EFFECTS OF VARIOUS HYPOBARIC HYPOXIA ON METABOLIC RESPONSE, SKELETAL MUSCLE OXYGENATION, AND EXERCISE PERFORMANCE IN HEALTHY MALES

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ABSTRACT

Objective
This study aimed to evaluate the effect of various levels of hypoxia versus normoxia on exercise performance, measured by metabolic parameters and skeletal muscle oxygenation profiles during graded exercise test (GXT) in healthy men.

Methods
In this randomized crossover trial, 11 healthy male participants (age 21.5 ± 2.3 years) performed the GXT using a cycle ergometer at sea-level (760 torr) and at various hypobaric hypoxia: 633, 526, and 433 torr, corresponding to simulated altitudes of 1500, 3000, and 4500 m, respectively. The GXT was started at 50 W and increased by 25 W every 2 min until the participants were exhausted. The pedal frequency was set to 60 rpm. Metabolic parameters (heart rate, HR; minute ventilation, VE; carbon dioxide excretion, VCO₂; respiratory exchange ratio, RER; peripheral capillary saturation, SpO₂; oxygen consumption, VO₂; and blood lactate, O₂ pulse) and skeletal muscle oxygen profiles (oxygenated hemoglobin and myoglobin, OxyHb; deoxygenated hemoglobin and myoglobin, DeoxyHb; and tissue oxygen saturation, StO₂) were measured for every 2 min during the GXT. Exercise performance was evaluated by maximal oxygen consumption, peak power, and duration of exercise time obtained through GXT.

Results
Regarding metabolic parameters, HR (P < 0.05), VE, (P < 0.05), VCO₂ (P < 0.05), RER (P < 0.05), and blood lactate (P < 0.05) showed significant increase under hypoxia compared to normoxia. Moreover,
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the increase was more pronounced as hypoxia became more severe. However, the $S_{\text{a}}O_2$ ($P < 0.05$) and $O_2$ pulse ($P < 0.05$) presented a significant decrease under hypoxia compared to normoxia. Similarly, the decrease was more pronounced as hypoxia became more severe. $V\text{O}_2$ ($P > 0.05$) did not show significant difference under different environmental conditions. In skeletal muscle oxygen profiles, none of the parameters showed noticeable changes. Regarding exercise performance, $V\text{O}_2^{\text{max}}$ ($P < 0.05$) and exercise time ($P < 0.05$) decreased significantly as hypoxia became more severe, and peak power ($P < 0.05$) decreased significantly at simulated altitudes of 3000 and 4500 m compared to normoxia.

Conclusion
A decrease in exercise performance is due to a decrease in metabolic function under various hypoxia compared to normoxia and the decrease was more pronounced as hypoxia became more severe.

Keywords: exercise performance; graded exercise test; hypoxia; metabolic function; NIRS; skeletal muscle oxygenation

INTRODUCTION

Under hypobaric hypoxia, the partial pressure of oxygen decreases due to low atmospheric pressure. This results in reduction of alveolar oxygen partial pressure, arterial oxygen saturation, and arteriovenous oxygen difference, thereby diminishing the capacity of oxygen delivery and utilization.\(^1\)\(^-\)\(^4\) These physiological changes under hypobaric hypoxia are known to cause deterioration in energy metabolism, hemodynamic function, and vascular function, and reduce oxygen transportation and utilization, thereby reducing exercise performance.\(^5\)

In the previous studies, the exercise time, maximal oxygen consumption ($V\text{O}_2^{\text{max}}$), and exercise load were reduced when graded exercise tests (GXT) were performed at various simulation altitudes with 75% maximal heart rate (HRmax). It has been consistently reported that acute exposure to various hypobaric hypoxia affects exercise performance negatively.\(^5\)\(^-\)\(^7\) Furthermore, hypoxia reduces oxygen consumption ($V\text{O}_2$) in skeletal muscles during exercise and accelerates the accumulation of fatigue-related metabolites because of reduced oxidative phosphorylation ability.\(^8\) In addition, as the altitude increases, the respiratory exchange rate (RER) and blood lactate concentration increase significantly. The researchers explained that exercise under hypoxia reduces oxygen transport and utilization to active muscles because of low oxygen partial pressure in the alveoli, thereby increasing substrate-level phosphorylation and carbon dioxide excretion ($V\text{CO}_2$) by hypoxic ventilation response (HVR).\(^9\)\(^-\)\(^10\)

