The Influence of High-Altitude Acclimatization on Ventilatory and Blood Oxygen Saturation Responses During Normoxic and Hypoxic Testing

by
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We investigated how acclimatization effects achieved during a high-altitude alpinist expedition influence endurance performance, ventilation (VE) and blood oxygen saturation (SaO2) in normoxic (NOR) and hypoxic conditions (HYP). An incremental testing protocol on a cycle ergometer was used to determine the power output corresponding to the Lactate (PLT) and Ventilatory Threshold (PVT) in NOR and HYP (FiO2=0.13) as indirect characteristics of endurance performance in both conditions. Furthermore, changes in VE, SaO2, blood pH and Pco2 were measured at a similar absolute exercise intensity of 180 W in NOR and HYP conditions. Seven experienced alpinists (mean ± SD: age: 50 ± 6 yrs; body mass: 76 ± 5 kg; body height: 175 ± 8 cm) volunteered to participate in this study after they had reached the summit of Gasherbrum II and Ama Dablam. They had therefore experienced the limitations of their acclimatization. Individual differences of PLT between values reached after and before the expedition (ΔPLT) correlated (r = 0.98, p = 0.01) with differences of SaO2 (ΔSaO2) in HYP, and differences of PVT (ΔPVT) correlated (r = -0.83, p = 0.02) with differences of VE (ΔVE) in HYP. The results suggest that the acclimatization may not have an equivocal and simple influence on the performance in hypoxia: enhanced blood oxygen saturation may be accompanied by increased endurance only, when the increase exceeded 2-3%, but enhanced ventilation, when increased more than 10 l/min in HYP, could detrimentally influence endurance.

Key words: hypoxia, normoxia, acclimatization, alpinist expedition, endurance.

Introduction
Alpinists who climb to high altitudes are exposed to extreme environments and experience profound alterations in the structure and functioning of their organism (Hornbein and Schoene, 2001; West, 1982). Perhaps the earliest response to hypoxia (HYP) is an increase in pulmonary ventilation (VE) while resting (hypoxic ventilator response, HVR) (Dempsey and Forster, 1982; Smith et al., 2001). The increase in VE is even more evident during exercise in HYP (Smith et al., 2001; Steinacker et al., 1996; West et al., 2007). The consequence is an increase in blood Po2 and a decrease in PCO2 which shifts the oxyhemoglobin saturation curve so that blood becomes more oxygenated at a similar Po2. (Wagner, 2001; West, 1982). It is believed that high HVR values represent better acclimatization (Katayama et al., 2001; Smith et al., 2001). Yet, Bernardi et al. (2006) showed that high HVR values did not accompany the response of high-level alpinists even when they were acclimatized. During exercise in acute hypoxic exposure, VE increases more than it can be predicted from changes during exercise in normoxia (Wagner, 2001). However, it is unclear whether this increase continues during chronic exposure to hypoxia in all subjects and in a

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similar manner. Ventilatory sensitivity to hypoxia during exercise is important in this adaptation (Lhuisser et al., 2012; Richale et al., 2011) which results from alterations in the sensitivity of baroreceptors in blood vessels (Lahiri and Cherniak, 2001; Lahiri et al., 2003; Smith et al., 2001), and also from sensitivity to hypoxia in the central nervous system (Paulin and Robbins, 1998; Severinghaus, 2001). In addition to acclimatization, climbing may influence adaptations in endurance performance. Although endurance training decreases $\dot{V}E$ in normoxic conditions (Byrne-Quinn et al., 1971), this phenomenon does not seem to regularly occur during exercise in hypoxia (Roach and Kayser, 2001; West et al., 2007). The question is whether alpinists as typical representatives who push their acclimatization possibilities to the limits adapt to hypoxic exercise with a parallel increase in $\dot{V}E$, HVR during exercise and SaO2?

The aim of the study was to identify the typical characteristics of $\dot{V}E$, HVR during exercise and SaO2 alterations as effects of acclimatization, which can influence endurance performance observed in a hypoxic environment.

