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Effect of intermittent normobaric hypoxia on total oxygen consumption and efficiency of cardio-respiratory mechanisms of oxygen supply in patients with a high risk of chronic obstructive pulmonary disease

Effect of intermittent normobaric hypoxic treatment (INHT) on total oxygen consumption (OC) and efficiency of cardio-respiratory mechanisms of oxygen supply was studied in adult patients with a high risk of chronic obstructive pulmonary disease (COPD). The 1st group (n=43) of patients received only conventional treatment. The 2nd group (n=103) received the same treatment in combination with INHT. INHT comprised of a daily 90 minute sessions in chamber "Orotron" for 2 weeks. The oxygen partial pressure was maintained in the automatic mode at 147-160 hPa. The heterogeneity of OC dynamics of both the amplitude and direction was observed in patients after INHT. The pattern and degree of changes were dependent on the initial level of OC and the functional status of the cardio-respiratory system. In this regard, the study group of patients was divided into three subgroups: 2-A – 33,1% of patients had a normal value of OC, 2-B – 52,4% of patients had a lower value of OC and 2-C – 15,5% of patients had a higher value of OC. INHT did not change the total OC but improved the efficiency of hemodynamic mechanisms of oxygen supply in patient subgroup 2-A. The total OC and efficiency of respiratory mechanisms of oxygen supply moderately increased in patient subgroup 2-B. The value of OC decreased moderately in patient subgroup 2-C, but respiratory and hemodynamic mechanisms of oxygen supply remained high enough. It was concluded that INHT optimized the oxygen consumption and improved the efficiency of cardio-respiratory mechanisms of oxygen supply in patients with a high risk of COPD .
Key words: intermittent normobaric hypoxia, chronic obstructive pulmonary disease

INTRODUCTION

Mountain climate has been used for treating patients with chronic pulmonary diseases for many years. Since the days of P.Bert (1878) and A.Mosso (1898), it has been postulated that high-altitude hypoxia is the most important factor that determines the specific nature and pattern of the physiological effects of mountain climate [17, 18]. It was found that even a relatively small decrease in oxygen partial pressure (PO_2) activated a number of compensatory and adaptive mechanisms, such as alveolar ventilation, systemic and regional hemodynamic, microcirculation, oxygen binding properties of hemoglobin, oxygen metabolism, etc. [2,7,10-13,20]. Oxygen delivery to tissue and total oxygen consumption (OC) are changed in patients with chronic pulmonary diseases at high altitude. The nature of these changes depends on the degree and duration of exposure to hypoxia, as well as characteristics of the disease. The individual genetic and phenotypic features are another important factors that determine the resistance of patients to hypoxia and specific features of their adaptation to mountain climate. Respiratory and hemodynamic mechanisms of oxygen supply provide tissues with oxygen in an amount that corresponds to their metabolic needs. Functional efficiency of these mechanisms determines the quality of adaptation to mountain climate and severity of hypoxic disorders in patients at high altitude.

Intermittent normobaric hypoxia (INH) is one of the effective non-pharmacological methods for care and rehabilitation of patients with different chronic pulmonary diseases, such as bronchial asthma, chronic bronchitis, etc. [1-6, 9, 13, 19]. This method is being more widely used in clinical practice now [8, 14, 15, 21-26]. But effect of INH on total oxygen consumption in patients with a high risk of chronic obstructive pulmonary disease (COPD) is not sufficiently investigated. This question is very relevant for prediction and evaluation of the therapeutic effect of INH in individual patients. In this paper we present the results of our studies regarding the INH effects on total oxygen consumption and efficiency of respiratory and hemodynamic mechanisms of oxygen supply in patients with a high risk of COPD.

