LUCIANI PERIODS ARISING BY THE ACTION OF ACETYLCHOLINE AND ESERINE ON AUTOMATIC ACTIVITY OF PURKINJE FIBERS

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Experiments on isolated rabbit hearts with complete atrioventricular block showed that Luciani periods arise under the influence of acetylcholine ($1 \cdot 10^{-7}-2 \cdot 10^{-6}$ g/ml) or eserine ($1 \cdot 10^{-7}-2 \cdot 10^{-6}$ g/ml). These periods disappear as a result of the action of atropine ($1 \cdot 10^{-6}$ g/ml). Microelectrode recordings showed that Luciani periods produced under the influence of acetylcholine or eserine are due to periodic inhibition of pacemaker activity of the Purkinje fibers. This suppression of pacemaker activity is regarded as the result of relative insufficiency of the process of active ion transport.

KEY WORDS: atrioventricular block; Luciani periods; acetylcholine; Purkinje fibers.

The writers showed previously that ouabain, an inhibitor of Na,K-ATPase, 2,4-dinitrophenol, and hypoxia all give rise to periodic ventricular asystole, i.e., to Luciani periods, under the conditions of complete atrioventricular block. The appearance of these periods has been explained by periodic suppression of automatic activity of the ventricular pacemakers as a result of relative insufficiency of the processes of active ion transport [1, 2].

Acetylcholine is known to facilitate poststimulation suppression of automatic activity of the cardiac pacemakers [4, 8, 9]. Accordingly the question arises: does eserine, which blocks cholinesterase, and does acetylcholine cause the appearance of Luciani periods?

To answer this question the investigation described below was carried out.

EXPERIMENTAL METHOD

Purkinje fibers of the false tendons of the hearts of rabbits and dogs and rabbits' hearts isolated by Langendorff's method, with complete atrioventricular block, were used. The block was produced by tying a ligature in the upper part of the ventricular septum.

Preparations of the false tendons and the isolated hearts of the warm-blooded animals were perfused with oxygenated (95% O_2 + 5% CO_2) Tyrode solution (composition in mmoles/liter: NaCl 137, KCl 2.7, $CaCl_2$ 1.8, $MgCl_2$ 1, $NaHCO_3$ 12, NaH_2PO_4 0.4, and glucose 5.5) at 36.5°C and pH 7.3-7.4. Potentials of single spontaneously excited Purkinje fibers were recorded intracellularly by glass microelectrodes filled with 3 M KCl solution. The potentials were led to a cathode follower (Biofizpribor Technical Design Office), then to a dc amplifier of the S1-19 oscilloscope. The actual recording was made on an N-700 oscilloscope. In the experiments on isolated rabbits' hearts, the ECG of the ventricles or atria was recorded with an Elcar-2 ink-writing electrocardiograph. The frequency of spontaneous excitation and the action potentials of the Purkinje fibers were investigated before and after the addition of acetylcholine ($1 \cdot 10^{-7}-2 \cdot 10^{-6}$ g/ml) or eserine ($1 \cdot 10^{-7}-2 \cdot 10^{-6}$ g/ml) to the Tyrode solution. The action of these substances was abolished by adding atropine ($1 \cdot 10^{-6}$ g/ml) to the perfusion fluid. Altogether 43 tests were carried out.

