THE INFLUENCE OF THE EXTRACARDIAC NERVOUS SYSTEM ON THE FUNCTIONAL STATE OF THE HEART IN EXPERIMENTAL MYOCARDIAL INFARCTION

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Some workers consider the leading factor in the etiology of myocardial infarction to be a functional disturbance of the coronary circulation, others – atheromatous changes in the vessels of the heart. In recent years these factors have come to be regarded as complementary to each other, and in addition the factor of the functional load has aroused increasing interest.

In 1953, for instance, in acute experiments on dogs with experimentally induced myocardial infarction, we showed that if the contractions of the heart were greatly intensified, myocardial infarction developed significantly more quickly and was more extensive than after ligation of the descending branch of the left coronary artery alone. Intensification of the contractions of the heart was produced by prolonged stimulation of the peripheral section of the vagus nerve with an electric current or by increasing the tonus of the vagus nerve center by the intravenous injection of adrenalin on a background of the action of morphine [6, 7, 8, 9].

From these experiments it can be seen that the discrepancy arising between the strength of the cardiac contractions and the coronary blood supply during coronary insufficiency may lead to the development of a myocardial infarct or may considerably aggravate the course of an already existing infarct.

Our findings were subsequently confirmed in work by A. I. Strukov and S. A. Vinogradov [2, 10].

The hypothesis of the discrepancy between the strength of the contractions of the heart and the blood supply to the myocardium as the cause of production of a myocardial infarct in man was first put forward by F. A. Andreev [1]. Recently clinicians have attached ever increasing importance to the functional load in the development of a myocardial infarct not only in coronary insufficiency but also in healthy young persons during excessive physical effort [11].

In the study of the pathogenesis of the myocardial infarct in our laboratory, as in the case of other workers, it was observed that in the process of development of the infarct itself and in its outcome, the state of the collateral coronary circulation and of the intima of the coronary vessels has great significances. Where there is a well developed collateral system ligation of the descending branch of the left coronary artery in dogs does not lead to extensive infarction [5].

It was shown by experiments of long duration on dogs in our laboratory that after ligation of the descending branch of the left coronary artery, severe polytopic ventricular extrasystole, which appear without compensatory pauses, arise during the first few days after operation. As the researches of A. I. Smirnov, A. I. Shumilina and O. V. Ul'ianov showed, extrasystole is closely connected with the influence of the vagus nerve on the heart [7]. This provided us with a basis for a more detailed study of the functional condition of the tonus of the vagus nerve center and of its influence on the heart during experimental myocardial infarction.

TABLE

Changes in the Cardiac Activity During Experimental Myocaridal Infarction

Name of dog	Date of observation / Indices of cardiac activity / Experimental conditions	Control experiment		Operation		Day after operation																	
						2 nd		3 rd		4th		5th		6th		7 th		8th		9th			
		13/VI 1957		17/VI 1957		18/VI 1957		19/VI 1957		20/VI 1957		21/VI 1957 r.		22/VI 1957				24/VI 1957			
		pulse rate	presence of extra-systoles	pulse rate	presence of extra-systoles	pulse rate	presence of extra-systoles	pulse rate	presence of extra-systoles	pulse rate	presence of extra-systoles	pulse rate	presence of extra-systoles	pulse rate	presence of extra-systoles	pulse rate	presence of extra-systoles	pulse rate	presence of extra-systoles	pulse rate	presence of extra-systoles		
Usach	Initial findings	120	Absent	—	—	120—140	Present	130—140	Present	130—140	Absent	110	Absent	100	Absent	—	—	96	Absent	—	—		
	After injection of morphine	56	»	—	—	—	—	130—140	Respiratory arrhythmia	130—140	Present	90	Present	66	»	—	—	78	»	—	—		
	After injection of $CaCl_2$	34	»	—	—	—	—	130—140	The same	140—150	»	74	»	56	»	—	—	50	»	—	—		
	Date of observation	4/IV 1957		8/IV 1957		9/IV 1957		10/IV 1957		11/IV 1957		12/IV 1957		13/IV 1957						16/IV 1957	
Dzhul'-bars	Initial findings	90	Absent	110	Absent	120—130	Present	112	Present	100	Present	110	Absent	96	Absent	—	—	—	—	110	Absent		
	After injection of morphine	50	»	44	»	—	—	130	»	88	»	76	Present	54	»	—	—	—	—	90	»		
	After injection of $CaCl_2$	36	»	—	—	—	—	140	»	74	»	68	»	42	»	—	—	—	—	68	»		
	Date of observation	28/II 1957		5/III 1957				7/III 1957		8/III 1957		9/III 1957				11/III 1957		12/III 1957			
Sultan	Initial findings	90	Absent	—	—	—	—	140	Present	130	Present	140	Present	—	—	130	Absent	100	Absent	—	—		
	After injection of morphine	70	»	—	—	—	—	140	»	130	»	120	»	—	—	110	»	90	»	—	—		
	After injection of $CaCl_2$	50	»	—	—	—	—	140	»	130	»	100	»	—		60	»	72		—	—		