MATERIALS AND METHODS

The total volume of oxygen consumption and the main characteristics of the functional efficiency of the respiratory and hemodynamic mechanisms of oxygen supply were studied in 146 adult patients. Patients ranged in age from 27 to 59 years (women – 52,1%, men – 47,9%). All of them had a cough, sputum production and under certain conditions – dyspnoea. The most of them were smokers, but they had no persistent violation of lung function. According to the Global Initiative for Chronic Obstructive Lung Disease, they were attributed to patients with high risk of COPD. All patients were divided into control (1^{st}) and study (2^{nd}) groups randomly. The 1^{st} group (n=43) of patients received only conventional treatment. The 2^{nd} group (n=103) received the same treatment in combination with INH. The intermittent normobaric hypoxic treatment (INHT) was performed in "Orotron" chamber within 2 weeks for 1,5 hours daily. Under conditions of normal atmospheric pressure, this device creates and maintains in automatic mode the following parameters: PO_2 - 147-160 kPa, relative humidity - 60-70%, ambient temperature - 16-18° C, and content of light negative ions - up to 6000 per cm^3. The total time of hypoxic exposure in intermittent regime was 21 hours. The total volume of oxygen consumption was measured using closed-system respirometer. Oxygen consumption per minute (VO_2), oxygen consumption index (VO_2I), coefficient of oxygen extraction from air (VO_2/V_e), ventilation equivalent (VE), oxygen consumption per one cycle of respiration (O_2rc), oxygen consumption per one cardiac cycle (O_2cc), hemodynamic equivalent (HE) were calculated by standard formulae. Corrections were made for barometric and vapor pressure and temperature to reduce all figures to standard conditions - STPD and BTPS. The methods of spirography, pneumotachography, electrocardiography and rheovasography were used for investigation lung ventilation and hemodynamic' function. All parameters were recorded before and after the course of conventional treatment and the same treatment in combination with INHT. Mean values of difference between control and study groups of patients before and after treatment were calculated and compared. Students "t" test was applied for evaluating the significance of differences.

RESULTS

The studies found no significant differences in the total oxygen consumption, as well as in characteristics of the efficiency of the respiratory and hemodynamic mechanisms of oxygen supply between the control and study groups of patients before treatment (Table 1).This fact indicated that the compared groups of patients were fairly uniform in the nature of the disease manifestations.

The value of oxygen consumption was not significantly changed in the 1^{st} group of high risk COPD patients after 2 weeks of conventional treatment. They had only a moderate increase in O_2cc and decrease a negative base excess (BE). It was found a moderate increase in VO_2, VO_2I, O_2 cc, pH, BE and decrease in VE, HR and HE in the 2^{nd} group of patients after conventional

treatment in combination with INH. Thus the number of parameters and the degree of their changes after treatment were more pronounced in the 2nd group of patients. The functional efficiency of the respiratory and hemodynamic mechanisms of oxygen supply was evidently higher in these patients.

The heterogeneity of the OC dynamic of both the amplitude and direction was observed in the 2nd group of patients after INHT. We analyzed this fact. It was determined that the pattern and degree of changes were dependent on the initial level of OC. For this reason, we divided all patients from study group into 3 subgroups according to initial level of OC: 2-A – 32,0% of patients had a normal value of OC, 2-B – 52,4% of patients had a lower value of OC and 2-C – 15,6% of patients had a higher value of OC before INHT.

Significant differences in VO_2 could be related to various height and weight in subgroups of patients. In this regard, we calculated the oxygen consumption index in all subgroups of patients according to their actual height and weight. The type and nature of inter-group differences in VO_2 and VO_2I remained unchanged. These results showed that established differences had a more complex mechanism of origin. We suggested that these differences were related to the individual characteristics of respiratory, hemodynamic and metabolic mechanisms of oxygen supply in individual patients. We refined this assumption.

The values of VO_2, VO_2I and the main respiratory and hemodynamic parameters of the oxygen supply efficiency were within the physiological range in the 2-A subgroup of patients before INHT. Disturbances of acid-base balance were absent (pH=7,36±0,03; BE=-1,22±0,05 $mmol \cdot l^{-1}$) (Table 2).