**Material and Methods**

**Participants**

Four experienced alpinists who reached the peak of Gasherbrum II (8,032 m), and three who climbed Ama Dablam (6,828 m) (age = 50 ± 6 yrs, body mass = 76 ± 5 kg, body height = 175 ± 8 cm) volunteered to participate in this study. Due to the comparable ascending (acclimatization) and descending strategies and similarities in power output determined by Lactate (PLT) and Ventilatory (PVT) Thresholds before the expedition, both groups were combined for data analysis. The study was approved by the National Ethics Medical Committee and all subjects read and signed a consent form prior to testing.

**Procedures**

One week before both expeditions departed, all subjects completed the first incremental cycle ergometer test in normobaric hypoxia (HYP; FiO2 = 0.13) conditions after an overnight sleep in those conditions. Both HYP sleeping and testing were administered in two rooms with controlled environmental conditions (“altitude room”; b-Cat, Tiel, Netherlands). Normobaric hypoxia was reached by a vacuum pressure swing adsorption system. This system generated and delivered oxygen-depleted air to both rooms. The subjects slept overnight in the rooms in such conditions from about 8 pm to 8 am (about 12 hrs). Testing in normoxic conditions (NOR: terrestrial altitude of 250 m, barometric pressure about 1011 hPa, FiO2 = 0.21) followed HYP tests in two days. This break was needed for preventing fatigue during HYP testing.

Each subject participated in four incremental tests on a mechanically braked cycle ergometer (Monark, Model 818E, Ergomedic, Sweden). The first incremental test in HYP started at 60 Watts (W) and increased by 40 W every 4 min until volitional fatigue. It was reached at 180 W in all except two subjects, who could perform 200 W for 2 and 3 min, respectively. Therefore, the power output of 180 W was used as a reference power limit (180 W) for the follow-up tests.

The mountain climbing ascent phase lasted ~4 weeks. In the first 7-day phase, the alpinists climbed to the base camp (~5,000 m). During the next 3 weeks, they gradually acclimatised via prepared altitude camps and subsequently reached the summit. The descent phase lasted 14 days, until the final testing.

The post-expedition procedure was identical to the first two tests. The third test was conducted in HYP after an overnight sleep in HYP conditions. A final post expedition test was administered in NOR two days after the third test.

**Measures**

During ergometer testing, blood samples (10 μl) were collected to determine blood LA with an LP400 laboratory photometer (Dr. Lange, Berlin, Germany). Measures of $\dot{V}E$, $\dot{V}O2$ and $\dot{V}CO2$ were recorded using a K4b (Cosmed, Rome, Italy) metabolic cart. In addition, capillary blood Po2, Pco2, pH, blood bicarbonate (HCO3) and blood oxygen saturation (SaO2) were assessed utilising an ABL 5 analyser (Radiometer, Copenhagen, Denmark). Capillary blood samples in the amount of 60-80 μl were obtained from a hyperaemic ear lobe. Arterial blood O2 saturation (SaO2) was measured using a TrueSignal pulse oximeter (Datex Ohmeda, Inc., Madison, WI, USA).

**Calculations and statistical analysis**

Blood LA data from the incremental testing protocol were used to determine the Lactate Threshold (LT) by using a log-to-log
transformation model (Beaver et al., 1984). Furthermore, $V_{E}$ data from the same testing protocol were used to assess the Ventilatory Threshold (VT) via a V-slope model (Beaver et al., 1986).

The ventilatory response to hypoxia was calculated using the following equation (Lhuissier et al., 2012; Richalet et al., 2011):

$$HVR_{VT} = \frac{\Delta V_{ET}}{(\Delta SaO_{2} \times BW)} \times 100 \quad (\text{Equation 1})$$

where $\Delta V_{ET}$ is the difference in $V_{ET}$ between the HYP and NOR testing and $\Delta SaO_{2}$ is the difference in $SaO_{2}$ between NOR and HYP. Unlike in Lhuissier et al.’s (2012) testing protocol, we used data which were determined by VT (a similar relative exercise intensity) measured during incremental protocols performed in NOR and HYP conditions and not by using a specific test.

Indirect measurements were taken to estimate endurance performance: Ventilatory Threshold (VT) and Lactate Threshold (LT) were used (Amann et al., 2004; Ušaj and Starc, 1996).

