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ACTIVITY OF THE RIGHT CARDIAC VENTRICLE AND METABOLISM IN HEALTHY PERSONS DURING AN ORTHOSTATIC TEST AFTER SHORT-TERM IMMOBILIZATION

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16. Abstract A 15-minute orthostatic test was performed on healthy male volunteers under conditions of catheterization of the right ventricle of the heart and the radial (or brachial) artery before and after 5-day bedrest in an antiorthostatic position of the body (with the foot of the bed raised 4.5 degrees). The change to a vertical position after immobilization was attended by a more marked increase in the rate of cardiac contractions, an increase of max dp/dt pressure in the right ventricle, and a decrease of cardiac and stroke indices. The decrease of the cardiac index was compensated for, to a certain measure, by a further increase in the extraction and utilization of O_2 by the tissues. The arterial blood pH did not change essentially, while the decrease in pCO_2 and content of standard bicarbonate was more marked.

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ACTIVITY OF THE RIGHT CARDIAC VENTRICLE AND METABOLISM IN HEALTHY PERSONS DURING AN ORTHOSTATIC TEST AFTER SHORT-TERM IMMOBILIZATION

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A combination of immobilization with gravitation redistribution */36 of blood observed in clinics for patients with strict bedrest or in healthy persons during space flight leads to orthostatic instability of blood circulation. The latter is evidenced by hypotonia, pronounced tachycardia and a sharp decrease in the stroke volume of the heart [6, 8, 12, 15]. It is still unknown how intracardiac hemodynamics and the ionotropic state of the myocardium change and also their interaction with the metabolic activity of tissue and oxygenation of the blood. Moreover, this presentation of the question makes it possible to deepen the concept of causes for orthostatic instability and to move on to development of effective means for its prophylaxis and therapy. The purpose of this work was to study the effect of short-term antiorthostatic hypokinesia (ANOG [antiortostaticheskaya, gipokinesiya, antiorthostatic hypokinesia, ANOH]) on the activity of the right cardiac ventricle and the metabolism of a healthy person during orthostatic tests.

METHOD

The studies were conducted on healthy male volunteers (average age 30, height 175 cm, weight 73 kg, body surface 185 cm^2), who had passed a thorough medical examination. Several days before the studies, an orthostatic test was conducted without intravascular and intracardiac manipulation and then nine test subjects had it re- /37 peated in catheterization conditions (contol). Of these, five men

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*Numbers in the margin indicate pagination in the foreign text.

were subjected to the effect of ANOH. The latter was modeled using five-days strict bedrest with an antiorthostatic position of the body (the foot of the bed was raised 4.5°); after this, the test subject again underwent the orthostatic test using invasive methods for the study. It was carried out on a rotating table which allowed the test subject to be put in a position 80° head upward for 15 minutes. After the orthostatic test, catheterization was done [1] and blood samples were taken for a total volume of 250-300 ml which were partially complemented with a physiological solution. During the test, one of the catheters (Kurnand No. 7) was in the cavity of the right cardiac ventricle and the other (teflon) -- in the radial or brachial artery.

Pressure was measured by Statham P 23 Db electromanometers which were placed at the level of the right auricle. The derived pressures in the right ventricle of the heart (+max dp/dt, max dp/dt/P, -max dp//dt) were obtained by means of electronic differentiation and subsequent calculations in which the presence of their peculiarities were considered [7, 13]. The hemodynamic indices were recorded on a Siemens-Elema apparatus. The minute volume of the heart was determined by the Fick's direct method and all of the indices studied were recorded; blood samples were taken between the 13th and 15th minute of the test. The hematologic indices were recorded on an American Optical Comp. apparatus, the gas composition of the blood -- on a micro-Astrup apparatus, the content of glucose was determined by a gluco-oxidase method [10], insulin was determined by a radio immune method [3]. The concentration of lactic acid was determined according to the Barker and Summerson method [5] and the β-lipoproteides by a turbidimetric method [2].

A statistical analysis was conducted using the Student t criteria.

