THE EFFECT OF PARTIAL PANCREATECTOMY ON ON THE ELECTROCARDIOGRAM IN DOGS

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Experiments have shown [2, 4-7, 9] that a few days after pancreatectomy in cold-blooded animals, or after partial pancreatectomy and ligation of the efferent ducts in warm-blooded animals, changes occur in the parasympathetic innervation of the heart. These changes consist of a decrease in the excitability of the vagus nerves, a decrease or total disappearance of the negative inotropic action of the parasympathetic nerves on the heart, and a shortening, or in some cases, absence of vagal arrest of the heart. The negative chronotropic effect is not appreciably affected by this procedure [5]. These changes described in the parasympathetic effects have been attributed to a disturbance of the formation and secretion of acetylcholine at the parasympathetic nerve endings in pancreatectomized animals.

The object of the present study was to investigate the effects of partial pancreatectomy on the electrocardiogram.

EXPERIMENTAL METHOD

Experiments were conducted on dogs under morphine-hexobarbital anesthesia. Lead 2 of the ECG was recorded by means of a type OB-2 cathode-ray oscillograph, using subcutaneous needle electrodes. The initial ECG was recorded before and after bilateral vagotomy in the neck. Stimulation of the peripheral end of the divided vagus nerve was carried out, as a rule, on the right side, by means of rectangular impulses from a type ISE-01 stimulator. Results were obtained from 26 experiments, conducted on 12 control and 14 pancreatectomized animals, from which about half the pancreas was removed and both ducts ligated 6-10 days before the experiment.

EXPERIMENTAL RESULTS

In the intact dogs the heart rate, as shown by the ECG indices, varied from 60 to 120 beats per minute, with an average value of 93. After partial pancreatectomy it rose to 110-245/min. The greatest increase was observed on the 7th-10th day after the operation. On the 6th day, for instance, the average heart rate was 136/min, on the 7th day 153/min, and on the 8th day 210/min. On subsequent days it fell with slight fluctuations (Fig. 1, 1 and 3).

After bilateral vagotomy, the heart rate of the control animals rose to 185-230/min (mean 206/min). Hence it rose on the average from 93 to 206 beats per minute, i.e., by 221% of its initial value. In the pancreatectomized animals the heart rate fell slightly after vagotomy to an average value of 197/min. The most marked fall took place on the 7th-9th days after operation. For instance, on the 7th day the rate was 160/min, on the 8th day 200, and on the 9th day 185/min (Fig. 1, 2, and 4). As a result of this factor and of the increased heart rate in the operated animals before division of the vagus nerves, the rate increased only very slightly after vagotomy, on the average from 175 to 197 per min, i.e., to no more than 112% of its original value.

These results indicate some degree of depression of the automatism of the heart and a sharp decrease in the tone of the vagus nerves after partial pancreatectomy. In many animals undergoing the operation, the heart rate generally was not increased after vagotomy, indicating a complete loss of the tone of the vagus nerves; in some dogs, vagotomy was followed by an actual slowing of the heart. For instance, in one animal on the 7th day after operation the rate fell after vagotomy from 195 to 140/min. This paradoxical reaction to vagotomy was actually reflected in the mean figures obtained on the 8th day after operation (see Fig. 1, 3 and 4). This reaction was possibly due to a lowering of the reflex tone of the sympathetic nerves after vagotomy, brought to light as a result of the sharp decline or absence of vagal tone. It is interesting to note that a decline or total absence of vagal tone has been observed in dogs after the preliminary extirpation of the adrenal medulla [7].

The decline or disappearance of the vagal tone after preliminary partial pancreatectomy and ligation of the pancreatic ducts could result either from changes in the reflex activity of the corresponding centers or from exclusion of the peripheral influence of the extracardial parasympathetic innervation on the heart. In order to test the latter hypothesis, the effects of stimulation of the peripheral end of one (usually the right) divided vagus nerve were investigated after bilateral vagotomy.

