MECHANISMS OF ACTIVATION OF CONTRACTION OF CORONARY ARTERY SMOOTH MUSCLE CELLS

V. M. Taranenko and N. G. Kochemasova

UDC 612.731:612.171.1

KEY WORDS: smooth muscles; electrotonic potentials; action potential; membrane polarization; potassium ions; contraction and relaxation.

The smooth muscles of blood vessels, especially of the vessels of the heart, continue to attract the increasing attention of investigators. Publications devoted to this problem describe mainly the study of the action of various drugs and K^+ on contractile activity [2, 3, 5, 6] and the resting potential [4] of muscle cells.

However, electrical properties and the connection between electrical processes on the membrane and contraction of the smooth-muscle cells (SMC) of the coronary arteries have not previously been investigated, although knowledge of these factors would undoubtedly help to find ways of effective and oriented influencing of the contractile activity of the coronary arterial SMC. The investigation described below was aimed at the study of this problem.

EXPERIMENTAL METHOD

Experiments were carried out on circular strips of the bovine left descending coronary artery (diameter 1.5-2 mm). The double sucrose gap method [1] with simultaneous recording of contractions was used to record electrical activity of the SMC of the coronary arteries. Changes in the degrees of polarization of the membrane were produced by changing the external calcium concentration and by the action of the polarizing current. The composition of the original Krebs' solution was as follows (in mM): NaCl 134, $NaHCO_3$ 16.3, NaH_2PO_4 1.38, KCl 5, $CaCl_2$ 2.8, $MgCl_2$ 0.1, glucose 7.8; pH 7.4 (35-36°C). Krebs' solution with an increased K^+ concentration (160 mM) was prepared by adding KCl and the dry salt to the Krebs' solution.

EXPERIMENTAL RESULTS

In response to the action of an electric current of different polarity on SMC of the coronary arteries (Fig. 1b) catelectrotonic and anelectrotronic potentials (CE and AE, respectively) were observed to develop. The shape and amplitude of the electrotonic potentials depended on the strength of the polarizing current. For instance, the amplitude of AE increased proportionally to the strength of the hyperpolarizing current up to 0.6 μA, whereas the linear relationship for CE was disturbed as early as at 0.4 μA (Fig. 1A, B). With a further increase in the strength of the hyperpolarizing current AE fell gradually after reaching its maximum, to form a distinctive "take off" (see Fig. 1B, d-f). Stopping the current was accompanied by disappearance of AE, but in no case did an anode-breaking response appear (Fig. 1B). Strengthening the depolarizing current led to the appearance of slow depolarization at the beginning of CE (Fig.1B, d, e), changing into a spike potential (Fig. 1B, f). The amplitude of the spike reached 10 mV and its appearance was accompanied by phasic contraction.

Dependence of the amplitude of contractions of SMC from the coronary arteries on duration of action of the depolarizing current is shown in Fig. 2. The strength of the current was chosen so that a spike potential appeared in response to short stimulation of maximal amplitude. Stimulation of the strip by a current lasting 200 msec evoked a spike potential accompanied by just perceptible contraction (Fig. 2). An increase in the duration of the stimulating pulse led to a marked increase in amplitude of the contraction. When the duration of the depolarizing current was between 200 msec and 8 sec, the graph of amplitude of contraction ver-

Department of Neuromuscular Physiology, A. A. Bogomolets Institute of Physiology, Academy of Sciences of the Ukrainian SSR, Kiev. (Presented by Academician of the Academy of Medical Sciences of the USSR N. N. Gorev.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 90, No. 10, pp. 387-389, October, 1980. Original article submitted December 19, 1979.

0007-4888/80/9010-1317$07.50

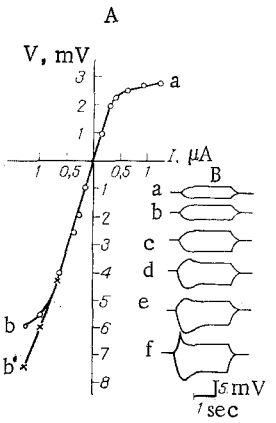

Fig. 1

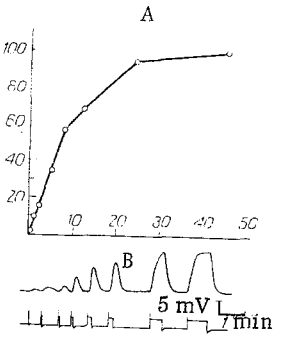

Fig. 2

Fig. 1. Action of polarizing current on electrical activity of SMC of bovine coronary arteries. A) Current-voltage characteristic curve of SMC: a) amplitude of CE, b, b') amplitude of AE before and after "take-off" respectively, B) AE and CE of SMC evoked by polarizing current of different strengths: a-f) at 0.15, 0.25, 0.35, 0.6, 0.9, and 1.2 μA, respectively. Here and in Figs. 2 and 3, upward deviation corresponds to depolarization, downward to hyperpolarization.

