ACTION OF ADRENALIN AND NORADRENALIN ON ELECTROPHYSIOLOGICAL PROPERTIES OF SMOOTH MUSCLES OF THE PORTAL VEIN

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Adrenalin and noradrenalin (10^{-6}) caused depolarization, strengthening of spontaneous electrical activity, increased excitability, and a decrease in the membrane resistance of smooth muscle cells of the portal vein. It is postulated that the excitatory action of catecholamines on muscle cells is connected with an increase in permeability mainly for calcium and sodium.

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Investigations of the mechanism of action of mediators on electrophysiological properties of smooth muscles of the gastro-intestinal tract have recently been published [2, 5, 6, 8]. So far, however, no such investigations have been carried out on the smooth muscles of blood vessels. In most studies the effect of catecholamines was investigated principally on spontaneous electrical activity and contractile activity of the smooth muscles of the vessels. In many respects the results of these investigations are contradictory [3, 7, 9-13].

It was therefore decided to study the effect of catecholamines not only on the spontaneous electrical activity (SEA) of muscle cells, but also on their excitability and on their membrane resistance.

EXPERIMENTAL METHOD

The test object consisted of segments of the rat portal vein 15-20 mm in length and 0.2-0.5 mm in diameter. The muscle strip was stretched by a weight of 2-3 g (its contractions under these circumstances were close to isometric) and it was placed in the chamber of a double sucrose bridge [1, 4]. Potentials were recorded and the object stimulated by means of Ag – AgCl electrodes. All electrodes were connected to the corresponding parts of the muscle strip through inflowing solutions. Before it entered the chamber, the Krebs' solution was aerated by a mixture consisting of 95% O_2 and 5% CO_2, and heated to a temperature of 33-34°. The recording electrodes were connected to the input of a cathode follower, from which the signals were fed into the input of a VÉKS-0.1M oscilloscope. Parallel recordings were made by means of a type N-700 loop oscillograph on photographic paper and by means of an ÉPP-09-M1 automatic writer on oscillographic paper.

The membrane permeability (resistance) for ions was estimated from the magnitude of the electrotonic potentials (ETPs) produced by a weak polarizing current. The 0.1% solutions of adrenalin and noradrenalin which were used were diluted with Krebs' solution to a concentration of 10^{-6} before each experiment. The duration of action of the catecholamines was 6-7 min.

EXPERIMENTAL RESULTS

In most experiments the action of noradrenalin was accompanied by depolarization of the membrane of the smooth-muscle cells, which reached a maximum of 2-3 mV after 2-3 min (Fig. 1A). Further action of noradrenalin did not change the level of the membrane potential (MP) of the cells. The frequency of the SEA was increased about 3 times during the first 2 min of action. The duration of the slow waves was reduced under these circumstances, and they were gradually changed into fast potentials. Further action of noradrenalin did not change the frequency of cell activity. The amplitude of the fast potentials fell

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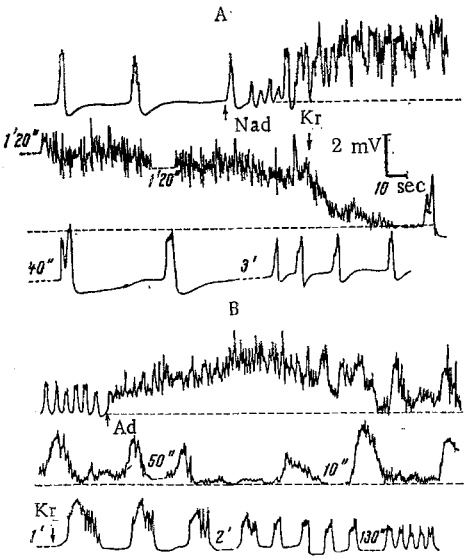

Fig. 1

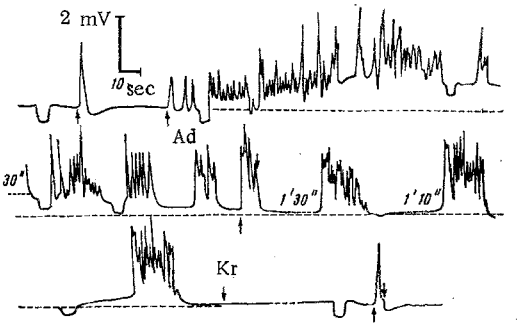

Fig. 2

Fig. 1. Action of noradrenalin (A) and adrenalin (B) on electrical activity of smooth muscles of portal vein. Nad – noradrenalin; Ad – adrenalin; Kr – normal Krebs' solution. Arrows indicate beginning and end of action of adrenalin and noradrenalin. In this and subsequent figures, upward deviation of curve denotes negativity, downward deviation positivity.

Fig. 2. Depolarization, appearance of electrical activity, and decrease in electrotonic potentials of muscle cells under the influence of adrenalin. In the initial state the cells possessed no spontaneous electrical activity. Arrows denote switching on and off cathode of polarizing current before and during adrenalin action. Electrotonic potentials produced by current of strength 0.7 μA.

throughout the period of action of noradrenalin, but only very slightly. In some experiments, at the 4th-5th min of noradrenalin action, isolated slow waves were observed. Their amplitude was 2-2.5 min and their duration from 12 to 15 sec, and frequent, fast potentials were superposed on them. Removal of the noradrenalin by rinsing with normal Krebs' solution was accompanied by gradual restoration of the MP and a decrease in the frequency of electrical activity. It returned to its intial level after 3-4 min.

