PHYSIOLOGY

Effects of Intermittent Hypoxic Training on Orthostatic Reactions of the Cardiorespiratory System

Zh. A. Donina, I. N. Lavrova, and M. A. Tikhonov*

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The possibility of using intermittent hypoxic training for stimulation of physiological mechanisms underlying the compensatory hemodynamic reactions to orthostatic load was studied in animal experiments. Intermittent hypoxic training had a favorable impact on circulatory reactions, which manifested in stabilization of blood pressure and heart filling pressure and in a decrease in orthostatic hypotension during the initial period of orthostasis. We hypothesized that the positive effect of intermittent hypoxic training on the correction of negative hemodynamic shifts is determined by the training effect aimed at the increase in the vascular tone and venous return to the heart. These results can serve as validation for preventive use of intermittent hypoxic training for reducing blood draining in the lower part of the body, correction of the compensatory orthostatic reaction of the circulatory system, and hence, for improvement of orthostatic resistance.

Key Words: *zero gravity; orthostatic instability; intermittent hypoxic training*

The absence of hydrostatic blood pressure under conditions of zero gravity, rearrangement of the circulatory and neurohumoral homeostasis, modification of afferent pulsation from the muscle proprioreceptors, and hypodynamia are the main causes of more pronounced orthostatic reactions of the cardiovascular system in aeronauts after space mission in comparison with the pre-mission period [3-5].

Therefore, the development of preventive means aimed at improvement of the orthostatic resistance is one of the main trends of aerospace medicine.

Methods simulating the hydrostatic pressure (air cuffs, anti-hypergravitation overalls, negative pressure for the lower part of the body, *etc.*) are used for prevention of the main consequences of zero hydrostatic pressure under conditions of weightlessness and orthostatic disorders after the mission [1,3]. Intermittent hypoxic training (IHT, inhalations of hypoxic mixture alternating with normoxic respiration) is widely used for the prevention and treatment of various diseases, improvement of nonspecific resistance to unfavorable environmental factors, exercises, and professional activity [2,6,7]. However, the use of IHT for preventing the reactions caused by the absence of hydrostatic blood pressure under conditions of zero gravitation and in on-earth experiments simulating physiological effects of zero gravity (antiorthostatic hypokinesia, immersion model of weightlessness) was in fact never studied. Hypoxic exposure during head-down tilt associated with reorganization of the mechanisms of nervous and humoral regulation of autonomic functions can be a means improving not only nonspecific resistance, but also preventing the de-

Laboratory of Respiration Physiology, I. P. Pavlov Institute of Physiology, Russian Academy of Sciences, St. Petersburg; *Institute of Biomedical Problems, Russian Academy of Sciences, Moscow, Russia. ***Address for correspondence***: breath@kolt.infran.ru. Zh. A. Donina

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velopment of sharp hemodynamic disorders during transition to the head-up tilt.

We studied the reactions of the cardiorespiratory system to orthostatic load before and after hypoxic exposure under conditions of a head-down tilt and tried to detect possible mechanisms of IHT effect aimed at alleviation of the negative hemodynamic shifts.

MATERIALS AND METHODS

The study was carried out on 10 rabbits (2.5-3.0 kg) narcotized with urethane (1 g/kg). During the experiment, constant recording of blood pressure (BP) in the common carotid artery and central venous pressure (P_{CVP}) in the anterior vena was carried out by direct catheterization, while intrathoracic pressure (P_{ITP}) was recorded by the balloon graphic method (in the lower third of the esophagus). Pressure transducers PDP-300 and PDP-1000 were used for pressure measurements. Respiration rate was evaluated by intrathoracic pressure fluctuations, HR was evaluated by electrocardiogram recorded using needle electrodes (bipolar lead); the right atrial filling pressure was calculated by the formula:

