CORONARY INSUFFICIENCY AND NECROSES OF THE MYOCARDIUM INDUCED IN CATS BY INJECTION OF POTASSIUM CHLORIDE INTO THE LATERAL VENTRICLES OF THE BRAIN

(UDC 616.132.2-008.64+616.127-002.4]-02:615.732.21-032:611.813.8)

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(Presented by Active Member AMN SSSR V. V. Zakusov)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 61, No. 1, pp. 37-40, January, 1966
Original article submitted December 14, 1964

Disorders of the nervous regulation of the coronary circulation are known to be of great importance in the pathogenesis of angina pectoris and myocardial infarction. Many workers have therefore attempted to produce an experimental model of coronary insufficiency of neurogenic nature. Reflex influences [2, 6] and direct action on the central nervous system [7, 9, 11, 13] have been used for this purpose. However, in most of these studies, the state of the blood supply to the heart itself has been estimated entirely on the basis of electrocardiographic findings. In such investigations, however, it is most important to use a combination of methods for making this assessment.

In this paper the authors discuss a new experimental model of acute coronary insufficiency produced by the action of potassium chloride on the central nervous system.

EXPERIMENTAL METHOD

Altogether 90 acute and chronic experiments were performed. The acute experiments were carried out on cats weighing 3-4 kg, anesthetized with chloralose (40 mg/kg) and urethane (600 mg/kg). The body temperature and respiration of the animals were maintained artificially.

Potassium chloride (0.5 ml of an M/4 solution) was injected into the lateral ventricles by means of a stainless steel cannula, using the method described by Feldberg and Sherwood [10].

To judge the state of the circulation of blood in the heart several methods were used. The index of the blood supply to the myocardium and of its energy metabolism was the volume velocity of the coronary blood flow and the oxygen consumption of the heart [4, 5]. In a separate series of experiments the tone of the coronary vessels was recorded by the method of resistography [3] and the arterial pressure and ECG were also recorded. To determine the mechanisms leading to constriction of the coronary vessels, the sympathetic nerve supply to the heart was interrupted and bilateral vagotomy performed in the neck. Atropine (1 mg/kg) and dihydroergotoxin (1 mg/kg) were used for the same purpose. In a special series of experiments the electrical activity of the inferior cardiac nerve was recorded.

The chronic experiments began 24 h after introduction of the cannula into the lateral ventricle of the brain by the technique described above. In the unanesthetized animals recordings were made of the ECG in three standard leads, and also of the autonomic and behavioral reactions. After 24 or 48 h the animals' hearts were removed for histological investigation.

EXPERIMENTAL RESULTS

Injection of potassium chloride into the lateral ventricles rapidly caused tachycardia in the animals, together with marked hypertension (220-240 mm Hg). After 1.0-1.5 min changes characteristic of acute coronary insufficiency developed in the ECG (negative T wave, displacement of the S-T interval from the isoelectric line) and the

