REGULATION OF DISORDERED RHYTHM OF THE HEART BY MEANS OF PROCAINE BLOCK OF EXTRACARDIAL NERVOUS FORMATIONS, AND OF OTHER AGENTS AFFECTING THE NERVOUS SYSTEM

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Numerous workers, both clinicians and physiologists, have remarked on the dependence of qualitative alterations in heart rhythm in disorders of the heart on nervous stimuli. The experiments of E. E. Epshtein [9], from V. N. Chernigovsky's laboratory, are of special interest; these experiments showed that very profound alterations in cardiac rhythm may result from stimulation of alimentary tract interoceptors, when the heart is under the action of calcium chloride.

The present paper deals with an investigation of the possibility of restoring normal rhythm in a number of types of cardiac arrhythmia, by means of factors affecting the nervous system. It should be noted that in different disorders of heart rhythm the effect of one and the same factor depends very largely on the nature of the arrhythmia, and on the actual mechanism of the process leading to its development.

We have shown in an earlier paper [7] that in strophanthin poisoning the same reflex reaction which favorably affects atrioventricular conductivity and raises myocardial excitability does not act in the same way in different types of arrhythmia. This reflex reaction totally abolishes all disturbances of atrioventricular conductivity in atrioventricular block of the second degree, but it aggravates arrhythmia in some cases of heterotopic rhythm.

The dependence of the effect of interference with nervous mechanisms on the nature of the given cardiac arrhythmia was very clearly shown in our experiments involving interference with extracardial nervous formations.

EXPERIMENTAL METHODS AND RESULTS

Cardiac arrhythmia was produced in experimental animals by administration of toxic doses of strophanthin, and in some cases also by ligature of large blood vessels of the heart (usually the anterior descending coronary artery).

The short experiments were most often performed under morphine-ether-chloroform anesthesia, and some isolated experiments under Barbamyl anesthesia. The dogs were given different intravenous doses of Strophanthin K. In order to bring about the gravest form of arrhythmia—paroxysmal ventricular tachycardia—we injected doses of 0.145 mg strophanthin per kg body weight. This gave rise to the expected effect.

It appeared from our experiments on strophanthin-poisoned dogs subjected to various forms of interference with the vagus nerves that the effect observed varies according to the acuteness of poisoning and with the given stage of development of arrhythmia. With comparatively light degrees of intoxication, with retention of the sinus rhythm of the heart, we observed that stimulation of the vagus nerves caused retardation of the sinus rhythm, impairment of atrioventricular conductivity, amounting in some cases to total block, and appearance of ventricular extrasystoles; ventricular rhythm, which is a feature of strophanthin poisoning, is also observed.

Severing the vagus nerves, or injecting procaine into them, led to a normalization of the heart rhythm, both in atrioventricular block and with heterotopic ventricular rhythm of comparatively low frequency. Exclusion of vagus nerve influences always caused restoration of atrioventricular conductivity in dogs with incomplete atrioventricular block, due to moderate degrees of strophanthin poisoning. We also found that abolition of vagus

effects restored normal heart rhythm in cases of heterotopic ventricular rhythm of 60-120 beats per minute.

Restoration of sinus rhythm was only exceptionally encountered following vagotomy in cases of severe strophanthin poisoning, in which the ventricular rhythm did not, however, exceed 200 beats per minute. With ventricular rates exceeding 200, interruption of vagus connections in no case restored sinus rhythm. Very large doses of strophanthin were given to a group of 20 dogs, 10 of which had previously been subjected to vagotomy, and the remaining 10 were vagotomized when the ensuing arrhythmia was at its height. In no case did preliminary vagotomy prevent the development of severe disturbances of cardiac rhythm: 9 dogs developed extrasystolic ventricular tachycardia (Figure 1), and one dog showed extrasystolic coupling of heart beats.