RESULTS AND DISCUSSION

In the control in two subjects at the 5th and 13th minutes of the orthostatic test, a pre-collapse state occurred and in the latter case when taking a blood sample from the right cardiac ventricle an accompanying group of ventricular extrasystoles. After the ANOH, the precollapse state occurred in one of the test subjects at the 4th minute of the test. Thus, the frequency of occurrence of precollapse states in the control and after ANOH was uniform and amounted to 20-22%.

The systolic pressure in the right cardiac ventricle during the orthostatic test in the control was decreased whereas +max dp/dt was essentially unchanged; on the other hand, after ANOH, the pressure was not changed and the first derivative was markedly increased (see Table). The directionality of changes and absolute values of arterial pressure were approximately the same.

PRESSURE IN THE RIGHT CARDIAC VENTRICLE AND ITS DERIVATIVE DURING AN ORTHOSTATIC TEST IN THE CONTROL AND AFTER ANOH (M ± m)

	Control			After ANOH		
Index	Initial	Orthostatic Test	Δ	Initial	Orthostatic Test	Δ
RVP_s mm Hg	21,0±0,6	17,6±1,3*	−3,4	19,7±0,6	19,5±1,8	−0,2
RVP_{in}	1,5±0,3	−1,1±1,0**	−2,6	2,0±0,8	−0,6±0,9**	−2,6
RVP_{ed}	4,9±0,5	−1,9±0,7**	−6,8	5,8±0,8	−0,8±0,5**	−6,6
+max dp/dt, мм рт. ст.×$с^{-1}$	97,1±3,6	110,5±7,5	+13,4	83,1±4,1	134,5±17*	+51,4
max dp/dt/p×$с^{-1}$	8,6±0,2	8,2±0,4	−0,4	7,7±0,3	7,3±0,9	−0,4
−max dp/dt, мм рт. ст.×$с^{-1}$	110,9±5,6	128,0±19,1	+18,0	131,2±7,0	150,3±13,7	+19,1

* $P<0{,}05$.
** $P<0{,}01$.

Notation. RVP_s, RVP_{in}, RVP_{ed} -- are systolic, initial and end diastolic pressure in the right cardiac ventricle; +max dp/dt is the maximum rate of increase of RVP_s; max dp/P -- is the ratio of max dp/dt to the pressure developed at this moment by the ventricle (Veragut index); -max dp/dt is the maximum rate of pressure drop in the ventricle.
[The commas in this Table and all succeeding Tables and Figures signify decimal points].

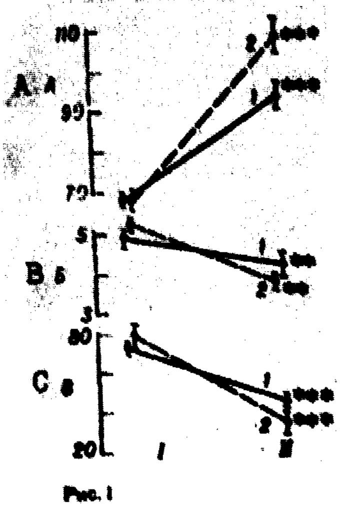

Fig. 1. The frequency of cardiac contractions, cardiac and stroke indices during the orthostatic tests in the control and after ANOH. Along the axis of the abscissa -- are the average indices before and after the orthostatic tests (I and II): I - control, II - after ANOH; along the ordinate axis A is the frequency of cardiac contractions per minute, B is the cardiac index, ℓ/min/m^2, C - is the stroke index, mℓ/m^2.

After ANOH in a vertical position, the increase in the frequency /38 of cardiac contractions and also the decrease in cardiac and stroke indices were more pronounced (Figure 1). Then, the increase in total peripheral resistance after ANOH amounted to 68% at the same time that in the control it was only 37%. Both in the control and after ANOH, the orthostatic test did not lead to a change in the pH of arterial blood, the pCO_2, the content of standard bicarbonate was decreased (Figure 2). The content of O_2 in the arterial blood was practically unchanged whereas in the mixed venous blood it was noticeably decreased due to a decrease in saturation of the hemoglobin by oxygen; as a result of this, the arterial venous difference for O_2 was increased both in the control and after ANOH. The coefficient of utilization of O_2 in orthostasis also increased whereas after ANOH it was higher than in the control.