The largest number of patients was in subgroup 2-B. The total volume of oxygen consump-

Table 1. Oxygen consumption and cardio-respiratory indices of oxygen supply in patients with a high risk of COPD before (I) and after (II) conventional therapy (1) and INHT in combination with conventional therapy (2)

Characteristics	Group of patients			
	1 (n=43)		2 (n=103)	
	I	II	I	II
VO_2, $ml \cdot min^{-1}$	289,02±12,51	293,70±17,42	273,20±10,52	305,60±9,48*
VO_2I,$ml \cdot min^{-1} \cdot m^2$	155,14±15,73	162,42±12,80	149,33±12,12	164,51±11,78*
O_2 rc, ml	18,67±1,33	19,48±1,17	17,43±0,93	19,15±1,16
O_2 cc, ml	3,73±0,20	4,29±0,24*	3,45±0,13	3,98±0,14*
VO_2/V_e, $ml \cdot l^{-1}$	25,05±1,86	26,10±1,98	24,60±1,25	28,78±1,10*
Vт , ml	749,8±51,1	704,1±38,3	726,7±33,8	717,9±40,1
f, min^{-1}	16,10±1,13	16,01±1,17	16,86±0,72	16,81±0,60
V_e, $l \cdot min^{-1}$	11,54±1,42	11,21±0,73	11,74±0,49	11,52±0,43
VE	39,81±2,90	38,82±2,85	45,53±2,39	40,35±1,65*
HR, min^{-1}	78,01±1,97	76,40±2,31	79,46±1,61	75,06±1,50*
HE	13,12±0,92	12,10±1,20	14,06±0,74	12,67±0,59*
Q, ml	46,11±1,56	45,87±1,81	44,79±1,60	45,40±1,70
Q, $ml \cdot min^{-1}$	3782,51±148,45	3692,89±167,78	3652,70±156,61	3637,50±164,89
pH	7,34±0,03	7,38±0,05	7,35±0,04	7,42±0,01*
BE $mmol \cdot l^{-1}$	-2,83±0,26	-0,51±0,04*	-2,33±0,19	+1,24±0,36**

Here and below: *p<0.05, **p<0.01- values are significantly different from the initial state.

tion did not exceed 216,92±5,62 ml·min^{-1} in these patients. The low respiratory indices of oxygen supply efficiency were typical: VO_2/V_e didn't exceed 21,26±1,69 ml·l^{-1}, O_2rc=13,88±1,04 ml, VE=52,58 ±3,65. But hemodynamic parameters remained fairly stable: O_2cc=5,19±0,11 ml, HE=16,80±1,11 ml/l, HR=75,69±2,24 beats per minute. The low efficiency of gas exchange led to the development of metabolic acidosis: pH=7,32±0,02, BE=-5,54±0,04 mmol·l^{-1}.

The total volume of OC was above 400 ml·min^{-1} in the 2-C subgroup of patients before INHT. The high intensity of OC combined with a substantial increase in expired

Table 2. Oxygen consumption and cardio-respiratory indices of oxygen supply in subgroup of patients with a high risk of COPD before (I) and after (II) INHT in combination with conventional therapy