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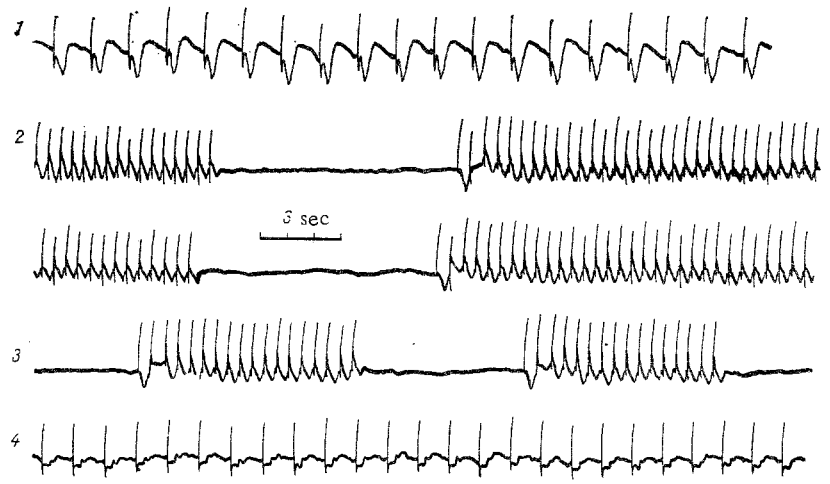

Fig. 1. Appearance of Luciani periods during action of acetylcholine on isolated rabbit heart with complete atrioventricular block. ECG of ventricles of isolated heart: 1) original idioventricular rhythm; 2, 3) Luciani periods recorded 20 and 30 min, respectively, after addition of acetylcholine ($1 \cdot 10^{-6}$ g/ml) to perfusion fluid; 4) restoration of idioventricular rhythm by atropine ($1 \cdot 10^{-6}$ g/ml).

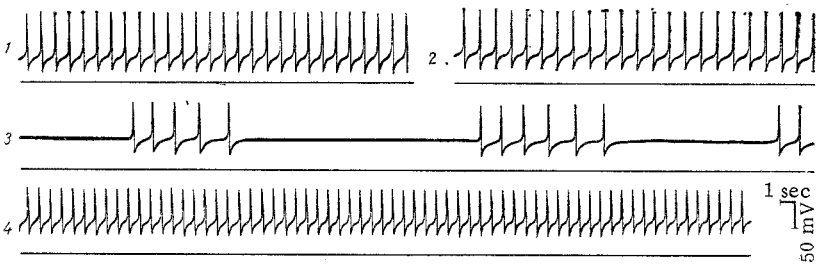

Fig. 2. Appearance of Luciani periods by the action of acetylcholine on Purkinje fibers of rabbit's heart. Recording of transmembrane potentials of Purkinje fibers: 1) original frequency of spontaneous excitation; 2) decrease in frequency of excitation after action of acetylcholine ($5 \cdot 10^{-7}$ g/ml) for 4 min; 3) Luciani periods arising after action of acetylcholine for 6 min; 4) restoration of rhythmic activity by atropine ($1 \cdot 10^{-6}$ g/ml).

EXPERIMENTAL RESULTS

The investigations on the isolated rabbits' hearts with complete atrioventricular block showed that acetylcholine (11 experiments) and eserine (nine experiments) had an identical action on ventrical pacemaker activity. During the first few minutes of action of these drugs no statistically significant change in the frequency of ventricular excitation occurred. However, during this period disturbances of idioventricular rhythm in the form of parasystoles or pulses bigeminus were observed. Periodic quickening and slowing of ventricular excitation followed, and after 10-30 min a short period (6-15 sec) of ventricular asystole suddenly occurred; this phenomenon began to be repeated periodically, i.e., Luciani periods developed (Fig. 1).

The appearance of Luciani periods was always preceded by a marked increase in the frequency of idioventricular excitation. The frequency of ventricular excitation between the periods of asystole usually exceeded the frequency of the original idioventricular rhythm. Luciani periods arising under the influence of acetylcholine were observed over a long period of time (40-60 min) in 10 of 11 experiments. In one experiment no disturbances of idioventricular rhythm were caused by acetylcholine.