Many aspects of hemodynamic and hemorheological functions, as well as energy metabolism, are considered while conducting studies on the mechanism of exercise performance reduction during hypoxia.\(^11\)\(^-\)\(^12\) In a study assessing cardiac function and hemodynamics, the cardiac output (CO) and stroke volume (SV) were significantly lower when performing the GXT under hypoxia than those measured under normoxia.\(^13\)\(^-\)\(^14\) It was reported that exercise during hypoxia might be associated with a decrease in end-diastolic volume (EDV) and end-systolic volume (ESV) and an increase in heart rate (HR), ejection fraction (EF), and CO during submaximal exercise.\(^15\) These hemodynamic changes are an acute compensation response to decreased oxygen delivery and utilization capacities under hypobaric hypoxia.\(^16\) Furthermore, under severe hypoxia, the RBC deformability, a hemorheological index that indicates ability to deliver oxygen to tissues, decreases.\(^6\) This decrease in hemorheological function plays a key role in reducing exercise performance because it lowers oxygen supply to microvessels and tissues.\(^7\)\(^-\)\(^17\)
Near-infrared spectroscopy (NIRS) is used to identify the physiological mechanisms of changes in exercise performance during exercise. NIRS enables the measurement of skeletal muscle oxygenation profiles and the ability to deliver and use oxygen in muscle tissues. The NIRS signal reflects a dynamic balance between muscle capillary blood flow and muscular VO$_2$ in microcirculation. In this regard, another study reported a static correlation between exercise performance and skeletal muscle oxygenation. Also, it was reported that assessing oxygen-transporting and utilizing capacity in muscles through NIRS is vital because it is highly associated with exercise performance ability. Most of the previously conducted studies have confirmed skeletal muscle oxygenation profiles in a single hypoxic condition using NIRS. However, there are few studies evaluating skeletal muscle oxygenation during exercise under various hypoxic conditions.

Therefore, the purpose of this study was to evaluate the effects of various hypobaric hypoxia (simulated altitude) versus normoxia (sea-level) on exercise performance via metabolic parameters and skeletal muscle oxygenation profiles during GXT in healthy men.

**MATERIALS AND METHODS**

**Participants**

We included 11 healthy men (age, 21.5 ± 2.1 years; height, 178.3 ± 5.5 cm; weight, 71.1 ± 4.2 kg) who did not participate in any planned exercise program for the past 6 months, did not take dietary supplements, and did not live at high altitudes for 3 months. The subjects were nonsmokers and had no history of musculoskeletal, cardiovascular, pulmonary, or metabolic disease. All subjects received information about the purpose and process of this study and provided informed consent prior to the start of the study. The characteristics of the subjects are presented in Table 1. This study was approved by the IRB at Konkuk University (7001355-201805-HR-241) and was performed in accordance with the provisions of the Declaration of Helsinki.

**Study Design**

The study design of this study is shown in Figure 1. The subjects visited the laboratory for five times during the experimental period. The subjects’ body composition was measured during the first visit at sea-level (760 torr). To minimize the adaptation effect of each condition during the main experiments, sea-level (760 torr) and various hypobaric hypoxia (1500 m, 634 torr; 3000 m, 526 torr; and 4500 m, 433 torr) were randomly selected, and each condition was set up with a wash-out period of 2 weeks. The GXT of exercise performance (started at 50 W and increased by 25 W every 2 min) was conducted with a bicycle ergometer (Monark Ergomedc 828E, Monark, Sweden) at sea-level (760 torr) and various simulated altitudes after resting for 30 min. Once the subjects began their exercise, HR, VE, VO$_2$, VCO$_2$, RER, O$_2$ pulse (K5, COSMED, Monte Savello, Italy), oxygen saturation (% S$_9$O$_2$, Radical-7 pulse oximeter, MASIMO, CA, USA) and NIRS (Astem, Mizonokuchi, Japan), which are the subjects’ energy metabolism parameters, were measured at every 10 s, while blood lactate concentration was measured at every 1 min. The average values at each exercise load during 2 min were used for all results. The GXT was performed in a chamber with environmental control, at a mean

