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Research Article

Controlled Breathing Plays an Important Role during the Adaptation to Highland

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Abstract: Possibilities for adaptation to highland conditions with the method of controlled breathing are investigated. It's revealed, that voluntary decreasing of respiratory rate (to 6 in minute) of pupils living in highland improves the heart functioning. It's shown the possibility to correct the disturbances revealed during the investigation by using of the method of controlled breathing.

Keywords: Adaptation to high altitude, Respiratory rate, Cardiovascular system, Controlled breathing.

INTRODUCTION

In recent years, there has been an increasing population living at high altitude (HA) due to immigration, work duty or tourism. With an increasing population living at a high altitude, the impact of high altitude residence on human cardiovascular functions has raised concerns [4].

The biochemical and physiological processes which meet the organism's vital activity is stipulated by the normal activity of the respiratory system. The respiration cycle is an intermittent process repeated during whole life. Its role is not limited with oxygen inspiration and assimilation, and carbon dioxide expiration. Respiration also regulates the rate of oxidative reactions, the work of cardiovascular system, the course of energetic metabolism, the synthesis of ATP etc.

The overall purpose of the respiratory system is to provide oxygen for metabolism and eliminate the carbon dioxide produced. In the steady equilibrium state oxygen uptake at the lungs is matched to oxygen consumption by the tissues, and carbon dioxide elimination at the lungs is matched to carbon dioxide production by the tissues.

The respiratory control system accomplishes this goal by adjusting pulmonary ventilation. The partial pressure of oxygen is kept at a level sufficient to supply tissue metabolic requirements. The partial pressure of carbon dioxide in the tissues is kept at a level that ensures hydrogen ion concentrations remain within the limits necessary for protein function.

The regulation of respiration is a complex circuit of different processes. It may be influenced by oxygen and carbon dioxide content in atmosphere, by barometric pressure, by different pathological events in organism etc. The most important for the respiration humoral regulation is the tension (partial pressure) of oxygen (PaO_2) and carbon dioxide ($PaCO_2$) in arterial blood, but the interaction of these two components is quite complicated.

The influence of arterial CO_2 partial pressure on cerebral autoregulation (CA) is well known. It has been characterized in the frequency domain [22]. The PaO_2 also influences at the breathing rate and oxygen assimilation. The deficiency of oxygen in organism may lead to hypoxy.

Nowtime because of the scientific and technical progress, air pollution increase, changes of the climate, wide using of tobacco and allergy there is an increase of respiratory system's illness. The most frequent illneses of the respiratory system are: acute larengytis, acute tracheitis, acute and chronic bronchitis, bronchial asthma, pleuritis, lung-cardiac insufficiency, bronchoectotic illnesses, and abscecces. The primary in occurance of malignances is lung tumor. It makes actual the effective treatment of respiratory organs and using of appropriate methods for the illness prevention.

One of such methods includes special trainings to strengthen respiratory muscles, to enlarge the mobility of the chest and diaphragm, to increase the elasticity of pleural membranes, to improve the mechanisms of breathing regulation and movements' coordination. The depth and frequency of breathing to some extent can be changed voluntary. It's a basic of breathing training.

Previous work [11] has shown respiratory rate to have powerful physiological effects, for example, on cardiac baroreceptor sensitivity (BRS) independent of direct effects on arterial blood pressure (ABP). Physiological studies have employed various controlled respiratory rates in the spectral analysis estimates of, for example, cerebral autoregulation (CA) using 6 breaths/min [8, 26], and cardiac BRS using 15 breaths/min [11]. However, work using the Valsalva and Mueller manoeuvres [7, 25, 29] has shown that changes in intrathoracic pressure can have a strong influence on the cerebral blood flow velocity (CBFV) response to transient changes in ABP. As the changes in intrathoracic pressure are likely to differ at different breathing rates, we postulate that this may influence estimates of cardiovascular functions.

To date, it is not clear what the effects of synchronized breathing at lower rates might be on cardiovascular functions. Breathing at different frequencies will induce oscillations in ABP that will change the heart work. These considerations led to the main hypothesis of our present study that synchronized breathing at different rates (e.g. 6 breaths/min) will have a significant influence on cardiac functions with results obtained during spontaneous breathing. Eames *et al*. [10] consider that the rate 6 breaths/min is the most effective.

