DEPRESSION OF AUTOMATISM OF POTENTIAL CARDIAC PACEMAKERS AND OF LUCIANI PERIODS IN HYPOXIA

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In rabbits with an artificially produced complete atrioventricular block the heart was isolated by Langendorff's method. Prolonged (30-60 min) hypoxia was found to increase the degree of depression of the automatism of potential ventricular pacemakers by fast stimulation. The duration of poststimulation asystole was increased by 3.5 times under the influence of hypoxia. In some experiments hypoxia led to the appearance of Luciani periods, i.e., short periods of ventricular asystole. The action of hypoxia was abolished by oxygenation of the perfusion fluid or by ATP in a concentration of 10^{-5} M. Lengthening of poststimulation asystole and the appearance of Luciani periods during hypoxia are regarded as the result of relative insufficiency of active ionic transport.

Periodic asystole [12] may be the result of depression of the automatism of potential cardiac pacemakers by an abnormally high frequency of excitation. This depression of automatism is due to the predominance of passive over active ionic transport [2, 3, 8]. A feature of the depression of automatism during Luciani periods is that the frequent excitation evoking this phenomenon is generated by the very fibers whose automatism is depressed. This phenomenon has been called "self-depression of automatism" [4]. It was shown previously that certain chemical agents inhibiting energy metabolism and active ionic transport (dinitrophenol, monoidoacetate, ouabain) prolong poststimulation asystole [2, 3, 8] and evoke the appearance of Luciani periods [1, 9]. In this connection it seemed probable that hypoxia, by disturbing ATP resynthesis and removing the source of energy for active ionic transport, ought to intensify the depression of automatism of the ventricular pacemakers during fast stimulation and to evoke the appearance of Luciani periods, i.e., short periods of ventricular asystole [5-7, 9-15].

The investigation described below was carried out to test this hypothesis.

EXPERIMENTAL METHOD

Rabbits' hearts were perfused through the aorta with an oxygenated ($95\%O_2+5\%CO_2$) solution of the following composition (in mM): NaCl 137, KCl 2.7, $CaCl_2$ 1.8, $MgCl_2$ 1, $NaHCO_3$ 12, NaH_2PO_4 0.4, glucose 5.5; pH 7.3; temperature 36.5 ± 0.3°C. At the beginning of the experiment a complete atrioventricular block was produced by clamping the region of the atrioventricular conducting bundle. The ECG was recorded by electrodes applied to the ventricles. Twice, for 3 min each time, the ventricles were stimulated by square electric pulses of above-threshold strength and with a duration of 3 msec. The frequency of stimulation was 2.5 times higher than the intrinsic frequency of ventricular excitation. The supply of oxygen to the perfusion solution was then stopped and the ventricles stimulated periodically for 40-60 min. At the end of the experiment the oxygen supply was restored or the sodium salts of ATP were added to the perfusion fluid in a concentration of 10^{-5} M. The ventricles were again stimulated under these new conditions and the duration of poststimulation asystole was determined.

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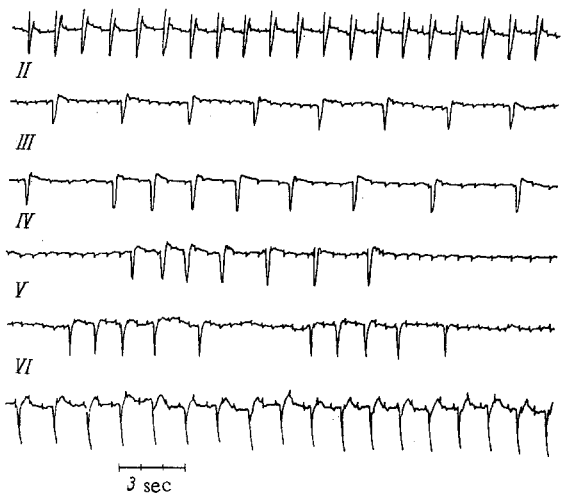

Fig. 1. Appearance of Luciani periods under the influence of hypoxia and restoration of normal idioventricular rhythm by subsequent oxygenation of perfusion solution: I) initial idioventricular rhythm; II) reduction of frequency of ventricular excitation after hypoxia for 15 min; III) periodic quickening and slowing of ventricular excitation after hypoxia for 25 min; IV) Luciani periods after hypoxia for 40 min; V) shortening of periods of asystole after perfusion for 5 min with oxygenated solution; VI) restoration of normal idioventricular rhythm after perfusion for 15 min with oxygenated solution.