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>21.5 ± 2.16</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>178.3 ± 5.52</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.1 ± 4.22</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>22.3 ± 1.32</td>
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<tr>
<td>Muscle mass (kg)</td>
<td>57.8 ± 4.82</td>
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<tr>
<td>Lean body mass (kg)</td>
<td>61.4 ± 5.08</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>9.6 ± 2.46</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>13.5 ± 3.57</td>
</tr>
</tbody>
</table>

BMI, body mass index, SD, standard deviation.

**TABLE 1** Participant Characteristics ($n = 11$).
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The average value measured at every 1 min during rest and until exhaustion, consistently, giving the average value of every 2 min.

The HR, VE, VO₂, VCO₂, RER, O₂ pulse, and VO₂max values were measured using the automatic metabolism analyzer K5 (COSMED, Monte Savello, Italy). The analysis performed indicated an average value of 2 min at each identical load during rest and GXT every 10 s. The K5 equipment was calibrated in each condition before the experiment started. The measured VO₂max was compared for each condition.

The analysis of levels of oxygenated hemoglobin (Oxy_Hb), deoxygenated hemoglobin (Deoxy_Hb), total hemoglobin (Total_Hb), and tissue oxygen saturation (StO₂) was performed using multi-channel tissue oxygenation monitor (Near Infrared Spectroscopy (NIRS), Astem, Mizonokuchi, Japan) by reviewing laser signals (wave length: 775, 810, and 850 nm). The signals were shot from the light-emitting area of the subject’s vastus lateralis muscle and were received at the absorber after it had returned penetrating the muscle tissues. The test recorded the average value measured every 10 s during rest and until exhaustion, consistently, giving the average value of every 2 min.

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while at rest and until exhaustion, consistently, giving an average value every 2 min.

In order to measure VO\textsubscript{2}\text{max}, an automatic analyzer K5 (COSMED, Monte Savello, Italy) and a bicycle ergometer (Monark Ergomedec 828E, Monark, Sweden) were prepared, after which the GXT was conducted. In each environment, the GXT was terminated when two or more criteria were met. The criteria used for achieving a threshold for exhaustion are plateau in VO\textsubscript{2} as workload increases, an RER greater than 1.15, and maximal HR is the predicted maximal HR (220 – age).

**Statistical Analysis**

All data obtained in the present study were analyzed using SPSS software version 25.0 for Windows (IBM Corp., Armonk, NY, USA). Data were presented as mean ± standard deviation. The assumption of normality and homoscedasticity was verified using the Shapiro–Wilks W-test before parametric tests. First, a two-way analysis of variance (ANOVA) with repeated measures was used to elucidate the interaction effects between environmental conditions and exercise time. Second, repeated one-way ANOVA was used to evaluate differences in dependent variables between all environmental conditions at each time point, and the post hoc test was used the Bonferroni test. A significance level of P < 0.05 was used to determine the statistical difference.

**RESULTS**

**Energy Metabolism during GXT**

Energy metabolism parameters at rest and during exercise are shown in Figure 2. A significant interaction (n\textsuperscript{2} = 0.236, P < 0.001) was observed between environmental conditions and exercise time in S\textsubscript{p}O\textsubscript{2}. As a result of post hoc analysis, S\textsubscript{p}O\textsubscript{2} was significantly lower (P < 0.05) at hypobaric hypoxia (433 torr) than all environmental conditions at most exercise loads. Furthermore, S\textsubscript{p}O\textsubscript{2} was significantly lower (P < 0.05) at hypobaric hypoxia (623 torr) than at sea-level (760 torr) and hypobaric hypoxia (633 torr), but hypobaric hypoxia (633 torr) was significantly lower (P < 0.05) than sea-level (760 torr) (Figure 2A).