Different controlled respiratory rates have been used in physiological studies where CA [8, 26] or cardiac BRS [25] have been measured. Disproportionately large changes in CBFV relative to the change in ABP have been recorded during the release phase of the Valsalva manoeuvre [7] and, on a smaller scale, changes in intrathoracic pressure during normal breathing may also add to CBFV variability on a breath-by-breath basis independent of their effects on ABP. Other sources of CBFV variability could be associated with systemic changes in mean $PaCO_2$ or oxygen tension, central modulating mechanisms, intrinsic cerebral vasomotion or mental activation [15, 27, 30]. Controlled respiratory rates might potentially control some of these variables by reducing the randomness of the respiratory effects and by ‘clamping’ mental activation through concentration on the light-emitting diode.

In other studies, changes thought to reflect impairment of CA with mean $PaCO_2$ levels have been seen using transfer function and time domain analysis when partial end tidal volume of CO_2 increased by 5 mmHg or more [22, 39]. Coherence function and gain frequency response increased for frequencies below 0.05 Hz, and phase frequency response decreased in the frequency ranges 0.02-0.1 Hz [22] and 0.07-0.20 Hz [39]. The coherence functions for the different controlled respiratory frequencies were significantly different from one another at the fundamental respiratory frequencies and their multiple harmonics, and the coherence function for all of the controlled respiration data was periodically higher and lower compared with the data recorded with spontaneous respiration. The observation showed that at 6 breaths/min, in contrast with the other respiratory frequencies, the peak in coherence at the fundamental frequency was lower than its first harmonic, could be interpreted as a sign of autoregulation in that frequency range that is less effective with increasing frequency.

The effect of phase is incorporated in the time domain measures. The step responses suggested that, in response to a step in ABP, CBFV would subsequently fall towards baseline in slightly less than 5 s in all recordings, consistent with active CA, as reported from previous observations [23]. The step responses were characteristic of improved CA [23], with decreasing CO_2 end tidal volume, associated with the increasing respiratory rate, although the effect of respiratory rate alone was just not significant [8].

It was proposed that during HA adaptation, hypometabolism was developed as a mechanism to cope with the hypoxic stress. Such hypometabolism was also observed in fMRI studies involving gustatory stimulation [14] and cognitive performance [1]. There are also data indicating reduced amount of HA group gray matter volumes at bilateral insula [7] which points to its reduced functionality among the HA group. In authors’ opinion one plausible interpretation would be that such reduced functionality contributes to the reduced ventilation associated with long term HA adaptation, in contrast with the hyperventilation typically experienced by new comers.

The goal of our investigations was to study some peculiarities of respiratory and cardiovascular systems of high altitude residents in Armenia.

METHODS

Participants in the current study included 40 pupils from Vardenis (Armenia, 2000 m above the sea level) divided into 2 groups: I – 13-14 years old, and II – 15-17 years old. We have studied the breathing rhythm, chest circumference during quiet and deep breathing, lungs vital capacity, erythrocites amount, hemoglobin concentration, colour index, systolic, diastolic and puls arterial pressure, before and after trainings. The control groups were consist with Stepanavan (1300 m above the sea level) 23 pupils of the same age. The appropriate parameters were investigated.

The experimental groups’ pupils should go through two month trainings on controlled breathing. During trainings participants should make 6 breathing movements per min, three times a day. Study of appropriate health parameters was done after the training period.

Significance of received data was determined by statistical analysis with package of SPSS programs (SD ±0.05). All studings were carried out in concordance with Universal Declaration of Bioethics and Human Rights.

RESULTS

Our data (see table) showed significant differences within control and experimental groups pupils (see the table). The basal breathing rate in control groups was 16.33±0.41 breath/min and 15.09±0.34 breath/min. In the experimental groups it was respectively 19.25±0.93 ($p<0.05$) and 23.22±0.74 ($p<0.05$) breath/min. So a significant increased rate of breathing in high altitude pupils was revealed. After the training period the breathing rate of pupils of both experimental groups has significantly decreased to 14.50±0.54 ($p<0.05$) and 16.89±0.42 ($p<0.05$), and became almost the same in comparison with control groups.

