Influence of mild hypoxia on cardiorespiratory responses and muscle oxygenation during incremental exercise

Kiyokazu Sekikawa[1)], Mitsuru Tabusadani[1)], Kazuyuki Tabira[2)], Kotaro Kawaguchi[3)] and Kiyoshi Onari[3)]

Key words：1. near-infrared spectroscopy 2. hypoxia
3. incremental exercise

This study investigated the influence of cardiorespiratory responses, blood lactate concentration and muscle oxygenation during incremental exercise tests in normoxia and hypoxia. Seven healthy subjects performed an incremental cycle ergometer exercise test breathing in random order either room air or a 15% O_2 gas mixture. Ventilation and pulmonary gas exchange were measured and computed breath-by-breath. Arterial oxygen saturation (SaO_2) was estimated continuously via pulse oxymeter. Forearm venous blood for measurement of blood lactate was collected every minute. Continuous-wave near infrared spectroscopy measured peripheral tissue saturation (SO_{2NIRS}) in the vastus lateralis muscle. Significant reduction in oxygen uptake ($p<0.01$), power output ($p<0.01$) and SaO_2 ($p<0.001$) was found in peak incremental exercise during hypoxia compared with normoxia. For the same power output in the two conditions, hypoxia significantly decreased SaO_2 (ANOVA: $p<0.001$) and blood lactate concentration (ANOVA: $p<0.05$) and increased minute ventilation (ANOVA: $p<0.01$). In the hypoxic condition, oxygen uptake and SO_{2NIRS} were not found when exercising at the same power output compared with normoxia. This study would suggest that mild hypoxia may be avoided through ventilatory compensation at the alveolar level, and oxygen consumption in alveolar and peripheral tissue oxygenation can be maintained while exercising for the same power output.

Introduction

It is well accepted that hypoxia, reduces the partial pressure of arterial oxygen and has an influence on ventilatory, circulatory and metabolic processes during exercise; measuring the gas exchange has been used to study cardiorespiratory response under hypoxic conditions. Recently, muscle metabolism and oxygenation, as well as arterial oxygenation and cardiorespiratory action, are seen as being limited in healthy subjects under hypoxic conditions, and also under conditions of pulmonary patient induced hypoxemia. To assess muscle metabolism, muscle biopsy during resting and phosphorus magnetic resonance spectroscopy during exercise are often used and to assess muscle oxygenation; using arterial and venous blood sampling. However, this requires invasive techniques, which limits its application to physiological and clinical measurements. Recently, measurements using near infrared spectroscopy (NIRS) have made it possible to noninvasively measure in vivo changes in tissue of both oxygenated and deoxygenated hemoglobin and myoglobin. Although several incremental exercise experiments in hypoxic conditions have been reported[5-7, 9, 10, 13, 15-17)], few investigations have been done in respect to the relationship between cardiorespiratory responses and oxygenation in exercising muscle during mild hypoxia. The purpose of this study was to determine the relationships among gas exchange responses, blood lactate concentrations, and NIRS responses during

・低酸素吸入が呼吸循環応答及び活動筋酸素動態に及ぼす影響
・氏名：関川 清[1)]，髻谷 満[1)]，田平一行[2)]，川口浩太郎[3)]，大成浄志[3)]
・所属：1）広島大学大学院医学系研究科保健学専攻 2）吉島病院 3）広島大学医学部保健学科理学療法学専攻
・英文所属：1）Health Sciences, Graduate School of Medical Sciences, Hiroshima University
2）Yoshijima Hospital 3）Division of Physical Therapy, Institute of Health Scinces, Faculty of Medicine, Hiroshima University
・広島大学保健学ジャーナル Vol. 2(1)：85～89，2002

incremental exercise under normoxic and acute mild hypoxic conditions.

Methods

Subjects

Seven healthy men, but not currently involved in active physical training, were recruited for this study. Age, height and weight were 23.4 (SD 1.6) yr, 170.4 (SD 4.2) cm and 63.9 (SD 7.4) kg respectively. Each subject gave informed consent after understanding the nature, purpose, and risks in this study.

