EFFECT OF CHOLINERGIC SUBSTANCES AND ADRENALIN ON DURATION OF PRESERVATION OF ELECTRICAL ACTIVITY OF THE HEART DURING ACUTE ASPHYXIA

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In Raab's view [19] the mediators of the nervous impulse regulate the energy metabolism of the myocardium: under the influence of catecholamines the coefficient of useful action of the heart is reduced, while under the influence of acetylcholine it is increased. Administration of acetylcholine increases the glycogen content in the heart [8] and facilitates the absorption of lactic acid by the heart muscle from the blood [9]. Raiskina [4] administered acetylcholine and found an increase in the ATP and creatine phosphate in a rabbit's heart, and her subsequent investigation [5, 6] showed that this increase was dependent on the slowing of the metabolism of these substances in the myocardium. In addition, many investigators have shown that acetylcholine in physiological concentrations reduces the oxygen consumption of the heart [10, 15, 18] and increases the energy efficiency of its work [14]. There are reports that adrenalin can increase the oxygen consumption of the heart [12-16]. Raiskina, Samoilova, and Khodas [7] found that adrenalin increases the oxygen tension in the myocardium and inhibits its utilization, leading to the development of tissue hypoxia, evidently as the result of its action on the tissue enzyme systems.

The object of the present investigation was to examine the effect of cholinergic substances and adrenalin on the resistance of the heart to acute asphyxia.

EXPERIMENTAL METHOD

Experiments were carried out on 212 albino mice. The animals were fixed on their back. The trachea was exposed and the ECG recorded continuously in lead II on an ink-writing oscillograph. The time from the moment of compression of the trachea to disappearance of the ECG waves was measured and provided an estimate of the duration of preservation of the cardiac activity during acute asphyxia.

The animals of group 1 received an intraperitoneal injection of 0.2 ml of physiological saline 5 min before ligation of the trachea; the animals of group 2 received 0.2 ml of eserine solution in a dose of 1 mg per kg; group 3 received 0.2 ml of carbachol solution in a dose of 0.01 mg/kg; and the animals of groups 4 and 5 received 0.2 ml of adrenalin solution in doses of 1 and 0.1 mg/kg.

EXPERIMENTAL RESULTS

In the control experiments compression of the trachea led to the development of bradycardia, arrhythmia, and the appearance of atrioventricular block of varying degree, sometimes to the extent of complete transverse dissociation with a change to a nodal rhythm. The voltage of all the ECG waves fell gradually.

In the experiments of series 1, the preliminary injection of eserine increased the time of preservation of the cardiac potentials from 14.5 ± 1.6 to 20.8 ± 2.6 min by comparison with its value in animals receiving physiological saline ($P < 0.001$). Injection of carbachol increased this period still further – to 27.3 ± 2.6 min ($P < 0.001$). The preliminary injection of adrenalin had the opposite effect: a dose of 1 mg per kg sharply reduced the time of preservation of the potentials to 5.8 ± 0.6 min ($P < 0.01$), and in one-tenth of this dose (0.1 mg/kg) adrenalin caused a less marked shortening of the survival period of the heart, which was not statistically significant (9.5 ± 1.1 min).

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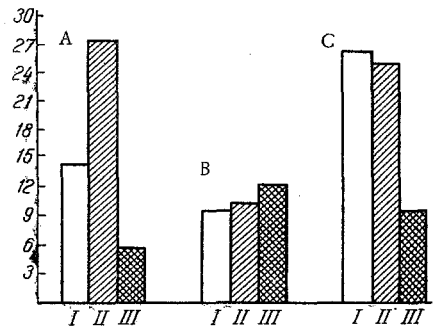

Fig. 1. Changes in duration of preservation of cardiac electrical activity in acute asphyxia under the influence of carbachol (II) and adrenalin (III) in control (A) and adrenalectomized (B) animals and animals receiving ACTH (C). I) Duration of preservation of cardiac potentials in animals receiving physiological saline. Ordinate – duration of preservation of cardiac potentials (in min).