As it's shown in the table, there are significant differences in the erythrocytes amount, and hemoglobin concentration between control and experimental groups. The colour index of control group was in norm limits, and in experimental groups it's at the minimal level. There are also significant differences in chest circumference during quiet and deep breathing.

Table 1: Some parameters of pupils living at low (1300 m above the sea level) and high (2000 m above the sea level) altitudes

Investigated parameter	Number of the group	Contrlol	Experimental groups before training	Experimental groups after training
Breathing rate (breath/min)	I	15.78±0.36	19.25±0.93*	14.50±0.54*
	II	15.09±0.33	23.22±0.74*	16.89±0.42*
Erythrocytes amount	I	3.75x10^{12}±600.01	4.48x10^{12}±910.07*	4.0x10^{12}±550.05*
	II	3.35x10^{12}±270.8	4.36x10^{12}±442.2*	3.91x10^{12}±300.3*
Hemoglobin concentration (g/l)	I	124.80±1.16	117.80±2.25*	133.6±1.85*
	II	125.50±3.05	113.60±2.41*	131.2±2.45*
Colour index	I	1.03±0.003	0.89±0.002	1.00±0.001
	II	1.10±0.005	0.88±0.003	1.01±0.002
Lungs vital capacity (ml)	I	3200±160.0	2971.0±158.4	3614.0±96.19*
	II	3300±270.0	2662.0±108.5	4188.0±246.0*
Chest circumference during quiet breathing (sm)	I	70.50±0.57	73.25±1.39	73.5±1.28*
	II	79.0±0.73	83.50±0.78*	91.0±1.22*
Chest circumference during deep breathing (sm)	I	75.75±0.25	81.62±1.53*	92.29±1.55*
	II	80.38±1.19	85.88±0.70*	94.25±1.0,8*
Heart rate (beat/min)	I	77.56±1,19	92.78±3.06*	75.22±1.69*
	II	78.38±1.62	91.38±2.07*	78.75±1.85*
Systolic pressure (mmHg)	I	100.0±2.13	113.60±1.23*	106.50±1.13*
	II	105.0±3.27	117.10±1.97*	105.4±1.48*
Diastolic pressure (mmHg)	I	55.0±1.89	61.50±1.24*	74.12±0.81*
	II	73.12±2.82	67.75±1.36*	77.75±1.81*
Puls pressure (mmHg)	I	40.83±3.61	51.77±1.46*	33.38±1.85*
	II	37.72±1.59	48.91±2.11*	35.27±1.17*

The differences of lungs vital capacity in control and experimental groups are not significant, but nevertheless this parameter is too low in the experimental groups. In many cases, the biochemical changes in response to high altitude exposure are so striking that almost everything is statistically significant when compared to baseline. However, uncovering the biological relevance of those alterations remains a challenge. Relatively small (and *statistically* insignificant) changes in the steady-state concentration of biomarkers and signalling molecules may be associated with *biologically* significant changes in physiology, in particular when regulatory circuits are operating at their limits. In other cases, statistically significant changes from baseline may simply indicate that the system is operating at a different setpoint (which may still be well within the regulatory range) [17].

Our data suggest that in the organism of high altitude residents there are mechanisms for adaptation to high altitude, for example high rate of breathing without changes of breathing volume. However the blood hemoglobin saturation is about the normal level, which means that there is also another mechanism underlying the adaptation process.

The pupils of experimental groups in comparison with pupils of the same age of the control groups had significantly higher level of systolic and dyastolic, and also the pulse pressures, which may suggest the myocard overloading. After two month trainings the decrease of systolic and dyastolic, and also the pulse pressures was revealed.

Medical examination revealed few cases of cardiopulmonary sickness in both experimental groups. 4 of investigated 16 pupils of the first group had sinus tachycardia, 2 – respiratory arrhythmia, 3 – myocarditis and hypoxy, and 1 – right bundle-branch block. For 20 investigated pupils of the second group it was revealed following: 2 cases of sinus tachycardia, 1 – respiratory arrhythmia, 1 – myocarditis and hypoxy, 1 – focal blockade with myocarditis and hypoxy, 1 – right bundle-branch block, and 1 – cardiac rhythm and conduction disturbance.