Characteristics	Stages of research	Subgroup of patients		
		2-A (n=33)	2-B (n=54)	2-C (n=16)
VO_2, ml·min^{-1}	I	298,75±5,31	216,92±5,62	412,50±13,59
	II	309,98±19,86	266,15±8,93**	362,50±18,68*
VO_2I, ml·min^{-1}·m^2	I	163,19±12,80	119,62±10,60	222,91±10,12
	II	169,40±13,59	147,01±11,70*	195,71±13,82*
O_2rc, ml	I	20,12±1,25	13,88±1,04	23,91±2,35
	II	20,60±1,82	18,05±1,36*	24,94±5,04
O_2cc, ml	I	3,56±0,15	5,19±0,11	4,9±0,16
	II	4,01±0,19	6,19±1,07**	5,11±0,40
VO_2/V_e, ml·l^{-1}	I	27,54±1,53	21,26±1,69	28,89±3,38
	II	27,14±1,65	25,98±1,59**	29,02±3,41
Vт , ml	I	729,87±46,38	691,54±55,70	860,01±57,69
	II	757,44±75,89	653,85±51,45	835,00±89,90
f, min^{-1}	I	15,12±0,91	17,62±0,19	18,00±1,24
	II	15,66±0,90	17,46±0,85	17,00±1,84
V_e, l·min^{-1}	I	10,77±0,57	10,97±0,67	15,37±1,49
	II	11,35±0,60	11,05±0,64	13,30±1,12
VE	I	36,19±1,96	52,58±3,65	37,77±4,03
	II	37,74±2,14	42,28±2,62*	37,82±4,25
HR, min^{-1}	I	82,94±2,58	75,69±2,24	84,75±3,48
	II	78,31±3,09*	73,85±1,90	72,50±3,42*
HE	I	12,41±1,10	16,80±1,11	9,80±1,12
	II	12,20±1,11	13,55±0,80*	10,61±1,62
Q, ml	I	45,20±3,40	43,90±2,01	46,8±3,90
	II	48,95±4,3	42,41±1,80	49,70±3,70
Q, ml·min^{-1}	I	3705,11±308,50	3525,01±216,49	3920,10±332,81
	II	3864,81±412,91	3479,00±169,90	3973,54±493,90
pH	I	7,36±0,03	7,32±0,02	7,40±0,02
	II	7,41±0,02	7,37±0,01*	7,44±0,03
BE, mmol·l^{-1}	I	-1,22±0,05	-5,54±0,04	+1,03±0,06
	II	+0,50±0,03*	-0,81±0,03*	+2,01±0,03*

volume (V_e=15,37±1,49 l·min^{-1}), tidal volume (Vт=860,01±57,69 ml) and heart rate (HR=84,75±3,48 beats per minute). A high level of oxygen consumption could be due to increasing of respiration and circulation work but their functional efficiency for oxygen supply still remained high enough. It was indicated by such characteristics as VO_2/V_e, O_2rc, VE, O_2cc and HE.

Analysis of the research data showed the specific patterns in changing of the total oxygen consumption and the efficiency indices of respiratory and hemodynamic function. These patterns were subjected to correlation analysis and calculation of the bivariate correlation coefficients (r). A positive correlation coefficients were found between VO_2 and V_e (r=0,405, p<0,05), HR (r=0,376, p<0,05), V_T (r=0,341, p<0,05), Q (r=0,342, p<0,05) in patient subgroup 2-A. Less strong positive correlation coefficients were found between VO_2 and BE (r=0,356, p<0,05), pH (r=0,305, p<0,05), Q (r=0,302, p<0,05) in patient subgroup 2-B. Different magnitudes of the correlation coefficients were found between VO_2 and V_T (r=0,506, p<0,05), HR (r=0,438, p<0,05), VE (r=0,383, p<0,05), pH (r=0,372, p<0,05) and Q (r=-340, p<0,05) in patient subgroup 2-C.

The volume and intensity of OC and efficiency indices of respiratory function did not significantly change in the 2-A subgroup of patients after INHT. However, the functional efficiency of hemodynamic improved mainly due to decreasing in HR from 82,94±2,58 to 78,31±3,09 beats per minute. The total volume of OC increased by 49,23±8,20 ml·min^{-1} (p<0,05) in the 2-B subgroup of patients. The metabolic acidosis severity decreased due to more effective function of respiratory and hemodynamic mechanisms of oxygen supply. The VO_2/V_e index reached up to 25,98±1,59 ml·l^{-1} (p<0,001) and VE decreased up to 42,28±2,62 (p<0,001). Oxygen cost of respiratory cycle increased by 4,17±1,03 ml (p<0,001), and cardiac cycle - by 1,00±0,27 ml (p<0,05). Amount of oxygen, which is extracted from 1 liter of blood reached up to 13,55± 0,80 ml (p<0,05). The total oxygen consumption decreased by 50,00±20,71 ml·min^{-1} (p<0,05) in the 2-C subgroup of patients after INHT. This effect may be associated with decreasing of respiratory and hemodynamic work: V_e reduced by 2,07±0,79 l (p<0,05) and HR - by 12,25±3,80 (p<0,05) beats per minute. The relative decreasing in OC remained within the physiological limits and did not reduce the efficiency of respiratory and hemodynamic mechanisms of oxygen supply.