Heart rate showed a significant interaction (n\textsuperscript{2} = 0.336, P < 0.001) between environmental condition and exercise time. HR was significantly higher (P < 0.05) at hypobaric hypoxia (433 torr) and hypobaric hypoxia (623 torr) than at sea-level (760 torr) at most exercise loads. Furthermore, HR was significantly higher (P < 0.05) at hypobaric hypoxia (433 torr) than hypobaric hypoxia (633 torr) (Figure 2B).

Minute ventilation presented a significant interaction (n\textsuperscript{2} = 0.679, P < 0.001) between environmental condition and exercise time. VE was significantly higher (P < 0.05) at hypobaric hypoxia (526 torr) and hypobaric hypoxia (433 torr) than hypobaric hypoxia (633 torr) and at sea-level (760 torr) at most exercise loads (Figure 2C).

VO\textsubscript{2} presented a significant interaction (n\textsuperscript{2} = 0.374, P < 0.001) between environmental condition and exercise time. Post hoc analyses found that VO\textsubscript{2} increased (P < 0.05) significantly at hypobaric hypoxia (526 torr) and hypobaric hypoxia (433 torr) than all other environmental conditions at rest. However, no main effect in environmental condition was observed (n\textsuperscript{2} = 0.147, P = 0.184) and there was no significant difference between sea-level and various simulated altitudes at most exercise loads (Figure 2D).

There was a significant interaction (n\textsuperscript{2} = 0.551, P < 0.001) between environmental condition and exercise time in O\textsubscript{2} pulse. Post hoc analyses found that O\textsubscript{2} pulse was significantly lower (P < 0.05) at hypobaric hypoxia (526 torr) and hypobaric hypoxia (422 torr) than other environmental conditions at most exercise loads (Figure 2E).

VCO\textsubscript{2} showed a significant interaction (n\textsuperscript{2} = 0.299, P < 0.001) between environmental condition and exercise time. VCO\textsubscript{2} was significantly higher (P < 0.05) at hypobaric hypoxia (433 torr) than all other environmental conditions at most exercise loads. Furthermore, VCO\textsubscript{2} was significantly higher (P < 0.05) at hypobaric hypoxia (526 torr) than hypobaric hypoxia (633 torr) (Figure 2F).
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FIGURE 2 Changes in metabolic parameters at rest and during GXT. (A) Change in S\(_pO_2\) (%), (B) change in HR (bpm), (C) change in VE (L/min), (D) change in VO\(_2\) (mL/min), (E) change in O\(_2\) pulse (mL/min), (F) change in VCO\(_2\) (mL/min), (G) change in RER, (H) change in blood lactate level (mmol/L); a = 760 torr, b = 633 torr, c = 526 torr, d = 433 torr; greater than (>), or less than (<) indicates significant difference. Different lowercase letters indicate significant differences in hypoxia groups. No alphabet of time indicates not significant. Red line: For comparison of each condition, statistical analysis was conducted with the results of up to 10 min; all subjects completed the GXT. GXT: graded exercise test, n\(^2\): partial eta squared, H: hypoxia, E: exercise, S\(_pO_2\): peripheral capillary oxygen saturation, HR: heart rate, VE: minute ventilation, VO\(_2\): oxygen uptake, O\(_2\) pulse: oxygen pulse, VCO\(_2\): carbon dioxide exertion, RER: respiratory exchange ratio.

There was a significant interaction in RER (n\(^2\) = 0.312, P < 0.001) between environmental condition and exercise time. RER was significantly higher (P < 0.05) at hypobaric hypoxia (433 torr) than all other environmental conditions. It was also significantly higher (P < 0.05) at hypobaric hypoxia (526 torr) than hypobaric hypoxia (533 torr) and sea-level (760 torr) at most exercise loads (Figure 2G).

Blood lactate level showed a significant interaction (n\(^2\) = 0.740, P < 0.001) between environmental condition and exercise time. Blood lactate level was significantly higher (P < 0.05) at hypobaric hypoxia (433 torr) than all other environmental conditions at most exercise loads. It was significantly higher (P < 0.05) at hypobaric hypoxia (526 torr) than at sea-level (760 torr) (Figure 2H).