Exercise protocol

All subjects performed two incremental exercise tests on an electrically braked ergometer (232c-XL, Combi, Co., Ltd) during random ordered breathing of room air or hypoxic gas mixture (15%O_2, N_2 balance). While breathing the hypoxic mixture, subjects breathed through a facemask with a J-valve from a reserve bag. Subjects performed ramp exercise at a work rate of 20W/min, after breathing the gas mixture for 5 min subsequent to 15min sitting at rest. The pedaling rate was maintained at 50 rpm. Workload was increased until maximal exercise effort occurred, which was determined as being when: no longer able to keep the 50 rpm pedaling frequency because of breathlessness or leg fatigue, or age predicted maximal HR calculated as 220 less their age in years reached, or oxygen saturation less than 85%.

Oxygen uptake ($\dot{V}O_2$, standard temperature and pressure, dry (STPD), carbon dioxide production ($\dot{V}CO_2$, STPD) and minute ventilation ($\dot{V}E$, body temperature and pressure, saturated with water vapor (BTPS)) were monitored via a metabolic cart system (AE-280S, Minato Medical Science Co., Ltd). The O_2 and CO_2 gas analyzer were calibrated before and after each test, using standard gas. Heart rate (HR) was continuously measured by electrocardiogram (DS-3140, Fukuda-Densi Co., Ltd.) and was then entered into the metabolic cart system. Pulmonary exchange and HR were calculated as the average over 30 seconds for each minute during exercise. Oxygen saturation (SaO_2) was estimated continuously via pulse oxymeter (MicroO_2, Siemens, Co., Ltd.) and was measured every minute. Forearm venous blood was sampled each minute of exercise by catheter for measurement of blood lactate (Aqu-Sports, Roche Diagnostics Co., Ltd.).

A near infrared spectrometer (BOM-L1TR, Omega Wave Inc,) was used to monitor tissue oxygenation. This instrument uses three wavelengths (780, 810 and 830nm), and absorption characteristics generally depend on the relative oxy- hemoglobin (OxyHb), deoxy hemoglobin (DeoxyHb) levels in tissue based on a Modified Lambert-Beer's law. The absorption coefficient of hemoglobin at each wavelength was based on data reported by Matcher et al.[12] Tissue oxygen saturation (SO_{2NIRS}) was calculated from the ratio of OxyHb to TotalHbMb (= OxyHb + DeoxyHb) values. For measurement, the distance between the incident point and the detector was 30mm, with a resulting depth of penetration of about 15mm. A NIRS probe was placed over the right vastus lateralis muscle 10-12cm above the knee and was protected by adhesive tape with a rubber sheet. Tapes were wrapped around the thigh to prevent displacement of the probe during exercise. NIRS data were inputted to a Macintosh personal computer at a sampling frequency of 10 Hz via an A/D transducer (Mac Lab 8s, AD Instrument Inc.). NIRS data were expressed by changes from the pre-exercise values (ΔOxyHb, ΔDeoxyHb, ΔTotalHb and ΔSO_{2NIRS}), which were determined as averages during the minute preceding the start of exercise using chart v3.6.8/s software.

Statistical analysis

The values were expressed as mean $\pm$ SE. The peak data were compared by paired t-tests. A two-way repeated measure ANOVA was used to evaluate the difference between the hypoxic and normoxic conditions from paired exercise data. Statistical analysis was performed using Stat View 5.0J software and the level of statistical significance on all tests was set at $p < 0.05$.

Results

Reasons for stopping hypoxic exercise were: five were breathless and two had SaO_2 less than 85%. The peak values for each condition are shown in Table 1. Hypoxia caused a reduction in maximal work performance as indicated by the reduction in the peak work rate from 228 $\pm$ 9.1 (range 180-240) to 178.6 $\pm$ 10.3 (range 140-210) Watt ($p<0.01$). A significant reduction in $\dot{V}O_2$, HR, $\dot{V}E$ and SaO_2 was found in peak exercise during hypoxia as compared to normoxia (Table 1). There were significant differences in Δ OxyHb and ΔSO_{2NIRS}($p<0.05$ respectively).