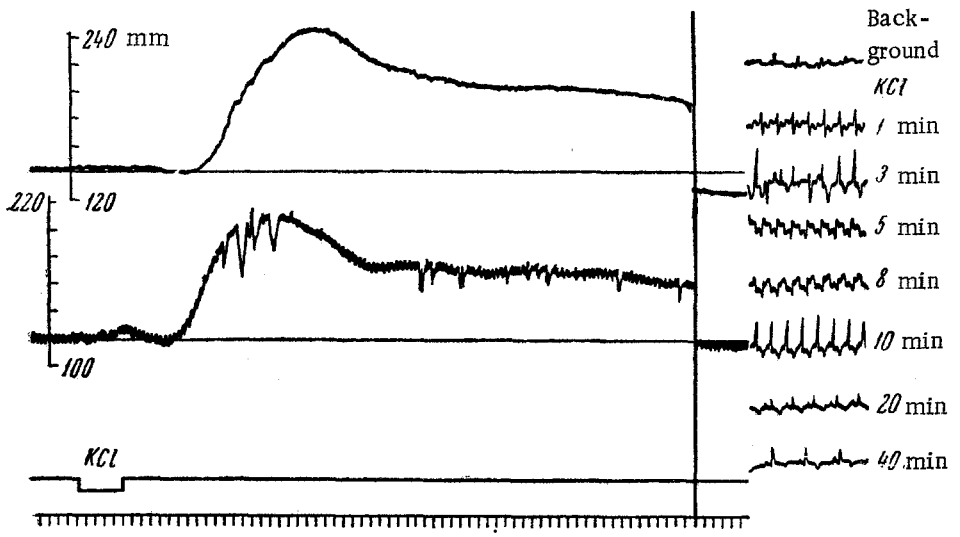

Fig. 1. Effect of potassium chloride injected into the lateral ventricles on the tone of the coronary vessels, the arterial pressure, and the ECG. From top to bottom: resistance of coronary vessels, arterial pressure, marker of injection of potassium chloride, time marker (5 sec). On the right: ECG in standard lead II, before and after injection of potassium chloride.

cardiac rhythm was disturbed (monophasic rhythms, sinus and ventricular extrasystoles, etc.). The changes in the ECG persisted at a high level for 40-50 min, and the normal ECG pattern was never fully restored.

Besides the "ischemic" changes in the ECG, potassium chloride caused an increase in the volume velocity of the coronary blood flow and a considerable increase in the uptake of oxygen by the heart. This effect was observed parallel with the increase in arterial pressure. Hence, the developing insufficiency of the coronary circulation was to some extent compensated hemodynamically. However, this compensation was evidently inadequate to satisfy the growing demands of the myocardium for oxygen, as was clearly demonstrated by the ischemic changes in the ECG. The volume velocity of the coronary blood flow is known to reflect changes in many of the factors taking part in the regulation of the blood supply to the heart. In the subsequent investigations the method of resistography was therefore used additionally for the purpose of analysis.

The results of these experiments showed that besides causing the arterial pressure to rise to a marked degree, potassium chloride produced a considerable increase in the resistance of the coronary vessels. In 22 experiments the tone of the vessels of the heart rose on the average by 41 ± 3.4% from the original level. As during recording of the arterial pressure, biphasic changes were observed in the tone of the coronary arteries. The second, depressor phase coincided in time with the development of hypotension. It is interesting that the changes in the ECG developed parallel with the increase in the tone of the coronary vessels and became less intensive when the pressure in the coronary arteries was lowered (Fig. 1).

Preliminary cervical vagotomy and atropinization of the animals did not prevent the increase in the tone of the coronary vessels and the disturbances in the ECG. On the contrary, when the sympathetic nerve supply to the heart was first interrupted, the tone of the coronary vessels rose by only 6.6 ± 1.4%, whereas in the control experiments spasm of the coronary vessels attained 41 ± 3.4% of the initial level. Sympathectomy and injection of dihydroergotoxin completely prevented the development of the electrocardiographic changes described above. In a special series of experiments in which the efferent impulses in the inferior cardiac nerve were recorded during injection of potassium chloride into the lateral ventricle, a significant strengthening of the tonic activity was observed.

In a series of chronic experiments dynamic observations were made on the development of the symptom-complex including acute coronary insufficiency and the development of autonomic and behavioral reactions by the animals. Immediately after the injection of potassium chloride into the lateral ventricles, the cats developed generalized restlessness and a marked mydriasis. After 1.0-1.5 min, parallel with the appearance of ischemic changes on the ECG (displacement of the S-T interval, inversion of the T wave), the animals gave a long cry and a groan.