**Muscle Oxygenation during GXT**

Muscle oxygenation profiles at rest and during exercise are shown in Figure 3. There was a significant interaction between environmental condition
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and exercise time in Oxy_Hb ($n^2 = 0.150$, $P = 0.045$) and StO$_2$ ($n^2 = 0.178$, $P = 0.010$). Post hoc analyses found that Oxy_Hb decreased ($P < 0.05$) significantly at hypobaric hypoxia (526 torr) than at sea-level (760 torr) at 50 and 75 watt of exercise load (Figure 3A). However, Oxy_Hb tended to be lower at sea-level than under most hypoxic conditions. StO$_2$ showed a significant decrease ($P < 0.05$) at hypobaric hypoxia (433 torr) than at hypobaric hypoxia (633 torr) at 100 watt of exercise load (Figure 3D). Overall, StO$_2$ presented a tendency similar to Oxy_Hb. Deoxy_Hb ($n^2 = 0.128$, $P = 0.124$) and Total_Hb ($n^2 = 0.063$, $P = 0.811$) showed no significant interaction between environmental condition and exercise time (Figures 3B and C).

Exercise Performance

There was a significant main effect within environmental condition in VO$_2$max ($n^2 = 0.941$, $P < 0.001$), peak power ($n^2 = 0.803$, $P < 0.001$), and exercise time ($n^2 = 0.921$, $P < 0.001$). As a result of post hoc analysis, VO$_2$max and exercise time showed a significant decrease ($P < 0.05$) proportionally with increase in simulated altitude (Figures 4A and C). Peak power also showed the same statistical changes as other exercise performance parameters (e.g., VO$_2$max and exercise time); however, there was no significant difference between sea-level (760 torr) and hypobaric hypoxia (633 torr) (Figure 4B).

DISCUSSION

Response to reduction phenomenon based on metabolic parameters and skeletal muscle oxygenation profiles for the change in exercise performance according to altitude was revealed. In metabolic parameters, HR, VE, VCO$_2$, RER, and blood lactate level increased, while O$_2$ pulse and SpO$_2$ decreased during the GXT at various hypobaric hypoxia conditions. 

FIGURE 2  Continued
Hypoxia exposure reduces exercise performance

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reported that the decrease in $S_{pO_2}$ is caused by the promotion of oxygen dissociation to compensate for the lack of oxygen in tissues. Considering that the oxygen dissociation curve is an “S” shape curve, it can be understood that when $PO_2$ of the x-axis decreases, the oxygen saturation of hemoglobin drops rapidly. It has been reported that individuals in hypoxic conditions have high respiratory frequency and increased dead space ventilation, which cause lower oxygen saturation than at sea-level.

The RER results of this study showed no difference between sea-level and hypobaric hypoxia (633 torr) at all exercise loads. However, there was a significant difference (P < 0.05) at both hypobaric

Energy Metabolism

In our results, the level of $S_{pO_2}$ was significantly lower (P < 0.05) at various hypobaric hypoxia than at sea-level at all exercise loads. A previous study
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J Mens Health Vol 16(4):e107–e120; 02 November 2020
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760 torr 633 torr 526 torr 433 torr

760 torr 633 torr 526 torr 433 torr

hypoxia (633 tor) and (433 torr) compared with other environmental conditions. In other words, the carbohydrate oxidation rate is high at hypobaric hypoxia (526 torr) and hypobaric hypoxia (433 torr) at all exercise loads. A previous study compared metabolic function during 60 min of aerobic exercise at 50% VO₂max at sea-level and normobaric hypoxia (inspired oxygen fraction, F_iO₂ = 12.4%). The results showed a significant increase in RER and carbohydrate oxidation at normobaric hypoxia compared with sea-level, which is consistent with our findings. Regarding acute exposure to hypoxic conditions, glucose is the most oxygen-efficient substrate, and the use of glucose metabolism increases as the oxygen transport capacity is limited to tissues. This can be explained by decrease in ability to generate aerobic energy because of low S_pO₂. In addition, increase in carbohydrate oxidation with increase in altitude is due to the increased activity of the sympathetic nervous system, leading to increased secretion of epinephrine and norepinephrine, which promotes carbohydrate oxidation. An increase in carbon dioxide emission due to a high respiratory frequency may lead to an increase in blood lactate and hydrogen, resulting in increased RER. In this study, we found that carbohydrate oxidation increased with increase in simulated altitude. These results can be explained