$$P_{tm}= P_{CVP}-P_{ITP}.$$

Intermittent hypoxic training was carried out by the "return respiration" method (closed cycle respiration), during which hypoxia gradually increased to 12% O_2 over 10 min. Hypoxic exposure was alternating with normoxic respiration. Head-down tilt is a common model for reproduction of zero gravity factors. The orthostatic test was carried out by passive tilting of the animal from head-down to vertical position. The orthostatic test directly after head-down position makes it possible to record the most intensive reactions of circulation to the orthostatic exposure [3]. Each experiment consisted of 3 stages with 1-h intervals; during the experiment, the animals exposed to head-down tilt were exposed to 3 IHT sessions, after which the orthostatic test was carried out. The protocol of stage 1 was as follows: horizontal posture (control), head-down tilt (-30°), orthostatic test (+75°), head-down tilt (-30°), 3 sessions of IHT, and orthostatic test (+75°).

The data were statistically processed using Student—Fisher test.

RESULTS

During the orthostatic test, BP tended to increase from stage to stage, while changes within one stage were negligible. The summary effect of 3 IHT sessions almost completely eliminated the BP drop during the transitional period of the orthostatic test, and in some cases BP corresponded to control values recorded in a horizontal posture. The systolic BP in the orthostatic test before IHT decreased by 21%, diastolic by 32% (p<0.05), while after hypoxic exposure only by 13 and 4%, respectively (p>0.05; Table 1).

The transitional period of passive orthostasis (first seconds) is characterized by a short-term BP drop, followed by its recovery (sometimes partial) during the compensatory phase (subsequent 30 sec). The orthostatic test before IHT was associated with a drop of systolic, diastolic, and mean BP, while after IHT no initial BP drop was observed, and the mean BP was compensated for not during the compensatory phase, but during the transitional period of the orthostatic test at the expense of significant increase in diastolic BP (Fig. 1).

The reduction of heart filling by 60% before IHT was associated with compensatory 5% increase in HR, aimed at venous return increase (Fig. 2). The orthostatic test after IHT did not increase HR, while heart filling pressure surpassed the control values in the horizontal posture by 3%.

Analysis of the respiratory values showed no appreciable differences in respiration rate and intrathoracic pressure in the orthostatic position after

TABLE 1. Orthostatic Reactions of Circulatory System before and after IHT

Parameter		Horizontal posture	HDT -30°	OT +75°	
				before IHT	after IHT
BP, mm Hg	systolic	135.6±7.9	141.9±7.7	112.5±10.0*	124.4±15.0
	diastolic	83.1±7.9	90.0±7.1	61.3±8.9*	86.1±13.2
HR, bpm		257±10	257±19	270±16	248±8
Transmural right atrial pressure, cm H_2O		-2.6±0.9	-0.5±0.8	-4.2±1.3*	-2.5±0.7

Note. OT: orthostatic test; HDT: head-down tilt. *p<0.05 compared to HDT.

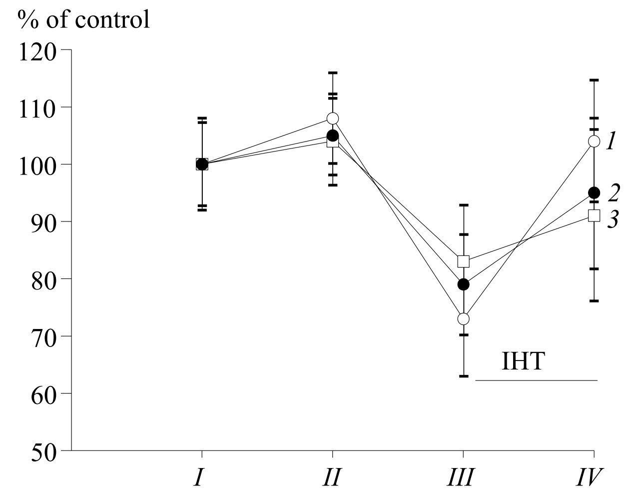

Fig. 1. Dynamics of BP during orthostatic load before and after IHT. *1*) diastolic BP; *2*) mean BP; *3*) systolic BP. *I*) horizontal position (control); *II*) head-down tilt; *III*) orthostatic test before IHT; *IV*) after IHT.