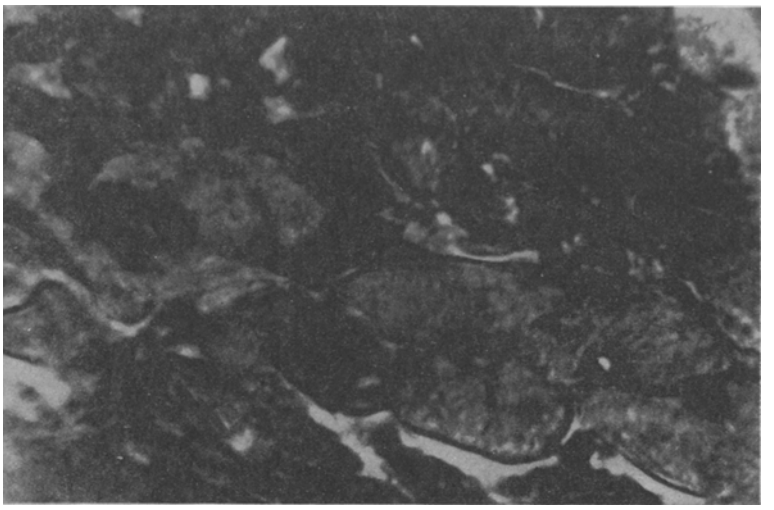

Fig. 2. Necrosis of a group of fibers of the myocardium after injection of potassium chloride into the lateral ventricle. Hematoxylin-eosin. Objective 40, ocular 7.

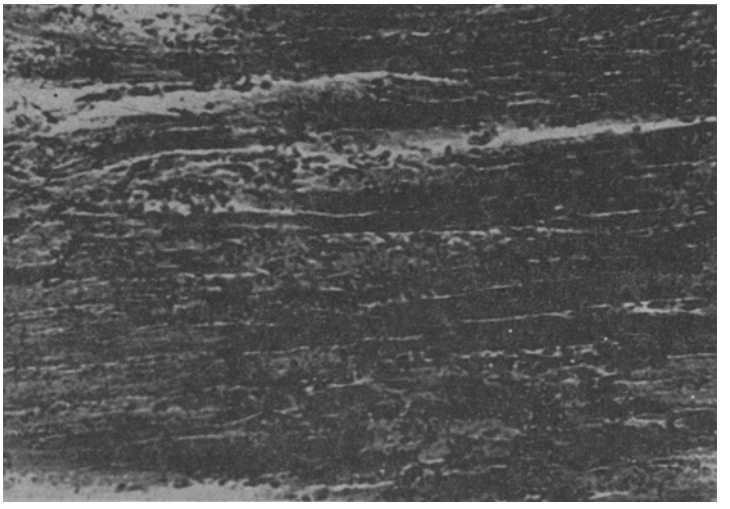

Fig. 3. Degeneration and necrobiosis of the muscle fibers and inflammatory reaction after injection of potassium chloride into the lateral ventricle. Hematoxylin-eosin. Objective 20, ocular 7.

This was followed by motor excitation, aggressiveness, and marked dyspnea. From 20 to 25 min after the injection of potassium chloride began, the animals assumed an enforced lateral position or lay with their limbs flexed. After 24 h some of the animals showed changes in the form of inversion of the T wave in all three standard leads. In the other animals the negative T wave and the deep Q were most marked in one lead; discordant T waves were often seen in leads I and III.

Microscopic examination showed that 24 and 48 h after injection of potassium chloride all the animals developed extensive pathological changes in the myocardium. These changes were characterized by swelling of the muscle fibers, disappearance of the myofibrillary structures, and by the development of a finely granular structure, staining weakly with eosin, of the myoplasm and by karyolysis. Cloudy swelling and fatty degeneration were also widespread in most of the animals, mainly 48 h after injection of the potassium chloride (Figs. 2 and 3).

This experimental investigation showed that the action of potassium chloride and on the central nervous system causes marked activation of the sympathetic nervous system of animals. As a result, the tone of the coronary

vessels is increased. The increase in the coronary blood flow developing parallel to the hypertension does not compensate for the growing oxygen demand of the myocardium, as is clearly demonstrated by the ischemic changes in the ECG. These cardiovascular disturbances are accompanied by focal necrotic and degenerative changes in the myocardium. These changes are evidently based on acute disturbances of the coronary circulation, leading to a discrepancy between the supply of oxygen to the heart and the demand for it. The accumulation of catecholamines in the heart muscle may play an important role in the development of acute coronary insufficiency and myocardial necrosis of neurogenic origin [1, 8, 12].

SUMMARY

An experimental model has been produced of acute coronary failure in response to potassium chloride injection into the lateral ventricle of the cat brain. It was found that under these conditions potassium chloride activates the sympathetic nervous system, causes a spasm of the coronary vessels, an increase in the oxygen requirements of the blood, and ischemic changes in the electrocardiogram. The above disturbances end in focal necrotic and dystrophic lesions of the myocardium.

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