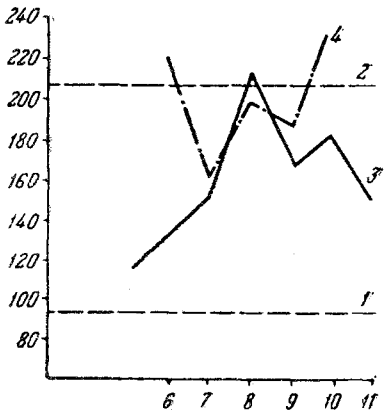

Fig. 1. Effect of partial pancreatectomy on the dog's heart rate. 1 and 2) Before and after vagotomy in intact animals; 3 and 4) the same after partial pancreatectomy and ligation of the pancreatic ducts. Along the axis of abscissas—days after operations; along the axis of ordinates—rate of the heart as shown by the ECG (mean values).

In all the pancreatectomized animals parasympathetic effects were observed on the heart, but they were significantly modified and weakened. The excitability of the vagus nerves at an optimal frequency of stimulation of 40 cps and duration of rectangular impulses of 1 msec was very slightly reduced (on the average 2.55 V compared with 2.37 V in the control animals). More significant changes took place in the rhythmic chronaxie of the vagus nerve, which increased on the average from 0.073 to 0.117 msec after the operation. Permanent arrest of the heart after optimal stimulation of the vagus nerve for 10 sec was absent in most dogs (in 6 of 9). Merely a slowing of the heart rate was observed, or a brief pause, followed by a negative chronotropic effect (Fig. 2, d, e). The range of frequencies causing marked cardiac arrest was narrowed from 15-200 cps in normal animals to 40-80 cps; the duration of the inhibitory after-effect was also shortened. For instance, in the intact animals the normal cardiac contractions were restored within a few seconds of the removal of the stimulus, while in the pancreatectomized animals recovery took place within tenths of a second (Fig. 2, b and c). It must be pointed out that cardiac arrest in some animals was masked by the development of heterotopic automatism in the form of single or rhythmic extrasystoles (Fig. 2).

In the pancreatectomized animals we also observed obvious weakening of the negatively chronotropic effects. These effects appeared at high frequencies of stimulation and were lesser in degree, i.e., their frequency was higher. It is clear from Fig. 2, for instance, that stimulation of a control animal with a frequency of 10 cps caused a negatively chronotropic effect (a), and with a frequency of 20 cps—lasting arrest of the heart (b). In the pancreatectomized animal this effect was observed at a frequency of 20 cps and was characterized by the higher frequency of its contractions (d).

A decrease of the negative dromotropic effect of the parasympathetic extracardial innervation was also observed in the pancreatectomized animals: stimulation of the parasympathetic nerves after partial pancreatectomy was accompanied by a smaller increase in the length of the P-Q interval, characterizing the function of atroventricular conduction. This phenomenon could be seen either in the conditions of the negative chronotropic effects or in the after-effects of vagal arrest of the heart (Fig. 2, a; see Fig. 2, c, d, f). The weakening of the effect of the parasympathetic nerves on the function of the conducting system of the heart was also revealed by the lower intensity of the disturbances of conduction of excitation (see Fig. 2, c and f) and by the presence of heterotopic automatism in the pancreatectomized animals (see Fig. 2). Hence, after partial pancreatectomy, all aspects of the effect of the parasympathetic innervation on the heart were weakened.

If we compare the degree of the changes in vagal innervation and tone, we cannot fail to note that the disturbance of tone was in all cases greater than the disturbance of the peripheral parasympathetic effects. Complete disappearance of the tone of the vagus nerves was frequently combined with a well defined or shortened period of vagal arrest, and more especially with negative chronotropic effects. The weakening and disappearance of the tone of the vagus nerves must therefore be attributed mainly to disturbance of the reflex activity of the corresponding centers. Disturbance of the reflex activity of the somatic nervous system, including disturbance of the reflex tone of the skeletal muscles, has been reported in earlier studies on both cold-blooded [3] and warm-blooded animals [1].

The shape and direction of the ECG waves after partial pancreatectomy were essentially unchanged, apart from a slight shortening of the P-Q interval compared with its length in the experiments on the control animals (on the average 39 compared with 45 msec), a slight widening of the R wave (on the average 38 compared with 32 msec), and sometimes a partial splitting of the R wave in the form of a depression in the ascending or descending part of

the curve. In approximately half the control and pancreatectomized animals, the T wave was negative. In most dogs a slight increase in the T wave was observed after the operation, irrespective of its direction, although it was usually smaller than the P wave. The high, pointed T wave described in dogs after total pancreatectomy [8] was not observed in our experiments. The S-T interval in the animals undergoing operation was slightly lengthened and sometimes displaced below the isoelectric line. As a result of the increase in the S-T interval the T wave was brought closer to the next P wave, and in some cases fused with it. Very similar electrocardiographic changes have been described in dogs with experimental pancreatitis [11].