The tonus of the vagus nerve center may be increased by injection of morphine. It is intensified still more if, in addition to the effect of morphine, calcium chloride or adrenalin [3, 4] are injected intravenously. We made use of these findings in our experiments.

EXPERIMENTAL METHOD

The experiments were carried out on 15 adult dogs, on which the operation of ligation of the descending branch of the left coronary artery was performed.

The operations were carried out under sterile conditions, under morphine-urethane or morphine-evipan anesthesia. After preparation of the field of operation with iodine solution an incision 10 cm long was made between the fourth and fifth left ribs. As a preliminary measure the dog was changed over to artificial respiration. After the pleural cavity had been opened, the ribs were displaced with retractors, the pericardium opened and ligation of the descending branch of the left coronary artery performed. The pericardium was then partially excised and the wound closed in layers. In order to prevent postoperative complications penicillin was injected intramuscularly during the first few days after the operation.

The development of an infarct of the myocardium as a result of this procedure was confirmed electrocardiographically, and later by morphological examination.

When 24 hours had elapsed after the operation, an increase in the tonus of the vagus nerve center was produced in each experimental dog every day for 1-1½ weeks by the injection of morphine and calcium chloride. Morphine was injected subcutaneously in a dose of 1-5 ml of a 1% solution, depending on the weight of the animal. Calcium chloride was injected intravenoulsy in a dose of 0.05 g per 1 kg body weight of the animal.

In control experiments on the same dogs before operation, an increase in the tonus of the vagus nerve center was produced in an identical manner.

In certain cases acute experiments were performed on the 3rd-4th day after operation in which, under morphine-urethane or morphine-evipan anesthesia, both vagus nerves were divided and their peripheral ends then stimulated with an electric current. Morphine was injected in a dose of 1 ml of a 1% solution per 1 kg body weight of the animal, and evipan was injected intraperitoneally or intravenously in the form of a 10% solution before the onset of anesthesia.

In individual experiments a 0.25% solution of novocain was injected into the trunk of the vagus nerve and atropine was injected subcutaneously in a dose of 1-2 ml of a 1 : 1000 solution.

In all the experiments the electrocardiogram was recorded, the rate of the cardiac contractions was measured, and during the actute experiments the arterial pressure was registered with a mercury manometer. Stimulation of the peripheral end of the vagus nerve was carried out by means of a Dubois-Raymond induction apparatus.

Altogether 10 control, 12 acute and 47 chronic experiments were performed.

EXPERIMENTAL RESULTS

The changes obtained by the influence of tonic impulses from the vagus nerve center during experimental myocardial infarction in dogs are illustrated in the Table and by kymograms and electrocardiograms of typical examples.

The investigations carried out showed that in all the control experiments the intravenous injection of calcium chloride, when superimposed on the effect of morphine, or prolonged stimulation of the peripheral portion of the vagus nerve with an electric current leads to a significant slowing of the rate and strengthening of the contractions of the ventricles of the heart (see Table and Fig. 1).

On the development of experimental myocardial infarction in the dogs, after 18-24 hours there appear polytopic ventricular extrasystoles of varying intensity, without compensatory pauses, and these gradually disappear on the 5th-6th day after operation (see Table and Fig. 2).

As already shown in our laboratory, extrasystoles appear only in case of development of experimental myocardial infarction. If the ligation of the descending branch of the left coronary artery did not result in the formation of a myocardial infarct, extrasytoles were absent.