For the same power outputs below 140Watts, SaO_2

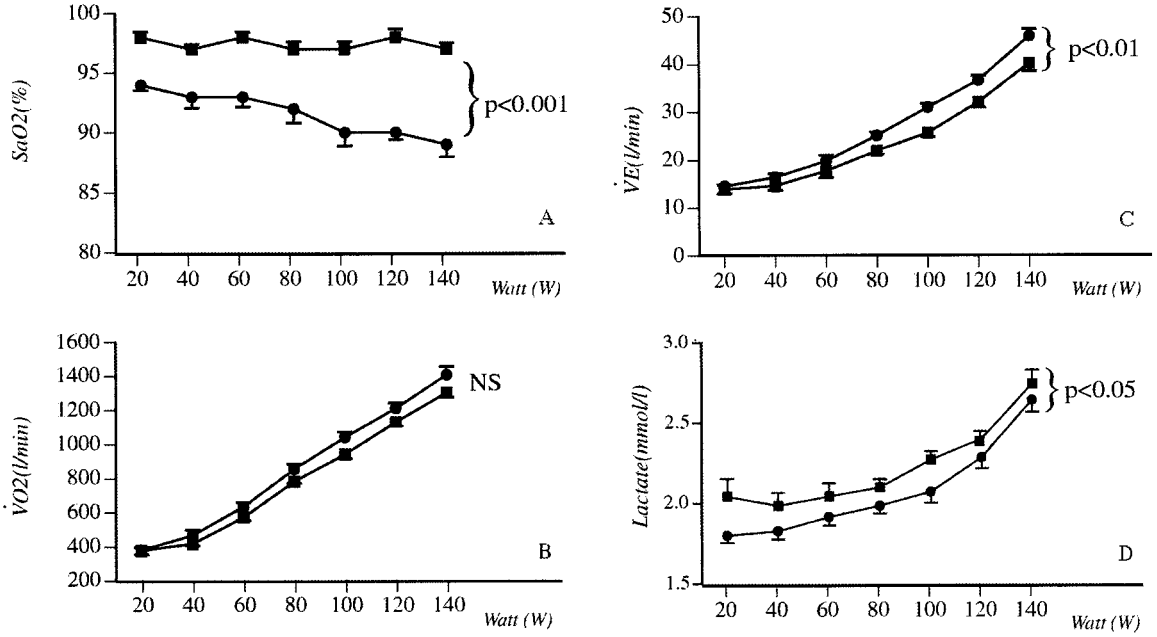

Fig.1. SaO_2(A), $\dot{V}O_2$(B), $\dot{V}E$(C) and Blood lactate(D) during exercise in normoxia(■) and hypoxia(●). Values are means ±SE.