The indices of carbohydrate metabolism both in the control and after ANOH were essentially unchanged. One should note a tendency toward a decrease in the content of β-lipoproteides which was already noticeable after immobilization.

The orthostatic test was subjectively fairly severely experienced by the test subjects even in the control with the use of catheterization and the manipulation accompanying it. In the test subjects who underwent a test without the use of invasive methods of research, the precollapse state did not occur and the orthostatic reaction

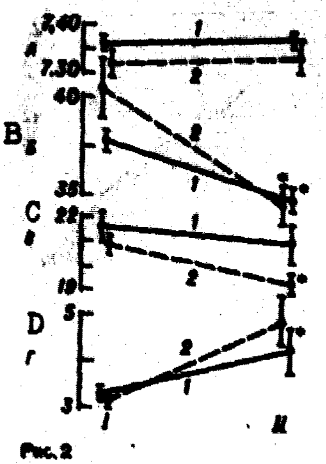

Fig. 2. The indices of the acid-alkaline state of arterial blood and arterial venous difference in oxygen during an orthostatic test in the control and after ANOH. **P<0.001; ***P<0.001. Along the axis of the ordinate A - is the pH of the blood, B - is the pCO_2, mm Hg C - is the standard bicarbonate, meqv/ℓ, 1 - is the arterial venous difference in oxygen, vol. %. *P<0.05. The remaining symbols are the same as in Figure 1.

was less pronounced. In this study, the percent of precollapse state in the control and after ANOH was the same and therefore can lead to the impression that the procedure itself of probing is capable of masking the immobilization effect. In this connection there is particular interest in an analysis of the peculiarities of a similar type of experiment [8] which made it possible to come to the following conclusions: 1. During standarization of research conditions the results obtained during catheterization of healthy persons before and after bedrest, including the time of orthostatic tests, are correct and valid. 2. The cause for breakdown in orthostatic stability is not the probe but the breakdown in circulatory homeostasis which is particularly clearly apparent during intracardiac and intravascular interference. 3. The use of invasive methods in a similar type of study is expedient and necessary inasmuch as they are low and make it possible to precisely evaluate changes in basic indices of circulation and obtain blood samples for biochemical analysis from different sections of the cardiovascular system.

Inasmuch as the research conditions in the control and after ANOH were identical, we could successfully detect a number of peculiarities of the effect of immobilization on the central circulation, the activity of the right cardiac ventricle and the metabolism of a healthy man during an orthostatic test.

After ANOH, the conduct of the orthostatic test was accompanied by more pronounced tachycardia and more noticeable decrease in cardiac and stoke indices. Similar changes recorded earlier by other authors are characteristic for the state of the cardiovascular system which occurs after bedrest or weightlessness [6, 8, 12, 15]. Then, attention is turned to the fact that tachycardia which occurs after remaining in weightlessness always is accompanied by hypotonia but the increase in frequency of cardiac contractions after bedrest is not accompanied by a decrease in arterial pressure [6] as would be expected in this study. The indices of the inotropic state of the right cardiac ventricle were also changed unevenly. For instance, the Veragut index which reflects, in the opinion of many authors, the "true"index, that is, hardly depending on the extracardiac factors of contractability of the cardiac muscle, essentially was unchanged both in the control and after ANOH. On the other hand, the rate of increase of intraventricular pressure after ANOH was noticeably increased at the same time that it was unchanged in the control. The increase of this index after immobilization can be evidence of an increase in the requirement for O_2 by the myocardium. It is well known that the value (dp/dt) of the intraventricular complex of pressure depends on a number of factors including the load of resistance, volume and frequency of cardiac contractions which are extremely important. Inasmuch as after immobilization in orthostasis, the resistance load of the right cardiac ventricle, in comparison with the control, is even increased [8], then tachycardia (the Bowditch effect) acquires the greatest significance in the increase of this index. Quickening of the frequency of cardiac contractions in orthostasis, more pronounced after immobilization, is due to the increase in activity of the sympathetic section of the vegetative nervous system and the β-adrenoreceptors of the myocardium [6, 9, 12, 14, 15]. However, in these conditions it apparently is not physiologically proven inasmuch as it is accompanied by a decrease in effectiveness of operation of the myocardium; a comparison of the increase in rate of intraventricular pressure and probably the requirement by it for O_2 with a decrease in the stroke index is evidence of this. Actually, as a result of the decrease in tachycardia by the introduction of β-adrenoblocking agents, the reaction of blood circulation is noticeably improved in the orthostatic test after 2-3 weeks of bedrest [12, 15].

