MECHANICAL ACTIVITY OF THE VASCULAR WALL: CHOICE OF OPTIMAL CONDITIONS FOR STUDYING ISOLATED ANNULAR SEGMENTS

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Mechanical activity of isolated preparations of blood vessels can be determined by physiological investigations and by a study of the action of new drugs. This can not only broaden our ideas on physiological mechanisms of regulation of vascular tone and its disturbances in certain pathological states, but it can also help us to judge the effectiveness of different kinds of medical treatment of diseases. The use of isolated preparations, free from hormonal and nervous regulatory influences, also greatly simplifies the interpretation of the results. However, the results of experiments in vitro depend on the conditions under which mechanical activity of the muscle cells is tested. Usually these investigations are conducted under isotonic, isometric, or auxotonic conditions [1]. The conditions differ considerably from those under which muscle cells of the vacular wall function in vivo. For example, in thin-walled blood vessels with constant transmural pressure, the ratio of complete stretching to the radius remains unchanged.

This paper describes what, in our opinion, are the optimal conditions for investigation of isolated annular segments of blood vessels in vitro.

EXPERIMENTAL METHOD

Inside blood vessels the hydrostatic pressure is higher than that of the external medium. The pressure is balanced by the tension in the vessel wall which, together with the level of smooth muscle activity, determines the diameter of the vessel. Let us examine the behavior of a thin-walled vessel exposed to the action of hydrostatic pressure from within. The tension in the vessel wall of such vessels is defined by the equation: $F = P \cdot R$, where F is the tension, i.e., the stretching force by unit of length, P the pressure within the vessels, and R its radius [3]. It will be clear from this equation that if the pressure P inside the vessel is constant, the ratio of total tension to radius must also be constant. To investigate the mechanical activity of the vascular wall in vitro, a ring is cut out of the vessel by means of a special die, and it is fitted on a holder. After the specimen has been removed from the animal, it is no longer subjected to the force of hydrostatic pressure. However, the effect of pressure on the vascular wall can be simulated by a model. For this purpose, the same relationship must be maintained between the force developed in the segment F_p and the distance between the two holders L as between $F \cdot \ell$ and $\pi \cdot R$:

$$\frac{F_p}{2L} = \frac{F \cdot l}{\pi \cdot R} = \frac{P \cdot l}{\pi}, \text{ whence } F_p = \frac{2 \cdot P \cdot l}{\pi} \cdot L,$$

where ℓ is the width of the segment and L is half the circumference of the segment. The relationship between the force developed by the segment of vessel and its circumference, when mechanical activity is measured under different conditions, is shown schematically in Fig. 1. Isometric contraction (the length of the circumference of the segment remains constant) is illustrated in Fig. 1a, isotonic (the force developed is recorded) in Fig. 1b,

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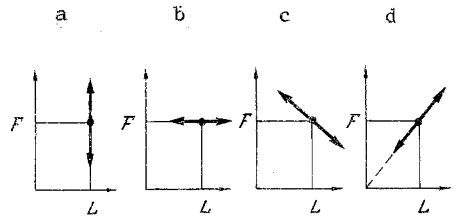

Fig. 1. Force developed by segment and length of its circumference when measured under different conditions. Abscissa, lengthening; ordinate, force.

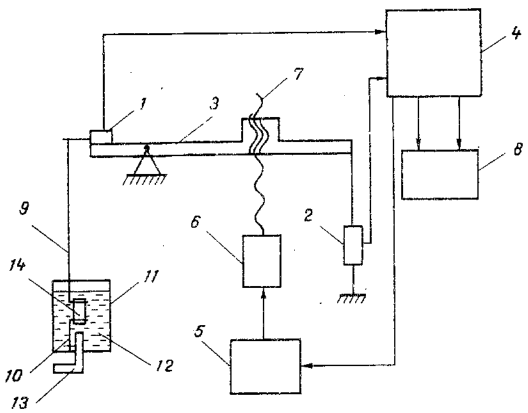

Fig. 2. Block diagram of apparatus: 1-8) explanation in text; 9, 10) holders; 11) constant temperature chamber; 12) solution; 13) oxygenation system; 14) specimen.