The action of adrenalin was qualitatively similar to that of noradrenalin. A recording of one of the experiments is shown in Fig. 1B. Depolarization reached a maximum 1-2 min after the beginning of adrenalin action, and reached 1-2 mV. Later, despite the continued action of adrenalin, the onset of adrenalin action was characterized by an increase in frequency of the SEA by about 3-4 times, with a gradual change of the slow waves into fast potentials. Further adrenalin action caused the appearance of slow waves from 2-3 mV in amplitude and up to 11 sec in duration, with frequent discharges in the form of single fast potentials on their peaks and between them. Removal of the adrenalin with Krebs' solution caused no change in the MP level of the cells. Recovery of electrical activity took place more slowly and was complete at the end of the 3rd minute. The fast potentials between the slow waves disappeared first, and then by the end of 1 min the frequency of the slow waves increased, while their amplitude and duration decreased.

The action of adrenalin on a muscle whose cells did not possess SEA is illustrated in Fig. 2. In the cells of this muscle it also caused depolarization of the membrane, and the appearance of electrical activity in the form of single fast potentials, the frequency and amplitude of which increased during the first 2 min. After 3 and 4 min the electrical activity had the form of alternating slow waves (duration 15-20 sec), up to 2 mV in amplitude, with fast potentials on their peaks, of high frequency and amplitude. Removal of the adrenalin with Krebs' solution led to disappearance of the electrical activity. In this, as in most other experiments, the effect of catecholamines on the amplitude of the ETP also was investigated. In the muscle in this experiment, anelectrotonus was produced by a current of strength 0.7 μA; under normal conditions it reached 0.6 mV.

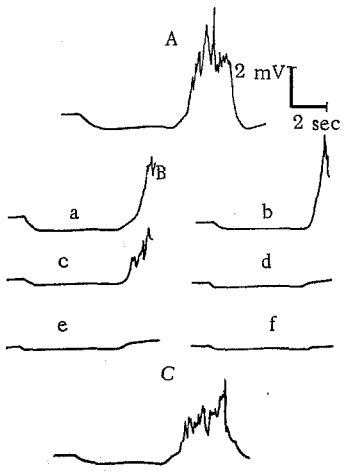

Fig. 3. Effect of adrenalin on electrical potentials of smooth muscles of portal vein possessing spontaneous electrical activity: A) anelectrotonus under normal conditions; B) anelectrotonus during adrenalin action; a,b,c,d,e,f) after 40 sec and 2, 3, 4, 5, and 6 min of adrenalin action, respectively; C) anelectrotonus at beginning of rinsing of muscle with normal Krebs' solution. Electrotonic potentials evoked by current of 0.5 μA.

At the beginning of adrenalin action the magnitude of the anelectrotonus fell by 0.2 mV, although the MP level was unchanged at this time. Switching off the polarizing current was accompanied by an anodic off-response, manifested as an increase in the frequency of electrical activity. The decrease in anelectrotonus reached its greatest degree after 7 min of adrenalin action. Removal of the adrenalin with normal Krebs' solution was accompanied, as a rule, by restoration of the anelectrotonus, for the anodic off-response was inhibited.

Before the beginning of adrenalin action, stimulation by the cathode of the polarizing current caused a small ETP, on which only one spike potential appeared. Switching off the current was accompanied by disappearance of the ETP and the development of a considerable after-hyperpolarization. During the action of adrenalin, the cathode of a polarizing current of the same strength caused appreciable depolarization and fast spike potentials. Switching off the current was accompanied by cessation of spike activity, but no after-hyperpolarization developed. Removal of the adrenalin with Krebs' solution led to restoration of the response to the cathode of the polarizing current. Changes in anelectrotonus during the action of adrenalin in an experiment in which the muscle cells possessed SEA are shown in Fig. 3. Wide scanning was used for this recording. The decrease in anelectrotonus took place at the very beginning of adrenalin action (Fig. 3B, a). The subsequent action of adrenalin led to a further decrease in the anelectrotonous, the amplitude of which after 5 min was almost reduced to one-quarter of its initial level. Switching off the polarizing current was accompanied by an anodic off-response (Fig. 3A), the latent period of which decreased during the first minutes of adrenalin action (Fig. 3B, a-c). During the further action of adrenalin, switching off the polarizing current did not produce an anodic off-response (Fig. 3B, d-f). Removal of the adrenalin with normal Krebs' solution was accompanied by restoration of the magnitude of anelectrotonus and by the appearance of an anodic off-response (Fig. 3C). The action of noradrenalin caused similar changes in ETP.

Investigation of the action of the polarizing current cathode on muscles whose cells possessed SEA was difficult because of the high frequency of electrical activity during the action of catecholamines.

During the first minutes, therefore, adrenalin and noradrenalin caused depolarization of the membrane and increased the frequency of the SEA of the muscle cells. During the next few minutes of adrenalin action, however, repolarization of the membrane took place and slow waves appeared with fast potentials on them, possibly as a result of adaptation of the cells to adrenalin action. Depolarization and strengthening of SEA produced by noradrenalin, on the other hand, persisted in most cases throughout the period of action of the mediator. The decrease in ETP under the influence of catecholamines discovered in these investigations is evidence of a decrease in the membrane resistance of the muscle cells, i.e., of an increase in its ionic permeability. This may be the way in which catecholamines exert their excitatory action on muscle cells. Preliminary investigations show that catecholamines increase the permeability of muscle cells primarily for calcium and sodium ions.

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