Fig. 2. Amplitude of contraction of SMC of bovine coronary arteries as a function of duration of action of depolarizing current. A) Force of contraction as a function of duration of action of depolarizing current. Abscissa, time (in sec); ordinate, amplitude of contraction (in %). Maximal contraction of SMC during action of depolarizing current taken as 100%. B) Combined electrical (below) and mechanical (above) responses of SMC.

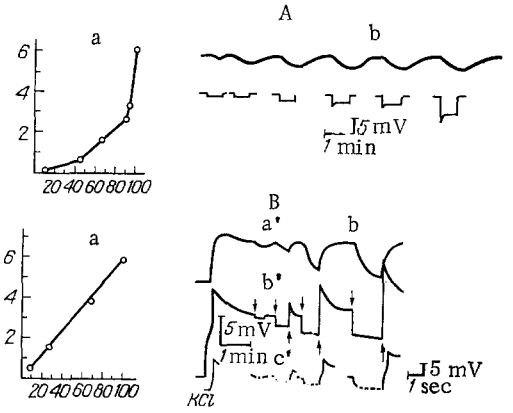

Fig. 3. Effect of hyperpolarization of membrane on tonic contraction of SMC of bovine coronary arteries. A: a) Degree of relaxation of SMC as a function of level of membrane hyperpolarization under normal conditions, b) electrical and mechanical responses for same experiment; B: a) degree of relaxation of SMC as a function of level of membrane hyperpolarization during potassium depolarization, b) electrical and mechanical responses in same experiment. Arrows indicate on and off of hyperpolarizing current. B: b, a', b') Records of contractile and electrical responses respectively, with small sweep, b, c') AP and anelectrotonic potentials recorded with large sweep. Graphs: abscissa, degree of relaxation of SMC (in %); ordinate, amplitude of AE (in mV). Maximal relaxation of SMC during AE taken as 100%.

sus duration of stimulation was a straight line. With a further increase in the duration of the stimulating current this proportionality was disturbed because of saturation of the contractile response (Fig. 2A, B).

The experiments showed that muscle strips from the coronary vessels possess initial tone, the value of which depends on the resting potential (RP) of the muscle cells (the results of one experiment, in which the effect of hyperpolarization of the membrane on tonic

contraction of SMC of the coronary arteries was studied, are given in Fig. 3). It will be clear from Fig. 3 that with only a very small shift of RP to the positive side relaxation of the muscle was observed. The degree of relaxation increased with an increase in the level of hyperpolarization. Maximal relaxation occurred when AE was 3-4 mV. A further increase in membrane hyperpolarization had hardly any effect on the degree of relaxation (Fig. 3A, a, b). The degree of relaxation continued as a linear function only as far as AE of 0.5-3 mV. A shift of RP toward hyperpolarization was thus always accompanied by a decrease in tonic contraction. By contrast a shift of RP toward depolarization (by the action of a polarizing current) had no effect on tonic contraction. Moreover, contraction was absent even when slow depolarization occurred at the beginning of CE. One cause of the absence of contraction in response to catelectrotonic depolarization may perhaps be the marked degree of rectification of the membrane of the muscle cells, which prevented any substantial shift of RP in the downward direction. Accordingly, in the next series of experiments K^+ was used as the depolarizing agent.

Data on responses of SMC of the coronary vessels to the action of 160 mM K^+ are given in Fig. 3b. Exposure to a high concentration of potassium caused depolarization of the membrane and contraction of the muscle cells. This depolarization at the beginning of its development consisted of two phases: initial — slow, and subsequent — fast. When slow depolarization reached a critical level (5 mV), this phase then switched to fast depolarization, i.e., an action potential (AP) was generated. During the action of K^+ partial repolarization of the membrane took place, after which the membrane potential was stabilized (Fig. 3B, b, b'). Simultaneously recording of the electrical and contractile responses during potassium depolarization (fast sweep) showed that during the action of K^+ the contractile response also consists of two phases: an initial slow tonic and a subsequent fast contraction. The slow contraction corresponds to the initial slow potassium depolarization, fast contraction to the AP.

A decrease in potassium depolarization of SMC by the action of a hyperpolarizing current showed that the degree of relaxation depends on the amplitude of AE (Fig. 3B, b, a', b', c'). Under these circumstances the degree of relaxation was an almost linear function of the amplitude of repolarization (Fig. 3B, a). Stopping the current caused disappearance of AE and the appearance of an anode-breaking response, accompanied by restoration of tonic contraction of the muscle to its original level (Fig. 1B, b, a', b', c'). With relatively weak hyperpolarization (AE) stopping the current was not accompanied by an anode-breaking response (Fig. 3B, b, b', c'). The amplitude of the anode-breaking response was determined chiefly by the degree of anelectrotonic polarization of the SMC membrane. The fact that during hyperpotassium depolarization the repolarization phase of the anode-breaking response was considerably increased can evidently be explained by the absence of an outward potassium current, for the K^+ concentration was approximately the same inside and outside the muscle cells.