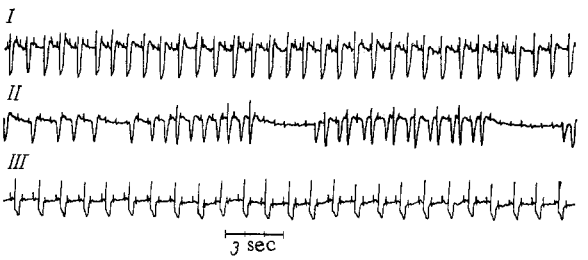

Fig. 2. Appearance of Luciani periods under the influence of hypoxia and their disappearance during perfusion of the heart with ATP solution: I) original idioventricular rhythm; II) moment of transition from arrhythmia with periodic quickening and slowing into Luciani periods after exposure to hypoxia for 30 min; III) restoration of normal idioventricular rhythm 5 min after beginning of perfusion with ATP solution.

EXPERIMENTAL RESULTS

The action of hypoxia on the isolated rabbit heart was studied in 17 experiments. In 15 experiments the effect of hypoxia was studied on the depression of automatism of the ventricular pacemakers by fast stimulation and on the appearance of Luciani periods. In two experiments no stimulation was applied in order to exclude its effect on the appearance of Luciani periods.

By 15-20 min after interruption of the oxygen supply the initial frequency of ventricular excitation (mean 64/min) had fallen by 48% ($P < 0.001$). The initial duration of poststimulation asystole (mean 14 sec) had increased by 246% ($P < 0.001$).

During subsequent perfusion of the heart with oxygenated solution (eight experiments) the duration of poststimulation asystole was again reduced ($P < 0.01$). The frequency of ventricular excitation also was restored almost to its initial level ($P < 0.001$).

During the action of the sodium salt of ATP on the heart after a period of prolonged hypoxia (5 experiments), within 5-10 min the duration of poststimulation asystole was reduced to a value below that observed at the beginning of the experiment (mean 90.6% of the initial value; $P < 0.02$). The frequency of ventricular excitation was increased to 71.2/min ($P < 0.001$).

In nine experiments (including those without artificial stimulation) the spontaneous appearance of periodic asystole, i.e., of Luciani periods, was observed during prolonged (not less than 30 min) hypoxia. Initially, against the background of a reduced frequency of excitation, periodic quickening and slowing of the idioventricular rhythm developed (Fig. 1, III); later, a phase of quickening of excitation was followed by a sudden onset of asystole (Fig. 1, IV). Having once appeared, the Luciani periods continued for 30-50 min. During subsequent oxygenation of the perfusion solution for 10-20 min the Luciani periods disappeared and the normal idioventricular rhythm was restored (Fig. 1, VI). During perfusion of the heart with ATP solution after a long period of hypoxia, the normal rhythm of ventricular excitation was restored after 3-8 min (Fig. 2, III).

Hypoxia thus sharply intensified the depression of automatism of cardiac-pacemaker activity by fast stimulation and can evoke Luciani periods. The effects of hypoxia disappear after perfusion of the heart with oxygenated solution or with solution containing ATP.

In deep hypoxia the active ionic-transport processes are evidently disturbed so severely that they no longer correspond even to the relatively low frequency of spontaneous excitation of the ventricular pacemakers. This leads to the development of short periods of ventricular asystole. During asystole the sodium pump, the activity of which does not cease completely, restores the disturbed ionic gradients and the pacemaker fibers regain their ability to generate excitation.

It can be concluded from the experiments described above that poststimulation asystole and the asystole during Luciani periods have a common origin: a relative insufficiency of the processes of active ionic transport relative to the actual frequency of ventricular-pacemaker excitation.

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