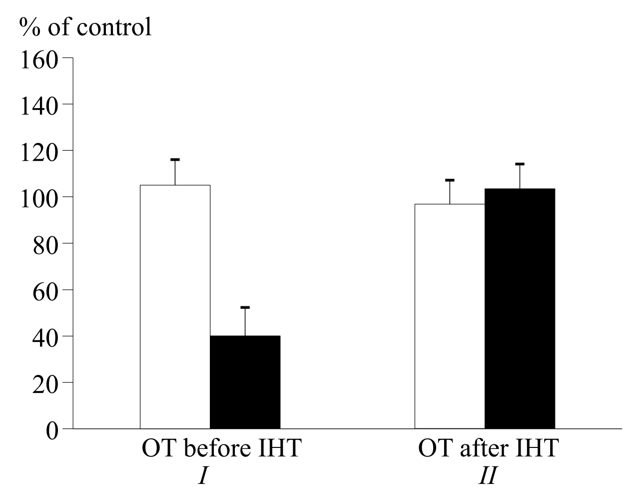

Fig. 2. Dynamics of HR and cardiac filling pressure during orthostatic test before and after IHT. *I*) orthostatic test before IHT; *II*) after IHT. Light bars: HR; dark bars: right atrial filling pressure. OT: orthostatic test.

IHT in comparison with the initial test, carried out before IHT. Minor changes in respiration rate and intrathoracic pressure presumably resulted from the shift of abdominal organs and diaphragm after changing the posture [1].

These findings are comparable with the results of studies demonstrating that breathing hypoxic mixture with gradually decreasing oxygen content caused significant BP rise, while repeated hypoxic exposure led to stabilization and even stimulation of the adaptive mechanisms, which manifested in longer maintenance of BP [7]. It was found that adaptation to short-term hypoxia after repeated exposure developed within one experiment, while the effect of subsequent exposure fortified the previous reactions [7]. Numerous experiments detected significant BP elevation under conditions of augmenting hypoxia [2]. Oxygen insufficiency causes a reflex increase in BP as a result of stimulation of the carotid and aortic chemoreceptors; stimulatory reflective effect (BP elevation) predominates in moderate hypoxia, while sharp hypoxia suppresses the vasomotor center, which leads to BP reduction [6,7].

In addition, the compensatory changes in the circulatory system during tilting are caused, among other things, by reflex vasoconstriction leading to reduction of the venous capacity, increase in venous return, and to HR increase, leading to an increase in cardiac output. However, in our study the orthostatic test after IHT was associated not with an increase (as before IHT), but with a decrease in HR to the control level (Fig. 2). This means that the compensatory activity of the cardiac component decreased in this case, while the participation of the vascular component increased, presumably due to the training effect of IHT aimed at increasing venous tone, which can be regarded as an adaptive reaction promoting the increase in venous return to the heart.

The fact that BP reduction during the initial period of orthostatic reaction depends on its initial level is particularly interesting. The higher is BP in a horizontal posture, the less pronounced is its reduction during tilting and the stronger is the trend to compensation during the final phase. Hence, prolonged (delayed) effect of IHT leading to the increase in the initial BP with each subsequent stage of the experiment promoted intensive recovery of BP as early as during the transitional period of the orthostatic test (Table 1).

The results indicate in general positive effects of IHT on reactions of the circulatory system, manifesting by reduction of orthostatic hypotension during the transitional period of orthostasis. Presumably, one of the mechanisms of positive effect of IHT on the correction of negative hemodynamic shifts is the training effect aimed at the increase in vascular tone and venous return to the heart. These data can serve as validation for preventive use of IHT for reducing blood deposition in the lower part of the body, correction of the compensatory orthostatic reactions of the circulatory system, and hence, improvement of orthostatic resistance.

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