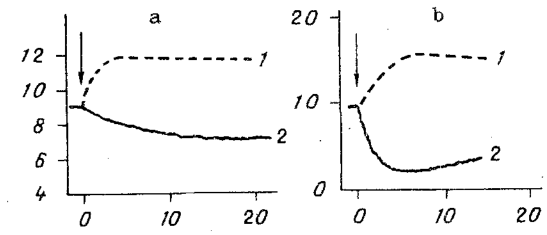

Fig. 3. Change in force developed by segment of vessel on measurement under isometric (1) and isobaric (2) conditions after addition of KCl (a) and NA (b). Abscissa, time (in min); ordinate, developed force (in g). Arrow indicates time of application of substance.

and auxotonic (an elastic element — a spring — is introduced into the system) in Fig. 1c. The relationship illustrated in Fig. 1d characterizes "isobaric" contraction. This state of affairs can be realized by using the feedback principle, i.e., with the aid of an automatically controlled system. A block diagram of such a system is shown in Fig. 2. The system contains transducers of force 1 and length 2, a bracket 3, a unit for programmed alteration of the diameter of the annular segment 4, the step motor control unit 5, a step motor 6, drive 7, and recorder 8. A fuller description of the system is given in [2]. The character of the required relationship between force developed by the segment and its diameter is assigned by the unit for programmed alteration of diameter 4, these values are measured, and if they do not agree with the chosen relationship, a mismatching signal is applied, triggering the effector mechanism 6 and 7. Thus at any moment of time, and during any change in the state of the vascular system, the developed force and diameter are adjusted and the ratio between them remains unchanged. In this way isobaric conditions are created for the muscle cells of the vessel wall to function, i.e., conditions are as near as possible to the mechanical conditions of the intact organism.

EXPERIMENTAL RESULTS

Graphs illustrating the use of the suggested isobaric conditions for investigating isolated annular segments are given in Fig. 3. The effect of KCl and noradrenalin (NA) on changes in the state of the wall of the dog's femoral artery was investigated. By means of a special die standard specimens were cut out, with an external diameter of 5 mm. Before the experiment started, the initial conditions in the system were assigned as follows. The unit assigning functional relations between the force developed by the specimen and its diameter was tuned according to the ratio between F_p and L given above. The "pressure" was chosen to be 80 mm Hg. Since the segment was 5 mm in length, the coefficient $\frac{2 \cdot P \cdot l}{\pi}$ was established as equal to 33.5 N/m.

After the initial conditions had been assigned the specimen for testing was fitted on the holders and immersed in a constant-temperature bath containing Henseleit's solution. The unit assigning functional relations was switched on, and in accordance with the assigned initial conditions and the state of the vascular wall, set the values of L and F_p in the specimen.

Next, KCl was added to the cuvette in a final concentration of 60 mM or NA in final concentrations 1 μm, and the force developed by the specimen was recorded throughout the experiment.

The continuous line in Fig. 3a, b denotes measurement of force developed by the specimen after application of KCl and NA, and measured under isobaric conditions. The broken line shows changes in force developed by the specimen under the influence of the same concentrations of KCl and NA measured under isometric conditions.

It will be clear from these results that, when tested under isometric conditions, KCl and NA increased the developed force by 35 and 55% respectively. Investigations using the suggested method show that, during exposure to the same factors, the force developed by the specimen was reduced by 22 and 77% respectively. Changes in the kinetics of development of the processes in the vascular wall after application of KCl and NA were observed.

To conclude, the suggested system is able to model more complex physiological situations also: responses of thick-walled vessels or the action of a variable hydrostatic pressure on the vessel wall. In these cases, more complex parameters, or parameters varying with time, for relations between the force developed by the test segment and its diameter are assigned by the unit 4, programming the change in diameter. The use of computers makes realization of the experimental conditions substantially easier.

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