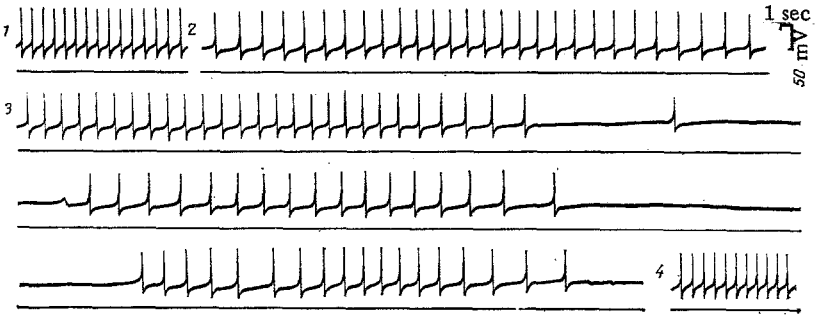

Fig. 3. Luciani periods produced by action of eserine on Purkinje fibers of rabbit heart. Records of transmembrane potentials of Purkinje fibers: 1) original frequency of spontaneous excitation; 2) decrease in frequency of excitation after action of eserine ($5 \cdot 10^{-7}$ g/ml) for 10 min; 3) Luciani periods arising after action of eserine for 15 min (2nd, 3rd, and 4th lines are direct continuations of each other); 4) restoration of rhythmic activity by atropine ($1 \cdot 10^{-6}$ g/ml).

Eserine caused the appearance of Luciani periods in six of the nine experiments. Periodic ventricular asystole under these circumstances was less stable: during continued perfusion with eserine solution, at times a regular idioventricular rhythm was restored.

Luciani periods arising as a result of the action of acetylcholine or eserine disappeared on all experiments on the addition of atropine in a concentration of $1 \cdot 10^{-6}$ g/ml to the perfusion fluid.

Similar results were obtained by the action of acetylcholine (12 experiments) and eserine (11 experiments) on pacemaker activity of the Purkinje fibers of the isolated false tendons of the rabbit or dog heart. By contrast with experiments on the whole heart, in experiments on Purkinje fibers the frequency of spontaneous excitation was reduced by acetylcholine and eserine during the first few minutes from 80 ± 12.7 to 44 ± 7.7/min ($P < 0.02$) and from 81 ± 8.3 to 49 ± 4.0/min ($P < 0.01$), respectively. Meanwhile, the action potentials of the Purkinje fibers were unchanged by these drugs. Against this background, just as in experiments on the whole heart, a periodic quickening and slowing of excitation occurred initially, followed by the appearance of Luciani periods, observable when the automatic activity of the single pacemaker fibers was recorded (Figs. 2 and 3). In response to the action of eserine, Luciani periods arose less frequently than to acetylcholine. The addition of atropine to the perfusion fluid led in every case to restoration of the rhythmic activity of the Purkinje fibers.

Luciani periods developed only by the action of acetylcholine or eserine on the activity of potential pacemakers of the ventricles. Automatic activity of the sino-atrial node was usually inhibited by these substances.

On the basis of earlier investigations of the mechanism of origin of the Luciani periods it was postulated that their appearance may be attributed to imbalance between the processes of active and passive ion transport, as a result of which the pacemaker fibers temporarily lose their ability to generate spontaneous excitation [1, 2]. The same mechanism lies at the basis of the origin of the preautomatic pause observed after the ending of rapid electrical stimulation of the ventricles during complete atrioventricular block [3].

The appearance of Luciani periods during the action of acetylcholine or eserine also evidently takes place on account of a disturbance of active ion transport, for there are indications that acetylcholine inhibits the activity of transport Na,K-ATPase in the microsomes and some subcellular fractions of neurons [6, 7].

The appearance of asystole during Luciani periods induced by the action of acetylcholine or eserine was usually preceded by high-frequency excitation of the ventricles. This high-frequency excitation, generated by the ventricular pacemakers, also contributed to the development of the relative insufficiency of active ion transport and to the appearance of the phenomenon of "self-depression" of automatic activity [3, 5]. As a result, periodic ventricular asystole developed, during which the disturbed ionic gradients on both sides of the excitable membrane were restored, and automatic activity of the Purkinje fibers resumed.

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