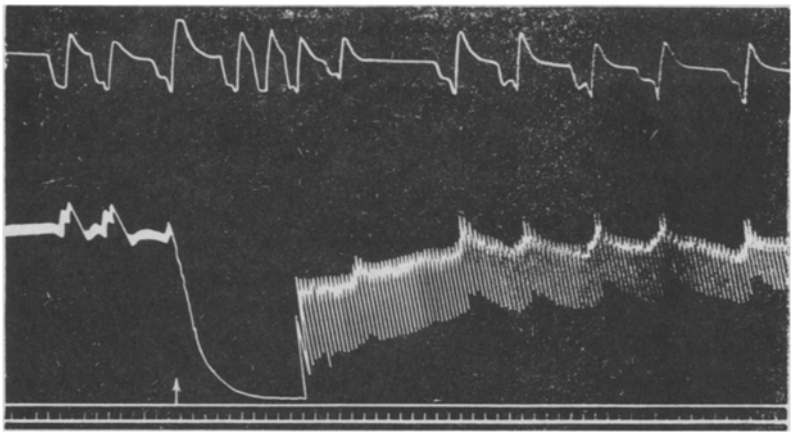

Fig. 1. Stimulation of the peripheral portion of the vagus nerve in a dog under morphine-evipan anesthesia before ligation of the descending branch of the left coronary artery. Significance of the curves (from above downwards): respiration, arterial pressure in the femoral artery, stimulation marker, time marker, which is also the zero line.

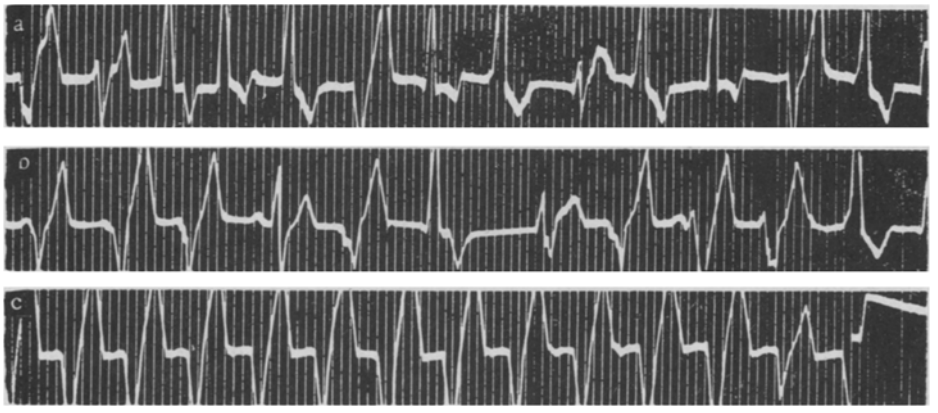

Fig. 2. Extrasystoles in the dog Sultan, lead II, experiment dated March 7, 1957. a) Polytopic ventricular extrasystoles on the 2nd day after ligation of the descending branch of the left coronary artery; b) electrocardiogram 10 minutes after intravenous injection of calcium chloride superimposed on the effect of morphine. The number of extrasystoles of the left ventricle is increased; c) electrocardiogram 30 minutes after the injection of calcium chloride superimposed on the effect of morphine.

After operation, increase of the tonus of the vagus nerve center by the intravenous injection of calcium chloride, superimposed on the effect of morphia, led to intensification of the existing extrasystoles for the first 5-6 days, without any slowing or strengthening action on the heart.

After the injection of calcium chloride the polytopic extrasystoles gradually changed into extrasystoles of the left ventricle (see Fig. 2).

After division of both vagus nerves, in more than 50% of cases the extrasystoles disappeared. In those cases where they continued, a considerable reduction in their number was observed. After vagotomy, stimulation of the peripheral portion of the vagus nerve with an electric current always led to the appearance of extrasystoles or to the sharp intensification of existing extrasystoles of the same type as before the vagotomy, and under these circumstances they lasted for the whole period of action of the electric current on the nerve [6] (Fig. 3). If after

division of both vagus nerves the extrasystoles disappeared, stimulation of the ansa of Vieussens did not cause them to appear, whereas in the same experiment subsequent stimulation of the peripheral portion of the vagus nerve led to reappearance of the extrsystoles. This was shown by O. V. Ul'ianova in our laboratory.