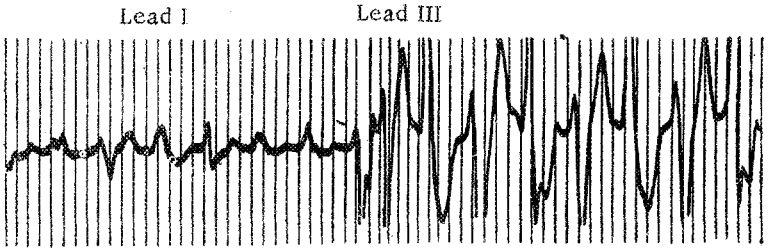

Fig. 1. Polytopic extrasystolic ventricular heart rhythm after administration of strophanthin to previously bilaterally vagotomized dogs; leads I and III.

When vagotomy was performed at the height of development of paroxysmal ventricular tachycardia, with a rate of 190-240 beats per minute, we observed a return to sinus rhythm in only one dog, with a ventricular rhythm of about 200 beats per minute. Restoration of normal rhythm was not observed in the other 9 cases.

Vagus stimulation in the most severe cases of strophanthin poisoning also had no effect on the heart rate. This finding is in full accord with I. P. Pavlov's experimental results; he found that vagal stimulation did not lower the frequency of the heart beat in dogs suffering from acute poisoning with the cardiac glucoside of Convallaria majalis.

It thus appears that in fully developed paroxysmal ventricular tachycardia restoration of normal heart rhythm cannot be achieved either by stimulation or by section of the vagus nerves. Even the most accelerated sinus rhythm possible after vagotomy does not in these cases exceed the ventricular heterotopic beat rate, and the disturbances in conductivity may depend not only on changes in the conducting system of the heart, and on heightened tonus of the vagus nerves, but also on the presence of simultaneously functioning foci of excitation in the auricles and ventricles (we have never, in the course of development of arrhythmia, seen deterioration of atrioventricular conductivity due to ventricular extrasystoles).

It is common clinical practice to apply stimulation of the vagus nerves to cut short attacks of auricular paroxysmal tachycardia [1, 3, 4, 8]. It is generally believed that suppression of the extrasystolic rhythm of ventricular paroxysmal tachycardia by means of vagus stimulation is not possible. We were, however, able to discern a stage in the development of arrhythmia in which stimulation of the vagus nerves causes definite inhibition of ventricular foci of excitation.

Only for an hour after administration of highly toxic doses of strophanthin, when the first signs of depression of the activity of ventricular automatism appear, does vagus stimulation cause change in the heart rhythm, by exerting an inhibitory effect on the foci of heterotopic excitation in the ventricles (more pronounced than in the sinus node).

In particular, we found that stimulation of the peripheral segment of a severed right vagus nerve, using an induction current, caused inhibition of both the heterotopic focus of excitation of ventricular rhythm and the sinus node. A very transient restoration of sinus rhythm was observed after terminating stimulation of the nerve. Stimulation of the left vagus nerve caused suppression of the focus of excitation of heterotopic ventricular rhythm, with retention of auricular sinus rhythm, and full atrioventricular block (Figure 2).

Stimulation of the same nerves at the stage of fully developed arrhythmia was without effect.

We were, however, able to restore normal sinus rhythm at the height of the most acute paroxysm of ventricular tachycardia, by acting on elements of the nervous system. Attempts have been made to treat paroxysmal tachycardia by surgical intervention, applied to the sympathetic nervous system [11].