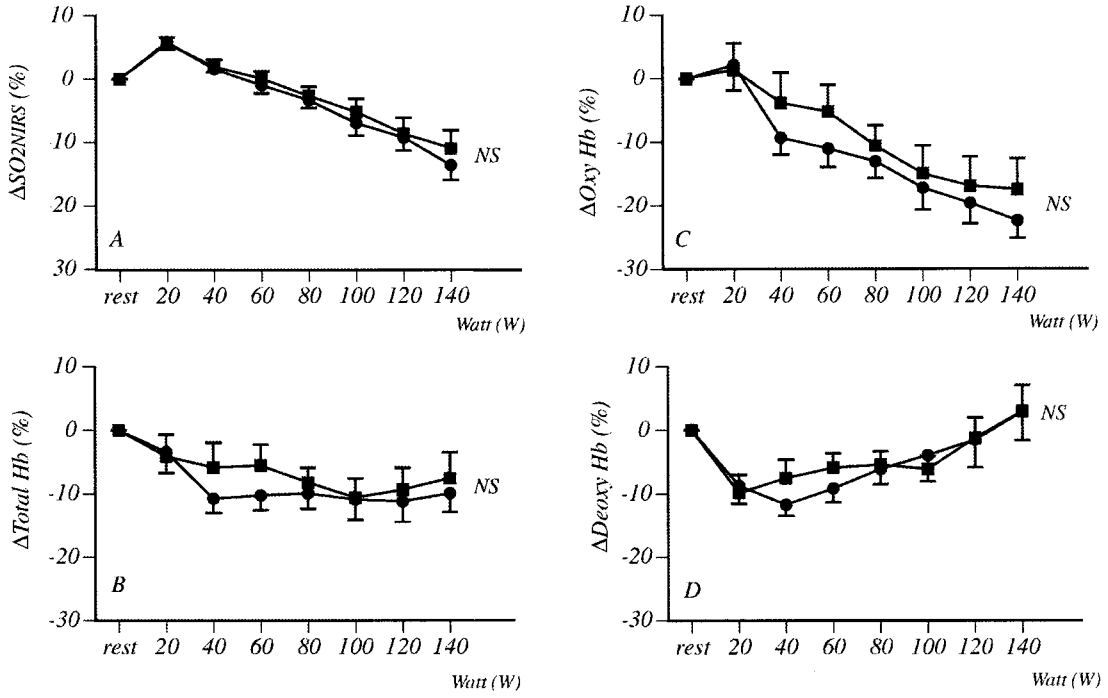

Fig.2. %change in SO2NIRS(A), Total Hb(B), Oxy Hb(C) and Deoxy Hb(D)during exercising in Normoxia(■) and hypoxia(●). Values are means ±SE

(Fig. 1A) was significantly lower in hypoxia than normoxia (ANOVA $p<0.001$). $\dot{V}E$ (Fig. 1C) increased progressively with exercise and hypoxic values significantly exceeded those found in normoxia (ANOVA $p<0.01$). Blood lactate concentrations (Fig. 1D) increased during exercise in the two conditions; however, blood lactate concentrations were significantly lower in hypoxia than normoxia (ANOVA $p<0.05$). $\dot{V}O_2$ (Fig. 1B), Δ SO2NIRS (Fig. 2A), Δ Total Hb (Fig.2B), Δ OxyHb (Fig. 2C) and Δ Deoxy Hb (Fig.2D) were not found in exercise during hypoxia compared with normoxia for the same power outputs.

Discussion

Cardiorespiratory responses

Reduced aerobic capacity has been found in acute hypoxia compared with normoxia, and a wide variability in reduction of $\dot{V}O_2$max decrements during hypoxic breathing has been reported [7, 10, 15, 16]. In this study under 15%O_2 conditions, we found that peak$\dot{V}O_2$ was reduced significantly compared with that under normoxic conditions. In breathing a gas mixture of 17%O_2 [5,13], however, $\dot{V}O_2$max was not changed compared with normoxia, findings that might be due to the difference in the fraction of oxygen in the inspired gas.

Several investigations have studied the influence of acute hypoxia on cardiorespiratory dynamics and blood lactate concentration for the same power output in incremental ergometer exercise protocols [6, 7]. Ibanez et al. [7] working with subjects under severe hypoxemia (10%O_2), found a significant increase in $\dot{V}CO_2$, $\dot{V}E$ and blood lactate concentration below 200 watt and a decrease in $\dot{V}O_2$ between 150 and 200 watt. Hughson et al. [6] found a significant decrease in $\dot{V}O_2$ and an increase in lactate concentration above 190 watt under 14%O_2 air breathing. In our study under 15%O_2 conditions, we found a significant increase in $\dot{V}E$ and an insignificant change in $\dot{V}O_2$ for the same workload below 140 watt. This would suggest that hypoxemia during mild hypoxia may be avoided through respiratory compensation at the alveolar level, shown by the increase in $\dot{V}E$, so minimizing the reduction in saturation with a mild decrease in partial pressure of oxygen in arterial blood.

Several investigations have reported that blood lactate concentrations were higher, for the same absolute exercise intensity, under acute hypoxia than in normoxia [7,18], and that increased $\dot{V}E$ was caused by the highest blood lactate concentration during hypoxic exercise [7]. However, no difference in blood lactate concentrations for the same relative intensity was found in 17%O_2 breathing exercises [5, 9]. Contrary to these reports, we found a significant decrease in blood lactate accumulation for the same power output. This suggests that the lowest blood lactate concentrations were caused by hypoxia-induced hyperventilation.