Furthermore, in the animals receiving carbachol a regular sinus rhythm and the original voltage of the R wave persisted longer than in the control. In the animals receiving large doses of adrenalin the voltage of the R wave fell more rapidly than in the control animals and complete block developed.

In the next investigations the effect of removal of the adrenals and injection of ACTH was studied on the action of cholinergic substances and adrenalin revealed in the experiments of series 1. Accordingly, in the experiments of series II, bilateral adrenalectomy was performed on the mice two days before the experiment. In the experiments of series III the animals received ACTH in a dose of 10 units/kg on four successive days. In each series the animals of group 1 received physiological saline by intraperitoneal injection 5 min before the experiment, the animals of group 2 received carbachol, and those of group 3 received adrenalin in a dose of 1 mg/kg. The experiments of series I on the intact animals served as the control for this series. It is clear from the figure that adrenalectomy slightly reduced the resistance of the heart to asphyxia. After compression of the trachea the voltage of all the ECG waves fell more rapidly in the adrenalectomized animals than in the controls, and conductivity was disturbed more quickly. In these animals the action of cholinergic substances in prolonging (survival of the heart 10.3 ± 1.4 sec) and the action of adrenalin in shortening (12.2 ± 1.5 sec) the preservation of the cardiac potentials during asphyxia were not manifested (in the animals receiving physiological saline this index was 9.8 ± 1.2 sec).

The experiments of series III in which ACTH was injected showed that after compression of the trachea the original voltage of the R wave and a regular sinus rhythm were maintained longer than in series I, and complete atrioventricular block developed later. This series of experiments also showed that injection of ACTH prolonged the period of preservation of the cardiac potentials to the same level (25.8 ± 2.1 sec; $P < 0.001$) as injection of carbachol in the experiments of series I. The "prolonging" action of carbachol against the background of saturation with ACTH no longer appeared (24.4 ± 2.45 sec; $P > 0.5$), while the "shortening" action of adrenalin remained (9.2 ± 0.7 sec; $P < 0.001$) but was less marked than in the analogous experiments of series I (see figure).

Hence, it follows from the results of the experiments of series I that during acute asphyxia cholinergic substances prolong the period of preservation of the cardiac potentials. In the experiments of Duchene-Marullaz and co-workers [11], injection of eserine also prolonged this time in rats after decapitation.

On the basis of observations on rabbits, the author also formed the impression some time ago that injection of acetylcholine may adversely affect the resistance of the heart to asphyxia [3]. However, the present investigation showed that acetylcholine does not lower resistance to asphyxia.

The results of these experiments, showing disappearance of the action of cholinergic substances and adrenalin on the duration of preservation of the cardiac potentials during asphyxia in adrenalectomized animals suggest that for these substances to act on tissue metabolism and on energy formation in the myocardium, the hormones of the adrenal cortex are essential. These observations are in agreement with those reported by Klimenko [2], who observed that the characteristic action of adrenalin on oxygen absorption by the tissues disappeared after adrenalectomy and with the findings of Dagaeva [1], who described a decrease in the creatine phosphate and glycogen content in the myocardium after adrenalectomy.

The absence of action of carbachol after preliminary administration of ACTH was possibly associated to some extent with the ability of ACTH to stimulate acetylcholine synthesis in nerve tissue [20, 21]. In addition, a decrease in the adrenalin concentration in the myocardium under the influence of ACTH has been described [17], and on the basis of the result of the experiments of series I, in which adrenalin was injected,

this must have helped to increase the duration of preservation of the automatism of the heart in acute asphyxia. Evidently when the body is saturated with ACTH, the resistance of the heart to asphyxia reaches its maximum and administration of carbachol in these conditions is unable to bring about any further increase in resistance. The positive effect of ACTH on the resistance of the heart to asphyxia evidently depends also on the fact that the "shortening" action of adrenalin in these animals, although it persisted, was less marked than in the control animals.

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