FIGURE 4  Exercise performance at all environmental conditions. (A) Change in VO₂max, (B) change in peak power, and (C) change in exercise time. a, b, c, and d: Different alphabets indicate significant difference, VO₂max: maximal oxygen consumption.
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by the fact that carbohydrates are more efficient in the use of oxygen in ATP production than fat oxidation. In addition, a previous study has reported that lactate production increased due to an imbalance in acetyl-CoA producing reactions because of accelerated glycolysis and decreased pyruvate dehydrogenase (PDH) activity during the GXT under hypoxic conditions.

Compared to sea-level, the HR response was higher as the simulated altitudes increased at all points during exercise. This increase in HR provides sufficient oxygen transfer to tissues, and the heart supplies more blood under hypoxia than normoxia. In addition, increase in HR in hypoxia is mainly due to increased catecholamine secretion caused by activation of the sympathetic nervous system and the beta-adrenaline receptor stimulation by epinephrine. In addition, as simulated altitude increases, breathing becomes faster, and oxygen through absorption increases the alveolar dead space rate without gas exchange in the pulmonary alveoli. It facilitates the transport of oxygen to tissues through increased HR.

In VE, the reaction increased significantly (P < 0.05) during exercise with increase in simulated altitude. A previous study conducted GXT with seven trained and sedentary women at sea-level and various hypoxia (1000 m, \( F_{O_2} = 18.7\% \); 2500 m, \( F_{O_2} = 15.4\% \); 4500 m, \( F_{O_2} = 11.7\% \)), and it reported results that were consistent with our findings. An increase in VE due to hypoxia maintains \( VO_2 \), and an increase in anaerobic metabolism increases the stimulation of the respiratory control center and the elimination of \( VCO_2 \) through breathing. There is less oxygen per volume of air in hypoxia than normoxia because hypoxia reduces air pressure. Therefore, to supply the same amount of oxygen for a given exercise intensity, more air must be exchanged in the lungs. Another study explained that respiratory alkalosis, caused by hyperventilation at the simulated altitudes, increased the affinity of hemoglobin to oxygen. This reaction increases oxygen transport to pulmonary alveolar capillaries and is intended to regulate the transport of oxygen necessary for tissues. Hypoxia is compensated by increasing VE to minimize decrease in the partial pressure of oxygen in arterial blood and reduction in oxygen saturation. The \( O_2 \) pulse refers to the amount of \( VO_2 \) per HR, which means that when the HR is low and the \( VO_2 \) is high, there is no stress on the heart, and the utilization of oxygen is positive. Consequently, hypoxia-induced reduction in \( O_2 \) pulse affects exercise performance negatively by reducing the rate of oxygen transfer to tissues.

**Muscle Oxygenation**

NIRS equipment was used to evaluate oxygen utilization rate in muscles during the GXT at sea-level and various hypobaric hypoxia. It was reported to have a high correlation with exercise performance as an index for evaluating oxygen utilization capacity in tissues. The measurable variable of this equipment is the combination of oxygen and hemoglobin in Oxy-Hb and the separate amount of oxygen and hemoglobin in Deoxy-Hb. Basically, it is desirable to have higher Oxy-Hb and lower Deoxy-Hb in terms of exercise science. Total_Hb is the amount of Oxy-Hb and Deoxy-Hb in total hemoglobin, and StO2 is the amount of oxygen saturation carried to tissues.