It is known that respiratory and hemodynamic mechanisms of human adaptation to mountain climate are closely interrelated and interdependent. However, it does not exclude the dominant role of one of them, especially in patients with pre-existing defects in one of the oxygen supply systems. The total oxygen consumption in patients with chronic pulmonary diseases has been studied for a long time. It is found that the nature and extent of changes in gas exchange is determined by many factors. The most important of these factors are the state of the lung's ventilation and hemodynamic [11, 16]. Changes of total oxygen consumption are absent in patients with the initial stages of COPD, although the functional efficiency of oxygen supply mechanisms may be decreased. These disorders become evident when the initial symptoms of airway obstruction and respiratory failure appeared. The total oxygen consumption is significantly decreased in patients with severe degree of respiratory failure. It is accompanied by the development of tissue hypoxia and metabolic acidosis.

The results of our research showed that pattern and degree of changes in OC were caused by INHT depended on the initial level of VO_2 and functional state of respiration and hemodynamics in patients with a high risk of COPD. The total volume of oxygen consumption and oxygen consumption index were at an adequate level in the 2-A subgroup of patient before INHT. The course of INHT mobilized reserves and improved the functional efficiency of hemodynamic mechanisms of

oxygen supply in these patients. Oxygen consumption was at lower level and symptoms of metabolic acidosis were present in the 2-B subgroup of patients. But the current level of the hemodynamic mechanisms efficiency prevented the development of more serious violations. INHT improved the functional efficiency of respiratory mechanisms of oxygen supply in these patients but the basic hemodynamic parameters remained stable. INHT reduced the functional overloading of cardio-respiratory system in the 2-C subgroup of patients. The breath frequency and tidal volume were decreased up to the level of physiological norm. Optimization of the total oxygen consumption was achieved by decreasing of the energy cost for work of respiration and hemodynamics.

Thus INHT normalized the total oxygen consumption in patients with a high risk of COPD. This effect was connected with moderate activation of OC and improvement of the functional efficiency of respiratory and hemodynamic mechanisms of oxygen supply. The pattern and degree of changes in total oxygen consumption were caused by INHT depended on the initial level of OC and the functional status of the patients' cardio-respiratory system. The results of this study may be used for prediction and evaluation of the therapeutic effect of INH in patients with a high risk of COPD.

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ВПЛИВ ПЕРЕРИВЧАСТОЇ НОРМОБАРИЧНОЇ ГІПОКСІЇ НА СПОЖИВАННЯ КИСНЮ ТА ЕФЕКТИВНІСТЬ РЕСПІРАТОРНИХ ТА ГЕМОДИНАМІЧНИХ МЕХАНІЗМІВ ЗАБЕЗПЕЧЕННЯ ОРГАНІЗМУ КИСНЕМ У ХВОРИХ З ВИСОКИМ РИЗИКОМ РОЗВИТКУ ХРОНІЧНОЇ ОБСТРУКТІВНОЇ ХВОРОБИ ЛЕГЕНЬ