The combination of tachycardia with respiratory alkalosis as was observed after ANOH, when the pCO_2 of the arterial blood was decreased more noticeably than in the control, is particularly undesirable. In this case, the probability of a breakdown in blood supply to the myocardium is increased as a result of a decrease in the coronary blood flow due to hypocapnia. To eliminate the unfavorable effect of the combination of these factors, some authors recommend a single inhalation of a 5% mixture of CO_2 and the injection of β-adrenoblocking agents [4]. An increase in hyperventialation after ANOH creates an unfavorable situation for blood supply to the brain because it leads to an increase in the tone ofprecapillary blood vessels and a shift in the curve of dissociation of oxyhemoglobin to the left (the Bohr effect). Inasmuch as the perfusion pressure in the aorta in the control and after ANOH was practically identical, the most important factor in leveling these changes was apparently played by the metabolic control of the brain tissue. Probably, the latter was ade- /40 quately effective thanks to which, after ANOH, we did not observe an increase in the number of cases of breakdown of cerebral blood circulation.

Transfer to a vertical position, as is known [11], is accompanied by a transitory hypoxia and a decrease in consumption of O_2 in the mixed venous blood; this once again is confirmed in our study. After immobilization, these changes are accompanied by more pronounced catecholemia [6] as a result of which, apparently, a shift toward metabolic acidosis becomes more pronounced. However, inasmuch as the concentration of lactic acid during the orthostatic test was unchanged, it is possible to assume that even in spite of the decrease in the cardiac index, the specific weight of the anaerobic phase of oxidation was the same as in the control. The supply of O_2 to the tissue in these conditions is accomplished by an increase in its extraction and use; the increase in arterial venous difference in oxygen and the coefficient of its utilization is evidence of this.

REFERENCES

1. Gazenko, O. G. V. I. Shumakov, Yu. M. Volynkin, et al., Kosmicheskaya biol., 5, 47-51 (1977).

2. Ledvina, M. Labor. delo, 3, 13-17 (1960).

3. Fedotov, V. P. and Ya. A. Dokolov, Sovremennyye voprosy endokrinologii [Modern questions of endrocrinology], Moscow, 4th edition, 1972, pp. 186-202.

4. Alexander, C., and L. U. Sheman-Ming, Cardiovas. Res. 10, 341-348 (1976).

5. Barker, A. and W. Summerson, J. biol. Chem. 138, 535-554 (1941).

6. Chobanian, A., R. Liller, A. Tercyak, et al., Circulation 49 551-559 (1974).

7. Curtiss, E., P. Reddy, J. O'Toole, et al. Ibid. 53, 997-1004 (1976).

8. Hyatt, K., L. Kamenetsky and W. Smith, Aerospace Med. 40, 644-650 (1969).

9. Ibrahim, M., R. Tarazi and H. Dustan, Am. Heart J. 90, 513-520, (1975).

10. Kadish, A., R. Little and J. Sternberg, Clin. Chem. 14, 116-131 (1968).

11. Loeppky, J. and U. Luft, J. appl. Physiol. 39, 43-47 (1975).

12. Melada, G., R. Goldman, J. Lentscher, et al., Aviat. Space Environm. Med. 46, 1049-1055 (1975).

13. Oboler, A., J. Keefe, W. Gaasch, et al., Cardiology 58, 32-44 (1973).

14. Spodick, D., M. Meyer and J. Pierre, Am. Heart J. 83, 719-722 (1972).

15. Zager, P., R. Goldman, J. Leutscher, et al., Ann. Sci. Meet. Aerospace Med. Ass. Prepr., 183-184 (1975).