A previous study reported a decrease in the amount of Oxy-Hb and an increase in Deoxy-Hb when performing leg resistance and submaximal exercise at various simulated altitudes. This explains why hypoxia induces reduction in the arterial oxygen difference by decreasing partial pressure of oxygen in the artery. This response is recorded as the oxygen dissociation curve moves to the right due to metabolic acidosis caused by the activation of glycolysis. The same result was observed when the GXT was performed, and this was explained as an increase in Deoxy_Hb in muscles due to a decrease in blood arterial oxygen saturation. It has been reported that the oxygen utilization rate in tissues decreases by 7% for every 1000-m increase in
Hypoxia exposure reduces exercise performance

altitude and that limited oxygen accelerates peripheral muscle fatigue. However, we confirmed that the use of oxygen in muscles did not significantly affect exercise performance. These findings show that decrease in exercise performance in hypoxia is more dependent on metabolic and cardiac functions than on muscle oxygenation functions. In order to clarify this, further studies are necessary.

Exercise Performance

In hypoxia, both the muscles and the brain have limited oxygen supply, so fatigue occurs earlier during exercise, affecting exercise performance. It has been found that cerebral oxygen plays an important role in performance decline during exercise in hypoxia. Acute exposure in a hypoxic condition also accelerates muscle fatigue by reducing alternative O content and leg blood flow. Previous study reported that exercise in hypoxia leads to low oxygen density, which means that the partial pressure of oxygen in the human body is low and affects VO\textsubscript{max}. In addition, when acutely exposed to hypoxia, HR and VE are higher than at sea-level (760 torr) due to the stimulation of sympathetic nerve and relative increase in energy metabolism, which affects VO\textsubscript{2max}. In addition, the cause of decrease in VO\textsubscript{max} at a simulated altitude of 5000 m (F\textsubscript{O\textsubscript{2}} = 10.5%) was that the maximal CO and blood flow to the muscles were low. Hypoxia revealed that hemoglobin concentration in the blood is low, causing a decrease in VO\textsubscript{2max}.

In this study, VO\textsubscript{max} showed a significant decrease (P < 0.05) proportional to an increase in simulated altitude. In particular, VO\textsubscript{max} was at its lowest value at hypobaric hypoxia (433 torr). A previous study reported that when exposed to extreme hypoxia; oxygen saturation in the blood is less than 70%, which is equivalent to 4500 m (433 torr). This causes fatigue of the central nervous system and affects VO\textsubscript{2max}, which is reported as one of the causes of its low value. It was also reported that as the simulated altitude increased, oxygen diffusion was insufficient due to low diffusion in pulmonary capillaries, and relative exercise intensity increased when absolute intensity increased, resulting in lower VO\textsubscript{2max}. However, it has been reported that oxygen diffusion is limited to capillary mitochondria in muscles under severe hypoxia. The decrease in VO\textsubscript{2max} with altitude is believed to reduce the peak power and exercise time during hypoxia. In addition, it has been reported that VO\textsubscript{2max} decreases by ~1.5–3.5% with every 300-m increase at altitudes above 1500 m.

In acute exposure to a hypoxic condition, exercise performance is deteriorated by hypoxia in terms of energy metabolism and cardiac function as mentioned above. Nevertheless, when applying training in this hypoxic condition, plasma and blood cells increase, and therefore red blood cells increase, thereby increasing the exercise performance. In addition, in the case of blood lactate concentration, it has the effect of showing a low value after training in a hypoxic condition. Training in such a hypoxic condition brought benefits, but it was confirmed that exercise performance decreased during acute exposure. In the future studies, the analysis of protein and RNA changes at molecular level, which is not confirmed in this study, could examine in multiple ways the causes of reduction in exercise performance in hypoxic conditions.

CONCLUSION

The results suggest that exercise performance decreased under various hypoxia compared to normoxia, and the decrease was more pronounced as hypoxia became more severe. In addition, it is confirmed that the difference between sea-level (760 torr) and hypoxia (633 torr) in a metabolic function is faint, but the difference is remarkable at hypoxia (526 torr) and above. From hypoxia (526 torr) and above, it has a greater negative impact on exercise performance because of a severe decrease in metabolic function. However, we confirm that muscle oxygenation profiles do not significantly affect the decrease in exercise performance.
CONFLICT OF INTEREST
The authors declare no conflicts of interest.

FUNDING
This work was supported by the Ministry of Education of the Republic of Korea and the National Research Foundation of Korea (NRF-2019S1A5A2A03034583).

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J Mens Health Vol 16(4):e107–e120; 02 November 2020
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