After the training period in the first group it was revealed 1 case of respiratory arrhythmia, 1 case of sinus tachycardia, and 1 case of myocarditis and hypoxy was changed to respiratory arrhythmia. All other pupils had no any disturbances. In the second group 1 case of sinus tachycardia was changed to sinus arrhythmia, and 1 pupil had respiratory arrhythmia. So, the trainings on breathing rate voluntary decrease had a positive effect. Fig. 1-4 presents the ECG results of four pupils from two experimental groups before and after training.

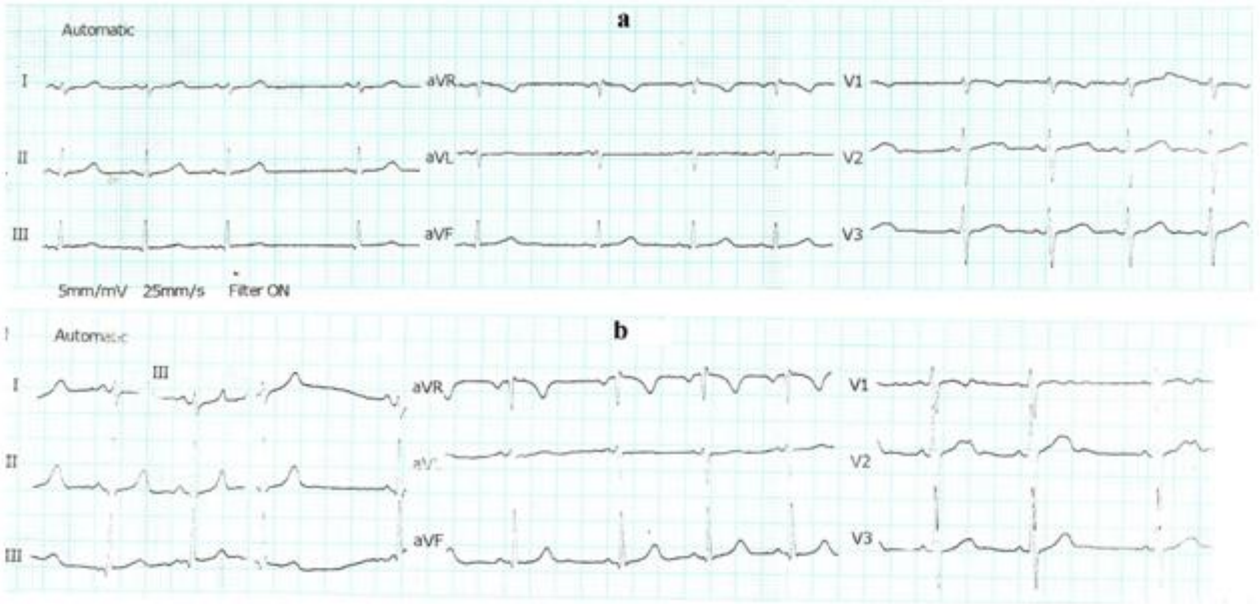

Fig. 1: ECG of the pupil B.V. (I group). I, II, III, aVR, aVL, aVF, V_1, V_2, V_3 – appropriate lead. a – before training (the patient had respiratory arrhythmia), b – after training (the patient has no any disturbances)