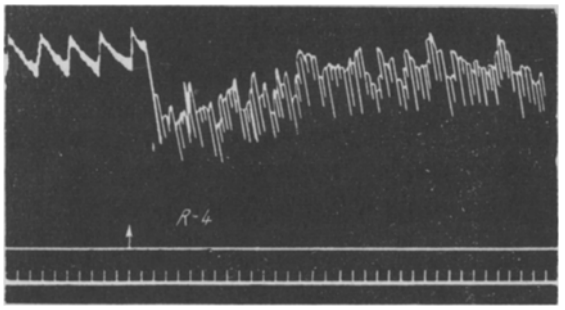

Fig. 3. Stimulation of the peripheral portion of the vagus nerve in a vagotomized dog on the third day after ligation of the descending branch of the left coronary artery. Polytopic ventricular extrasystoles.
Significance of the curves (from above downwards): arterial pressure in the femoral artery, stimulation marker, time marker, which is also the zero line.

The extrasystoles were intensified during mechanical stimulation of the vagus nerve by means of injection of 2-3 ml of physiological saline into its trunk, and they disappeared after injection in a similar manner of 3-4 ml of a 0.25% solution of novocain.

Subcutaneous injection of 1-2 ml of a 0.1% solution of atropine did not abolish the extrasystoles.

Restoration of the usual influence of the vagus nerve, in the form of slowing of the rate and strengthening of the contractions of the heart, was noticeable on the 5th-6th day (see Table). The slowing down of the rhythm and strengthening of the contractions of the heart took place both after intravenous injection of calcium chloride in association with the action of small doses of morphine, and during prolonged stimulation of the peripheral section of the vagus nerve with an electric current.

In none of our experiments did the extrasystoles, intensified by raising the tonus of the vagus nerve center or by stimulation of the peripheral section of the vagus nerve, lead to the development of ventricular fibrillation in the heart.

As already shown by research in our laboratory, the appearance of extrasystoles is characteristic of experimental myocardial infarction. In the development of such extrasystoles an important part is played by impulses coming from the vagus nerve center. This is also confirmed by our present investigation. The findings mentioned above show that during the first few days after the development of experimental myocardial infarction, the influence of the vagus nerve on the heart is shown not by slowing of the rate and strengthening of the contractions of the heart but by the appearance of ventricular extrasystoles, which may be in consequence of the change in the functional condition of the heart during infarction.

After 5-6 days, when the initial organization of the myocardial infarct takes place, the functional stage of the heart gradually returns to its original, and concurrently with the gradual disappearance of the extrasystoles the usual action of the vagus nerve is restored, in the form of slowing of the rhythm and strengthening of the contractions of the heart.

It may be mentioned that the extrasystoles which we observed, which were mainly due to tonic impulses from the vagus nerve center, did not significantly complicate the activity of the heart, since they rapidly passed off (on the 5th-6th day) and in our experiments on dogs they never led to ventricular fibrillation.

The results obtained indicate yet again that in the study of the pathogenesis of myocardial infarction it is essential to take into consideration both the functional condition of the heart and also the influence exerted on it by the extracardiac nervous system.

SUMMARY

Experiments were performed on 15 dogs in acute and chronic experiments. Myocardial infarction was induced by the ligature of the descending branch of the left coronary artery. To raise the tone of the vagus intravenous injections of calcium chloride were given on the background of morphine action before and after the operation. ECG readings were taken, the blood pressure measured and the number of cardiac contractions and respirations recorded.

Experiments demonstrated that increased tone of the vagus nerve center during the first 4-5 days after the

induction of the experimental myocardial infarction does not result in the decrease of the rhythm of intensification of the cardiac contractions. However, it intensifies the extra systoles of the cardiac ventricles. The inhibiting effect of the vagus nerve on the heart is reestabished on the 4th-25th day after the operation which coincides with the disappearance of the extrasystole.

The above-mentioned changes in the action of the vagus nerve on the heart depend to a great extent on the changes in the functional condition of the heart as a result of myocardial infarction. An explanation of the genesis of extrasystoles in human myocardial infarction may be sought in these data.

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