Table1. Mean ±SE of selected varibales during peak incremental exercise in normoxia and hypoxia

Variable	Normoxia	Hypoxia	
Power output (W)	228.6±9.1	178.6±10.3	**
$\dot{V}O_2$, STPD(l/min)	1.94±0.07	1.58±0.08	**
$\dot{V}CO_2$, STPD(l/min)	2.51±0.14	2.10±0.18	NS
HR (bpm)	185±3.2	166±4.8	**
$\dot{V}E$, BTPS (l/min)	92.7±4.4	64.3±7.1	*
Blood Lactate(mmol/l)	5.5±0.6	3.5±0.3	*
SaO_2 (%)	97.7±0.5	87.7±1.1	***
ΔOxy Hb (%)	-14.8±7.3	-30.1±4.4	*
ΔDeoxy Hb (%)	7.9±4.7	5.7±4.6	NS
ΔTotal Hb (%)	-4.2±5.7	-11.4±3.0	NS
ΔSO_{2NIRS} (%)	-11.7±3.6	-18.0±4.7	*

Differences between normoxia and hypoxia
NIRS data were expressed by changes from resting values
Significance level: *:p<0.05 **:p<0.01 ***:p<0.001

Muscle oxygenation responses

Recently, measurements using NIRS have made it possible to noninvasively measure in vivo changes in the oxygenated and deoxygenated hemoglobin and/or myoglobin of tissue. Previously, few studies have found any influence of hypoxia on muscle oxygenation measured by NIRS during incremental exercise, although several investigators have reported oxy- and deoxygenation in vastus lateralis muscle during ergometer cycle exercise [1-4, 8, 17]. We found in the hypoxic condition (15%O_2) that peak workload, peak SaO_2 and peak ΔSO_{2NIRS} were significantly lower compared with normoxia (Table 1).

The changes of total Hb represent those of blood volume, and SO_{2NIRS} those of the averages of arterial, capillary, and venous hemoglobin oxygen saturation, as well as the contributions from intracellular myoglobin oxygen saturation [2, 14]. This would suggest that when the condition is 15%O_2, it contributes to the differentiation of changes in oxygen content and metabolic demand in exercising muscle during peak exercise.

The time course of the NIRS change comparing normoxia and hypoxia was evaluated by steady state exercise. Costes F. et al. [3] have reported that during 30-min steady state exercise, muscle oxygenation was significantly lower in hypoxia (inspired oxygen fraction=0.105) than in normoxia when PaO_2 was shown to be 38torr at onset of exercise and 35torr at a maximum of 30min in hypoxic conditions. However, Macdonald et al. [11] showed that during 5-min steady state exercise, there were no significant changes in oxygen saturation in exercising muscle between normoxia and hypoxia (17% O_2). The results of the present study indicated that $\dot{V}O_2$

and ΔSO_{2NIRS} did not significantly change in the two conditions when exercising at the same power output. These findings suggested that hypoxemia during mild hypoxia (15%O_2) may preserve oxygen consumption in alveolar and peripheral tissue oxygenation at the same power output exercise.

The muscle oxygen content depends on oxygen delivery, which is determined by the arterial oxygen content and blood flow. NIRS techniques have been used to assess changes in blood volume, and the balance between O_2 delivery and O_2 utilization. In the present study, blood flow to individual muscles of the thigh was not measured, and needs to be studied further.

In conclusion, the results of the present study would suggest that the condition, breathing 15%O_2, contributed to the differentiation of changes in oxygen content and metabolic demand in exercising muscle at a peak exercise. We found that hypoxemia during mild hypoxia may be avoided through ventilatory compensation at the alveolar level, and that oxygen consumption in alveolar and peripheral tissue oxygenation can be maintained while exercising for the same power outputs.