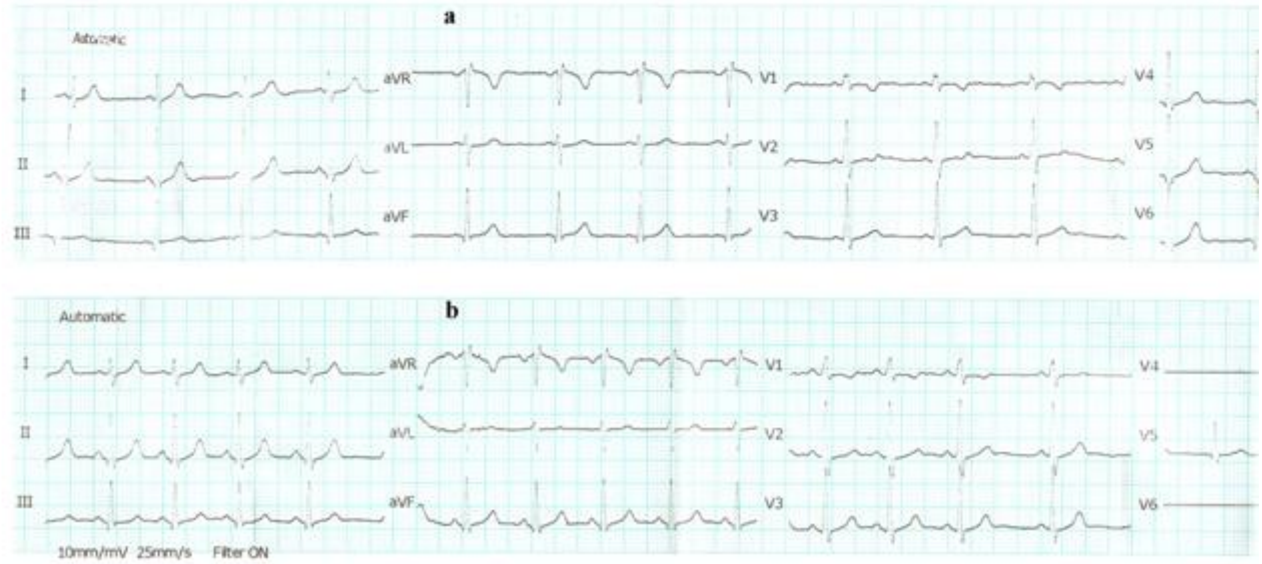

Fig. 2: ECG of the pupil M.M. (I group). I, II, III, aVR, aVL, aVF, V_1, V_2, V_3, V_4, V_5, V_6 – appropriate lead. a – before training (the patient had right bundle-branch block), b – after training (the patient has no any disturbances)

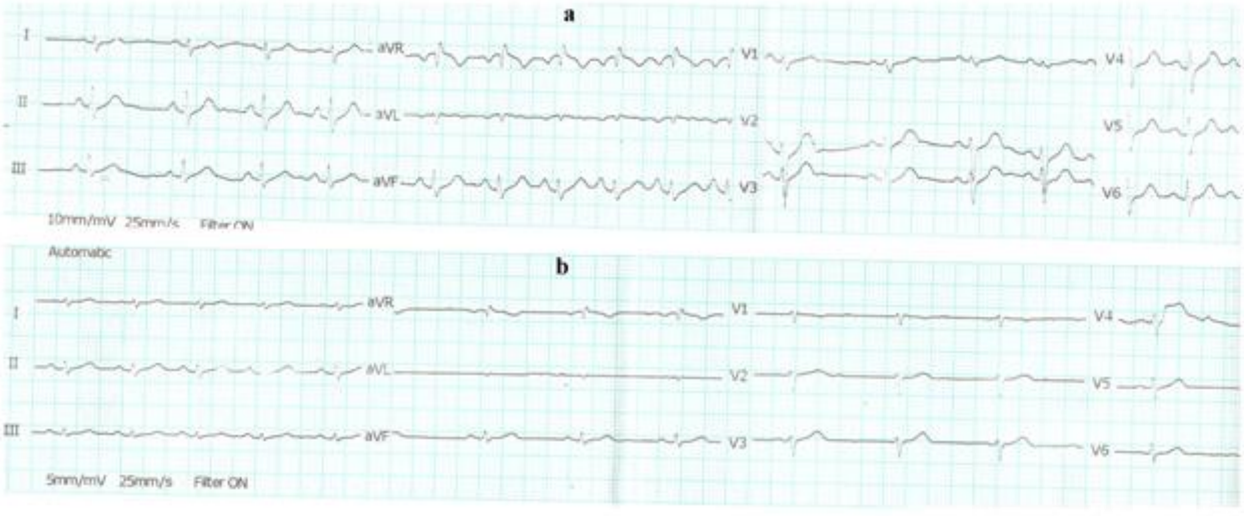

Fig. 3: ECG of the pupil H.M. (II group). I, II, III, aVR, aVL, aVF, V_1, V_2, V_3, V_4, V_5, V_6 – appropriate lead. a – before training (the patient had sinus tachicardia), b – after training (the patient has no any disturbances)