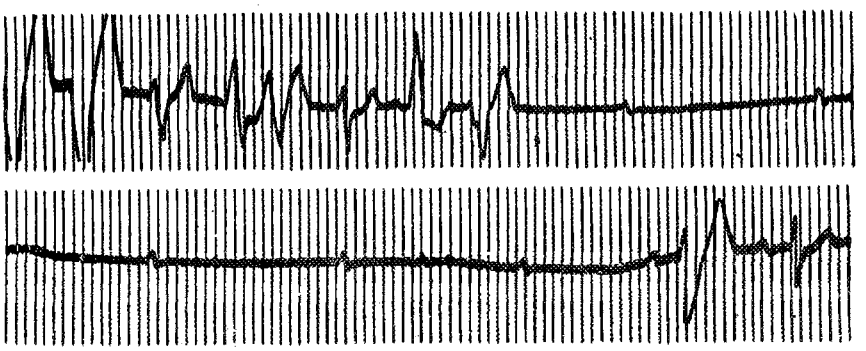

Fig. 2. Suppression of heterotopic ventricular rhythm, with retention of sinoauricular rhythm and full atrioventricular block, during stimulation of the peripheral segment of the severed left vagus nerve.

Of the drugs applied to the treatment of arrhythmias connected with enhanced automatism of the heart, wide use has been made of quinidine, and, more recently (according to the foreign literature), of procaine amide. Some authors [13] relate the effect of intravenous procaine amide to its direct action on the heart, while others believe that it has a sympatholytic action [12]. Procaine amide is not, however, efficaceous in all cases [10].

In view of the successful introduction of procaine block, which has, thanks to the work of A. D. Speransky [5, 6], been widely applied to the treatment of a number of different diseases, and on the basis of the concepts developed by this author, we undertook the study of the effects of procaine block of extracardial nervous formations on cardiac arrhythmias caused by administration of highly toxic doses of strophanthin, or by ligature of major coronary arteries. We performed 4 groups of experiments, in which strophanthin was administered at dosage levels of 0.145 mg per kg body weight.

In the first, control group of experiments we gave strophanthin alone to a group of 6 dogs, without applying any other measures. All the animals developed ventricular paroxysmal tachycardia, the rate of the ventricular rhythm attaining 200-240 beats per minute 20 minutes after the injections.

The second group of 6 dogs received strophanthin at the same dosage levels, after preliminary procaine block of the vagosympathetic trunks and the stellate and upper thoracic sympathetic ganglions. Normal sinus rhythm was found in all cases after administration of strophanthin.

The third group of 12 dogs was given strophanthin at the same dosage levels as before, and paroxysmal ventricular tachycardia was allowed to develop, after which procaine block of extracardial nervous formations was instituted. Sinus rhythm was restored in all cases 5-10 minutes after the block had been established (Figure 3). The sinus rhythm was normal in 10 cases, and in the other two the paroxysms of ventricular tachycardia underwent conversion to sinus rhythm, but disturbances of atrioventricular and intraventricular conductivity persisted for a certain time.

In the fourth group of 6 dogs, intravenous injection of strophanthin was combined with synchronous intramuscular injection of procaine. We observed that intramuscular administration of procaine depresses the activity of heterotopic ventricular foci, reducing the ventricular rhythm from 200-220 to 100-130 beats per minute. Restoration of normal rhythm was not, however, observed in any of the animals of this group.

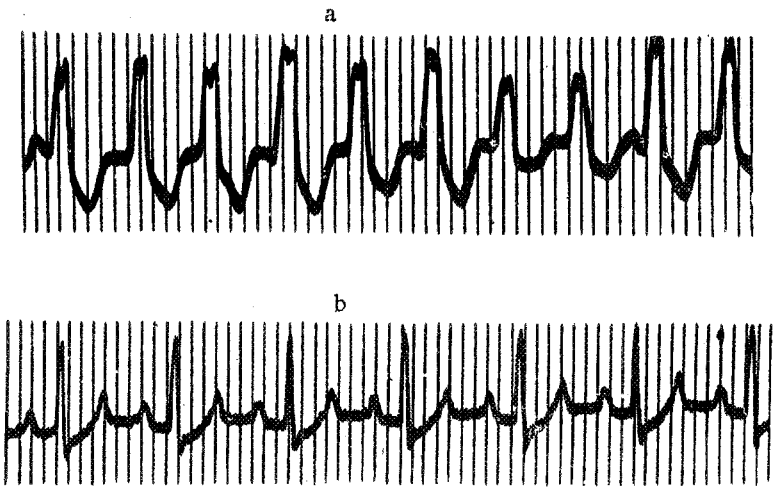

Fig. 3. Restoration of normal heart rhythm following procaine block of extracardial nervous formations.
a) Right ventricular extrasystolic rhythm of the heart following administration of strophanthin; b) sinus rhythm following procaine block of the vagosympathetic trunks and upper thoracic sympathetic ganglions.