References

1. Belardinelli, R., Georgiou, D. and Barstow, T. J. : Near infrared spectroscopy and changes in skeletal muscle oxygenation during incremental exercise in chronic heart failure: a comparison with healthy subjects. G. Ital. Cardiol., 25: 715-724, 1995.
2. Boushel, R., Langberg, H. and Olesen, J. et al. : Monitoring tissue oxygen availability with near infrared spectroscopy (NIRS) in health and disease. Scand J. Med. Sci. Sports, 11: 213-222, 2001.
3. Costes, F., Barthelemy, JC. and Feasson, L. et al. : Comparison of muscle near-infrared spectroscopy and femoral blood gases during steady-state exercise in humans. J. Appl. Physiol., 80: 1345-1350, 1996.
4. Grassi, B., Quaresima, V. and Marconi, C. et al. : Blood lactate accumulation and muscle deoxygenation during incremental exercise. J. Appl. Physiol., 87 : 348-355, 1999.
5. Hogan, MC., Cox, RH. and Welch,HG. : Lactate accumulation during incremental exercise with varied inspired oxygen fractions. J. Appl. Physiol., 55: 1134-1140, 1983.
6. Hughson, RL., Green, HJ. and Sharratt, MT. : Gas exchange, blood lactate, and plasma catecholamines during incremental exercise in hypoxia and normoxia. J. Appl. Physiol., 79: 1134-1141, 1995.
7. Ibanez, J., Rama, R. and Riera, M. et al. : Severe hypoxia decreases oxygen uptake relative to intensity during submaximal graded exercise. Eur. J. Appl. Physiol., Occup Physiol., 67: 7-13, 1993.
8. Kawaguchi, K., Tabusadani, M. and Sekikawa, K. et al. : Do the kinetics of peripheral muscle oxygenation reflect systemic oxygen intake? Eur. J. Appl. Physiol., 84: 158-161, 2001.
9. Knuttgen, HG. and Saltin, B. : Oxygen uptake, muscle high-energy phosphates, and lactate in exercise under acute hypoxic conditions in man. Acta Physiol. Scand., 87: 368-376, 1973.
10. Lawler, J., Powers, SK. and Thompson, D. : Linear relationship between VO2max and VO2max decrement during exposure to acute hypoxia. J. Appl. Physiol., 64: 1486-1492, 1988.
11. MacDonald, MJ., Tarnopolsky, MA. and Green,HJ. et al. : Comparison of femoral blood gases and muscle near-infrared spectroscopy at exercise onset in humans. J. Appl. Physiol., 86: 687-693, 1999.
12. Matcher, SJ., Elwell, CE. and Cooper, CE. et al. : Performance comparison of several published tissue near-infrared spectroscopy algorithms. Anal. Biochem., 227: 54-68, 1995.
13. Mateika, JH. and Duffin, J. : The ventilation, lactate and electromyographic thresholds during incremental exercise tests in normoxia, hypoxia and hyperoxia. Eur. J. Appl. Physiol. Occup. Physiol., 69: 110-118, 1994.
14. McCully, KK. and Hamaoka, T. : Near-infrared spectroscopy : what can it tell us about oxygen saturation in skeletal muscle? Exerc. Sport Sci. Rev., 28: 123-117, 2000.
15. Murphy, PC., Cuervo, LA. and Hughson, RL. : study of cardiorespiratory dynamics with step and ramp exercise tests in normoxia and hypoxia. Cardiovasc Res., 23: 825-832, 1989.
16. Paterson, DJ., Pinnington, JH. and Pearce, AR. et al. : Maximal exercise cardiorespiratory responses of men and women during acute exposure to hypoxia. Aviat Space Environ Med., 58: 243-247, 1987.
17. Wadazumi, T., Kimura, Y. and Oshima, Y. et al. : Differences in breakpoint patterns in the muscle oxygenation curve measured by NIRS during ramp exercise. Ther Res., 17: 153-157, 1996.
18. Wagner, JA., Miles, DS. and Horvath, SM. : Physiological adjustments of women to prolonged work during acute hypoxia. J. Appl. Physiol., 49: 367-373, 1980.