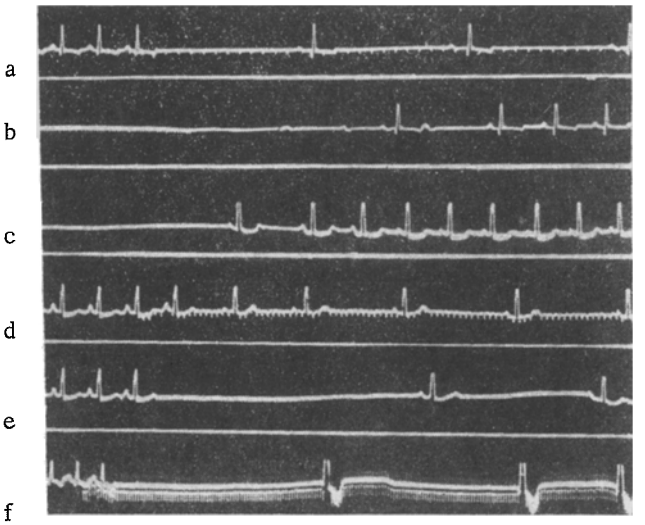

Fig. 2. Vagal effects after stimulation of control (a, b) and pancreatectomized (c, d, e, f) dogs with different frequencies. ECG. a) Chronotropic effect during stimulation with a frequency of 10 cps; b) arrest of the heart and an inhibitory after-effect due to stimulation with a frequency of 40 cps; d, e) chronotropic effects of stimulation with a frequency of 20 and 40 cps; c) inhibitory after-effect due to stimulation with a frequency of 40 cps on the 7th day after operation; f) heterotopic atrioventricular automatism, imitating a negative chronotropic effect, on the 10th day after operation. Velocity of film movement 25 mm/sec (time marker 0.05 sec).

It is easy to see that the changes we have described are to some extent opposite to those observed during stimulation of the vagus nerves or due to the action of acetylcholine [10]. On the one hand, in our opinion they demonstrate some degree of depolarization of the conducting system of the heart in pancreatectomized animals, as a result of which the velocity of spread of excitation throughout the heart is increased (shortening of the P-Q interval) and the development of heterotopic automatism is facilitated. On the other hand, these changes indicate a slowing of the processes of repolarization and recovery, as a result of which the duration of electrical systole of the heart (QRST) is increased and the level of automatism of the heart is slightly depressed.

There is every reason to suppose that partial pancreatectomy leads, after a definite interval of time, to a disturbance of the metabolism and synthesis of acetylcholine both in the parasympathetic nervous system and in the tissues of the heart. In order to test this hypothesis, we carried out five experiments in which compensatory, exogenous acetylcholine was administered to animals after the operation. These showed that the systematic intravenous injection of 2-5 ml of 1 : 10,000 acetylcholine solution (daily, starting on the 3rd-4th day after operation) considerably diminished the ensuing disturbances although it did not prevent them entirely. For instance, the heart rate increased after vagotomy on the average from 140 to 217/min (155% of the initial value). The excitability of the vagus nerves was increased; in all the animals cardiac arrest was observed, although the range of frequencies causing it remained somewhat narrowed. The negative chronotropic and dromotropic effects of the vagus nerves were

strengthened, the S-T interval shortened, and so on. However, all the indices remained more or less lowered by comparison with normal. The failure to achieve complete compensation was probably attributable to the inadequate dose of acetylcholine and, in particular, to the fact that the acetylcholine was not injected on the day of the experiment.

SUMMARY

Excision of a part of the pancreas and ligation of its ducts causes on the 6-10th postoperative day a marked diminution and disappearance of the vagus tone, provoked chiefly by the disturbed activity of the corresponding reflex centers. There is also a reduction of the range of frequencies causing the parasympathetic effects to shorten, and in some cases disappearance of the vagus cardiac arrest, as well as weakening of the negative chronotropic and dromotropic effect of the parasympathetic innervation. In the animals operated there is a shortenining of the P-Q interval, prolongation of the QRST complex, and a partial splitting of the R wave.

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