Bearing in mind the complexity of the physiological changes taking place in the organism following introduction of considerable amounts of procaine in the vicinity of the vagosympathetic trunks and the upper thoracic sympathetic ganglions, we attempted to act on the sympathetic innervation of the heart in a more selective way, by introducing 2 ml of 2% procaine solution subdurally into the cerebrospinal fluid, at the level of the 2nd thoracic segment. Subsequent injection of highly toxic doses of strophanthin did not give rise to ventricular tachycardia, although conductivity disturbances were observed.

It thus appears that procaine block of the extracardial sympathetic formations and vagus nerves prevents the development of premature beats and of ventricular tachycardia, as well as of disturbances of conductivity. Subdural injection of procaine prevents paroxysmal ventricular tachycardia, but does not avert conductivity disturbances.

We also examined the effect of procaine block of the vagosympathetic trunks and the upper thoracic sympathetic ganglions on extrasystolic ventricular arrhythmia resulting from high ligature of the anterior descending coronary artery. It was found that procaine block of extracardial nervous formations restored normal rhythm (at least for a number of hours) in dogs suffering from impaired coronary circulation, with an extrasystolic heart rhythm of high frequency. This effect was also achieved at those stages of development of extrasystolic ventricular arrhythmia not responding to interruption of vagus nerve impulses alone.

Certain possible side-effects may result from the application of procaine block of extracardial nervous formations. These may appear during the first few minutes after injection of procaine. Rapid injection of procaine into the vicinity of both vagosympathetic trunks and of the stellate ganglions may cause arrest of respiration. Forced respiration should then be instituted, and can save the life of the animals if it is begun in good time, and maintained for several minutes.

A second complication is the possibility of rapid suppression of ventricular automatism before atrioventricular conductivity has been re-established. In one of our experiments we found that procaine block was immediately succeeded by an asystolic state of the ventricles, lasting for several seconds, until partial restoration of atrioventricular conductivity supervened.

It may be concluded from the results of our experiments that procaine block of extracardial nervous formations is very effective in the treatment of severe cardiac arrhythmias. It is probable that blocking sympathetic formations depresses ventricular automatism, while elimination of vagus nerve influences enhances atrioventricular conductivity.

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FUNCTIONAL DISTURBANCES FOLLOWING MASSIVE INFUSIONS OF PHYSIOLOGICAL SALINE

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The sensitivity of the organism to loss of blood is not dependent solely on the amount of blood lost, or on the rate at which it is lost. Experiments carried out in I. R. Petrov's laboratory [3] have shown that over-heating, trauma, starvation, and other factors greatly aggravate the consequences of hemorrhage. Loss of blood leads more quickly to hemorrhagic collapse in anesthetized [1] or shocked [2] subjects. Replacement therapy, involving transfusion of blood or blood extenders, is most effective during the early stages of collapse. Infusions of blood or physiological saline are given after loss of blood in order to avert collapse. Saline is sometimes infused in very large amounts, with the intention of providing the organism with the largest possible reserves of fluid.

Arterial pressure is not significantly affected by slow intravenous infusion of even very large amounts of physiological saline. On this basis it has been thought that massive infusions of physiological saline are quite safe, and are therefore not only permissible, but even desirable in cases in which there is a risk of hemorrhage. It should not, however, be overlooked that intravenous infusion of physiological saline is not without effect on the reaction of the organism to loss of blood.

We have investigated the reaction of the organism to loss of blood following intravenous infusion of large volumes of physiological saline.

* In Russian.