Вплив переривчастої нормобаричної гіпокситерапії (ПНГТ) на загальне споживання кисню (СК) та ефективність респіраторних та гемодинамічних механізмів забезпечення організму киснем вивчали у хворих з високим ризиком розвитку хронічної обструктівної хвороби легень (ХОЗЛ). 1-а група (n=43) пацієнтів отримала тільки стандартну терапію. 2-а група (n=103) отримала також лікування у поєднанні з ПНГТ. Двотижневий курс ПНГТ складався з щоденних 90-хвилинних сеансів лікування у камері "Оротрон". Протягом усього сеансу PO_2 у середині камери підтримувався на рівні 147-160 гПа. Зміни СК у пацієнтів після курсу ПНГТ були неоднорідні як по амплітуді, так і за спрямованістю. Встановлено, що характер і ступінь змін у окремих пацієнтів залежали від початкового рівня СК і функційного стану стану кардіо-респіраторної системи. У зв'язку з цим, основну групу пацієнтів було розділено на 3 підгрупи: 2-А - 33% пацієнтів мали нормальні значення СК, 2-В - 53% пацієнтів мали знижене СК і 2-С - 14% пацієнтів мали високе СК. ПНГТ суттєво не змінювала СК, але підвищувала ефективність гемодинамічних механізмів забезпечення організму киснем у пацієнтів 2-А підгрупи. СК та ефективність респіраторних механізмів доставки кисню помірно підвищувались у пацієнтів 2-В підгрупи. Величина СК наближувалася до рівня фізіологічної норми у пацієнтів 2-С підгрупи, але ефективність респіраторних і гемодинамічних механізмів доставки кисню залишалася відносно високою. Таким чином, ПНГТ оптимізує споживання кисню у пацієнтів з хронічними легеневими захворюваннями, підвищує ефективність респіраторних та гемодінамічних механізмів забезпечення організму киснем.

Ключові слова: переривчаста нормобарична гіпоксія, хронічне обструктивне захворювання легень.

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ВЛИЯНИЕ ПРЕРЫВИСТОЙ НОРМОБАРИЧЕСКОЙ ГИПОКСИИ НА ПОТРЕБЛЕНИЕ КИСЛОРОДА И ЭФФЕКТИВНОСТЬ РЕСПИРАТОРНЫХ И ГЕМОДИНАМИЧЕСКИХ МЕХАНИЗМОВ ОБЕСПЕЧЕНИЯ ОРГАНИЗМА КИСЛОРОДОМ У БОЛЬНЫХ С ВЫСОКИМ РИСКОМ РАЗВИТИЯ ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНИ ЛЕГКИХ

Влияние прерывистой нормобарической гипокситерапии (ПНГТ) на общее потребление кислорода (ПК) и эффективность респираторных и гемодинамических механизмов обеспечения организма кислородом изучали у больных в высоким риском развития хронической обструктивной болезни легких (ХОБЛ). 1-я группа (n=43) пациентов получила только стандартную терапию. 2-я группа (n=103) получила такое же лечение в сочетании с ПНГТ. Двухнедельный курс ПНГТ состоял из ежедневных 90-минутных сеансов лечения в камере "Оротрон". На протяжении всего сеанса PO_2 внутри камеры поддерживалось на уровне 147-160 гПа. Изменения ПК у пациентов после курса ПНГТ были неоднородны как по амплитуде, так и по направленности. Установлено, что характер и степень изменений у отдельных пациентов зависели от исходного уровня ПК и функционального состояния кардио-респираторной системы. В связи с этим, основная группа пациентов была

разделена на 3 подгруппы: 2-А - 33% пациентов имели нормальные значения ПК, 2-В - 53% пациентов имели сниженное ПК и 2-С - 14% пациентов имели высокое ПК. ПНГТ существенно не изменяла ПК, но повышала эффективность гемодинамических механизмов обеспечения организма кислородом у пациентов 2-А подгруппы. ПК и эффективность респираторных механизмов доставки кислорода умеренно повышались у пациентов 2-В подгруппы. Величина ПК приближалась к уровню физиологической нормы у пациентов 2-С подгруппы, но эффективность респираторных и гемодинамических механизмов доставки кислорода оставалась относительно высокой. Таким образом, ПНГТ оптимизирует потребление кислорода у пациентов с хроническими легочными заболеваниями, повышает эффективность респираторных и гемодинамических механизмов обеспечения организма кислородом.

Ключевые слова: прерывистая нормобарическая гипоксия, хроническая обструктивная болезнь легких.

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