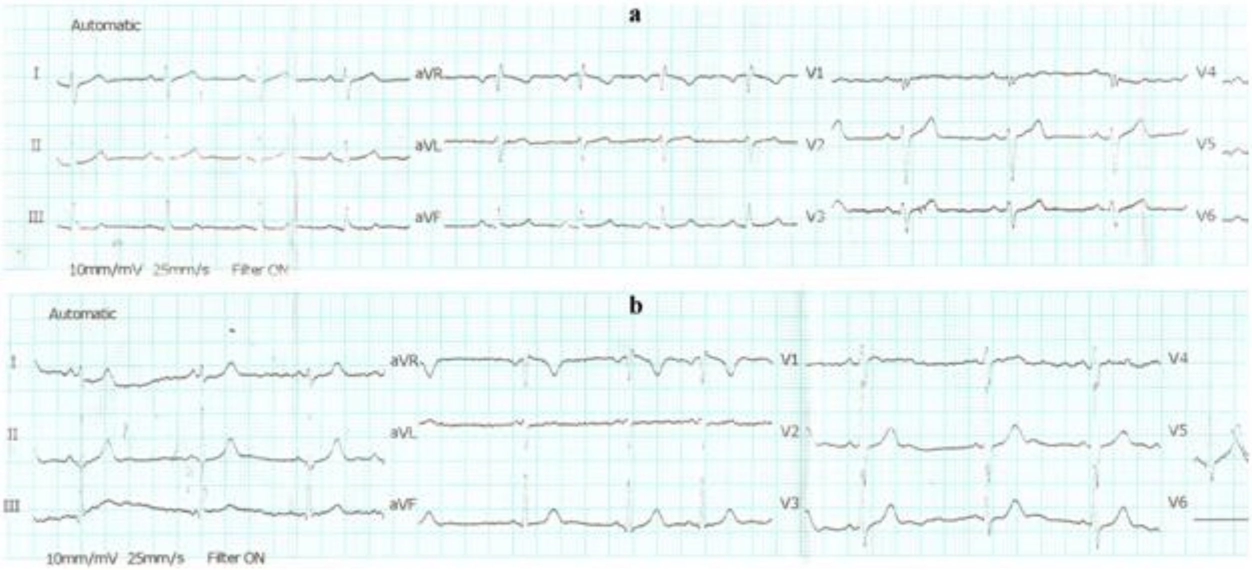

Fig. 4: ECG of the pupil M.V. (II group). I, II, III, aVR, aVL, aVF, V_1, V_2, V_3, V_4, V_5, V_6 – appropriate lead. a – before training (the patient had right bundle-branch block), b – after training (the patient has no any disturbances)

DISCUSSION

Barometric pressure falls with increasing altitude whilst the percentage of oxygen within the atmosphere remains constant. The consequent reduction in inspired oxygen impairs physical performance and may even threaten survival [24]. Graded and continued altitude exposure permits acclimatisation, a progressive tolerance to hypoxia traditionally ascribed to cardiopulmonary and haematological responses that support global convective oxygen delivery [34]. These changes tend to reduce the gradient of oxygen partial pressure from ambient air to tissues [33] by increase of erythrocites amount, systolic volume and hemoglobin concentration, which was shown also in our studies. It was reported that peripheral physiological parameters, especially hemoglobin concentration, adapt very quickly to hypoxia/normoxia changes in the scale of weeks [21].

