which died 2 1/2 hours after ligaturing the artery (Fig. 3). Special attention was aroused by marked disturbance of blood circulation

in the whole of the myocardium, which grew and reached the maximum on the second and third days. The marked edema hindered proliferation of the connective tissue elements, and re-formation of the capillaries. The vessels of the myocardium were very enlarged, overfilled with blood, and stasis and formation of thrombi were observed. The myocardium was flooded with erythrocytes as a result of diapedesis or rupture of the capillaries. In the dogs in which stimulation of the peripheral segment of the vagus nerve was carried out 2 or 3 days after ligaturing of the artery, signs of degeneration of the sympathetic fibers were seen in the form of an increase in the number of nuclei in the wall of the artery and Schwann cells of the nervous trunk.

Apart from these experiments, we investigated the heart in dogs which, after ligaturing the frontal descending branch of the left coronary artery in the post-operative period, were injected with mesotan intravenously (injected by N. G. Polyakov). The results of radiography and histological examination showed that the effect of mesotan was similar to that which we observed upon stimulation of the peripheral segment of the vagus nerve, since mesotan raised the tonus of the center of the vagus. In the control experiments conducted by N. G. Polyakov in the laboratory of Prof. A. I. Smirnov, it was shown that after ligaturing both vagus nerves, introduction of mesotan did not produce intensification of the cardiac contractions. Mesotan exerted an adrenal-like effect on the center of the vagus nerve.

On the basis of the experiments conducted, one can say that stimulation of the peripheral segment of the vagus nerve, which to a certain degree imitates an increase in the tonus of the center of the vagus nerve when the artery is ligatured, leads to a serious disturbance of blood circulation, exerts an unfavorable effect on formation of collateral blood circulation It seems that stimulation of the peripheral segment of the vagus nerve in the condition of the arterial ligature produces a disparity between the functional load of the heart (intensification of contraction) and its blood supply.

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