It can thus be concluded from the results that SMC of the coronary arteries have well-marked rectifying properties, and the fact that spike potentials of SMC of the coronary arteries are potassium in nature [7] may possibly indicate that the fast contraction is activated by the same Ca^{++} ions that participate in spike generation and enter the muscle cells through fast potential-dependent calcium channels.

The second (tonic) component, however, evoked by long-lasting potassium depolarization or by depolarization by a steady electric current also is activated, evidently, mainly by extracellular Ca^{++} ions, entering through the so-called slow potential-dependent calcium channels of the plasma membrane.

In the initial state the calcium channels of muscle cells are in an open state and they help to maintain tonic contraction of the muscle cells on the coronary arteries. Since anelectrotonic hyperpolarization of SMC is accompanied by relaxation of the strip on account of inactivation (closure) of these channels, deliberate action on RP of the muscle cells may be an effective means of influencing the initial tone of the coronary arteries.

LITERATURE CITED

1. D. N. Artemenko and M. F. Shuba, Fiziol. Zh. (Ukr.), No. 10, 403 (1964).
2. G. D. Baron, R. N. Speden, and D. Bohr, Am. J. Physiol., 223, 878 (1972).
3. L. Borda, R. Schuchleib, and P. D. Henry, Circ. Res., 41, 778 (1977).
4. P. A. Murray and H. V. Sparks, Circ. Res., 42, 35 (1978).
5. H. Mekata and H. Niu, Jpn. J. Physiol., 19, 599 (1969).

6. U. Peiper and E. Schmidt, Pfluegers Arch. Gesamte Physiol. Menschen Tiere, 337, 107 (1972).
7. W. T. Woods, R. E. Katholl, F. Urthaller, et al., Circ. Res., 44, 182 (1979).

VARIABILITY OF THE SINUS RHYTHM OF THE HEART DURING DEEP BREATHING

B. M. Tsukerman, A. M. Svetukhin,
A. R. Abul'khanov, K. A. Sergeeva,
and V. A. Kryukov

UDC 612.213:612.172.2

KEY WORDS: sinus rhythm; statistical parameters; physiological arrhythmia; severity of state.

Ever increasing attention is being paid nowadays to the study of the characteristics of the sinus rhythm of the heart as an important source of information on a person's state. This information is obtained from long-term continuous recording of the ECG (2-5 min), by calculating various statistical characteristics of the sequence of RR intervals of the ECG. This approach has been used to study neurohumoral regulation of the cardiac rhythm [1] and also to study problems in applied physiology. In particular, investigation of the characteristics of the sinus rhythm is widely used in aviation and space physiology [2], in sport physiology [3], work physiology, and engineering psychology [4]. Finally, analysis of the cardiac rhythm is becoming increasingly important in clinical physiology. It has been found that the greatest change in the sinus rhythm (physiological arrhythmia) occurs in healthy people; when pathological states (essential hypertension, angina pectoris, myocardial infarction, burns, etc.) arise the intensity of the physiological arrhythmia is reduced and an absolutely regular pulse may be established [5]. These features of the behavior of the sinus rhythm have enabled its analysis to be effectively used as a means of monitoring preoperative preparations and the patient's state during operations [6], to predict postoperative complications [7], for individual selection of drugs for the treatment of disturbances of cardiac rhythm [8], and in many other cases.

During investigation of the characteristics of the sinus rhythm of the heart, attempts have been made to increase their information content by the use of various function tests. The orthostatic test [9] and graded physical exertion [10] are most frequently used. Various pharmacological tests, such as injection of atropine [11], also are used.

A promising trend in the investigation of variability of the sinus rhythm is the development of methods for the objective evaluation of the severity of a patient's state on this basis. To increase the informativeness of the investigation, function tests must evidently be useful in this case also. The function tests already mentioned, as a rule, cause an increase in the pulse rate and a decrease in physiological arrhythmia; however, the cardiac rhythm may also change in the same direction under the influence of diseases. Accordingly, in patients with acquired heart disease the results of a function test with physical exertion have proved uninformative [12]. This points to the need for carrying out a function test which would cause a shift in the opposite direction, i.e., which would increase the dispersion of the rhythm. Breathing with increased depth of inspiration has been shown to have this effect [13]. This suggested that the change in variability of the sinus rhythm of the heart during deep breathing might prove a useful indicator of the functional state of the subjects tested. The object of the present investigation was to test this hypothesis.

EXPERIMENTAL METHOD

Three groups of patients with suppurating wounds, admitted for treatment to the A. V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, were investigated.

Laboratory of Physiology, A. V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR M. I. Kuzin.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 90, No. 10, pp. 389-391, October, 1980. Original article submitted April 10, 1980.

 0007-4888/80/9010-1320$07.50