However, such responses do not provide a full explanation of the acclimatisation process given that exercise tolerance remains limited even though arterial oxygen content returns to sea-level values [6, 13]. Furthermore, genetic selection pressure amongst high-altitude residents of the Tibetan Plateau (*in situ* for >20,000 years) favours lower rather than higher levels of oxygen-carrying haemoglobin [3, 36]. Finally, the marked inter-individual differences which exist in the ability to adapt to hypoxia sometimes are not explained by differences in arterial oxygen content [6]. Changes in tissue oxygen handling, mediated in part through changes in the microcirculation and in mitochondrial oxygen use, are increasingly considered more important to the development of hypoxia tolerance than is the augmentation of its global convective delivery [2, 13, 18].

Significant correlations were found between specific aspects of pulmonary function (IRV & ERV) and BOLD signal variation at specific brain regions [35]. These correlations indicate the contribution of specific aspects of pulmonary function to cerebrovascular response (CVR). It seems that IRV had a wide influence on BOLD signal across multiple brain regions, not only in cortices involved in respiratory modulation (e.g., the insula, thalamus, and the precentral cortex), but also other cortices such as the fusiform cortex. The HA group indeed showed a larger IRV than the control group, while other aspects of pulmonary function maintained at a similar level [35]. In authors' opinion, it could be possible that it took a longer time for the oxygenation level of the HA group to reach peak, considering that the HA group had similar levels of respiration rate and haemoglobin concentration with the only observed difference at IRV; and this delay was eventually reflected in the delay of BOLD signal. It could also be related to the involvement of these brain regions in respiratory modulation.

As it's shown by a number studies, adaptation to high altitude describes changes that have occurred over a number of generations as a result of natural selection in a hypobaric hypoxic environment, and this can be observed in some groups of high-altitude residents [12]. The mechanisms responsible for such adaptation probably involve alterations in the control of breathing [5, 19].

It's known that the cardiovascular responses to voluntary delay of breathing are definded by interaction of different reflexes between lung vessels and mechano- and chemoreceptors of reflexogenic zones [11, 31]. Significant role in these interactions have changes of pressure in lungs, chest and abdominal cavity, which influences at the venous flow into the heart, and arterial pressure during breathing delay. Delayed deep breathing decreases the pressure in the chest and facilitates venous flow to the heart. Besides the cumulation of carbon dioxide in organism during breathing delay leads to extension of coronary vesels, and therefore improves myocard delivering.

After controlled breathing trainings all investigated parameters became comparable with the same parameters of the control group. Therefore the method of voluntary decrease of the breathing rate is effective for the pupils living high altitudes. Obviously after breathing trainings the adaptive mechanisms of metabolism and activity of aerobic breathing ferments are changed, which lead to the new level of oxygen delivery, and consequently to changes of oxygen delivering organs and systems. It is confirmed by positive correlation of breathing with decrease of seakness, improvement of heart work, physical and mental workability. Practically the volitional control of breathing leads to positive changes in cardiovascular system. In summary, our results suggest the possible contributions of pulmonary functions in cardiovascular reaction.

Vardenis region lies at the level 2000 m above the sea level (atmosphere pressure 809.92 mbar): It's important, that today in the Vardenis out-patient clinic there are registered 468 patients with ischemic heart disease, 678 patients with hypertension, 60 patients with acute bronchitis, and 29 patients with bronchial asthma. Most probably there are more persons with arterial blood pressure oscillations who are not registered.

The control of breathing can be divided into chemoreflex and non-chemoreflex drives to breathe. Non-chemoreflex drives (e.g. wakefulness drive, voluntary cortical drive, hormonal factors) have never been measured in highlanders, while a single study of acclimatization in lowlanders showed that these drives remain unchanged from sea-level values after 5 days of high altitude exposure [28]. Chemoreflex drives to breathe can be further divided into central and peripheral drives. Both central and peripheral chemoreceptors respond to changes in hydrogen ion concentration ($[H^+]$) in their immediate environments [20, 32], while peripheral chemoreceptors are also responsive to changes in PO_2 via hypoxia-mediated changes in their $[H^+]$ ion sensitivity [16, 37]. As a result, highlanders have induced acute changes in PO_2 and PCO_2 and measured the ensuing changes in ventilation to assess the chemoreflex control of breathing [9].

CONCLUSION

By using of the method of breathing rate voluntary optimal changes it may be possible to improve the high altitude residents adaptive mechanisms, and health status of patients with cardiovascular deseases.

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