Power outputs obtained using both methods ($P_{LT}$ and $P_{VT}$) were compared before (PRE) and after (POST) the expedition in the NOR and HYP conditions utilising a two-way ANOVA and paired $t$-tests via Sigma Plot ver. 11 (Systat Software, Inc., Erkrath, Germany). The level of statistical significance was set at $p < 0.05$.

Alterations at similar absolute exercise intensities (120, 140 and 180 W) were analysed as difference between POST and PRE values in NOR and HYP conditions using a two-way ANOVA and paired $t$-tests.

Results

**Testing in normoxic conditions (NOR)**

$P_{LT}$ and $P_{VT}$ in NOR conditions did not show any significant effect of the alpinist expedition estimated by their differences between POST and PRE values (Table 1, Figure 1, filled circles). $P_{LT}$ had similar values PRE (151 $\pm$ 9 W) and POST expedition (155 $\pm$ 18 W). Similarly, $P_{VT}$ also showed no effect of the alpinist expedition: PRE, the values (162 $\pm$ 35 W) were similar to those reached POST (145 $\pm$ 23 W) (Table 1). No correlation existed between PRE and POST, $P_{LT}$ and $P_{VT}$ (Figure 1, filled circles).

**Testing in hypoxic conditions (HYP; FiO$_{2}$ = 0.13)**

In HYP conditions, $P_{LT}$ and $P_{VT}$ did not show any significant effect of the alpinist expedition (Table 1, Figure 1, open circles). $P_{LT}$ exhibited a growing tendency from 117 $\pm$ 14 W to 137 $\pm$ 31 W ($p=0.06$, NS). $P_{VT}$ also revealed a tendency to increase from 125 $\pm$ 20 W to 135 $\pm$ 29 W ($p=0.50$, NS) (Table 1). When changes between the NOR and HYP conditions were compared between the PRE and POST expedition, a significant decrease of $P_{LT}$ by 34 W (Table 1, $p=0.05$) and similarly for $P_{VT}$ by 37 W (Table 1, $p=0.05$) observed PRE disappeared POST the expedition and became negligible for $P_{LT}$ and $P_{VT}$ (Table 1).

There were significant correlations between $P_{LT}$ PRE and POST ($r = 0.74; p=0.05$) (Figure 1) and between $P_{VT}$ PRE and POST ($r = 0.76; p=0.05$) (Figure 1).

In HYP conditions, blood $SaO_{2}$ values increased significantly ($p<0.05$) at 180 W in POST in comparison to the PRE values (Table 2). The difference between the POST and PRE values in $SaO_{2}$ ($\Delta SaO_{2}$) was well correlated ($r=0.98; p=0.01$) to the difference between $P_{LT}$ reached POST and PRE expedition ($\Delta P_{LT}$) (Figure 2). About a 4% increase in $\Delta SaO_{2}$ at a 180 W intensity was required to increase the values of $P_{LT}$ POST expedition in HYP conditions. However, due to the single highest $\Delta SaO_{2}$ value, which accompanied the highest value of $\Delta P_{LT}$ (Figure 2), this correlation became high. Therefore, it should be interpreted cautiously.

When the changes in $V_{E}$ at 120, 140 and 180 W between the POST and PRE expedition ($\Delta V_{E}$) were compared to the changes in $P_{VT}$ ($\Delta P_{VT}$) in HYP conditions, correlations existed (using a parabola model) for 120 W ($r = -0.83; p=0.02$) and for 180 W ($r = -0.83; p=0.02$), but not for 140 W ($r = -0.67; p>0.05$, NS) (Figure 3). They showed that the decrease in $\Delta V_{E}$ was correlated with the increase in $\Delta P_{VT}$ (left side of the diagram, Figure 3), but the increase in $\Delta P_{VT}$ did not seem to be strongly correlated with changes of $\Delta V_{E}$ (right side of the diagram, Figure 3).

When hypoxic ventilatory responses (HVR$_{VT}$) during a similar relative exercise intensity at $P_{VT}$ were compared between the POST and PRE expedition, the values showed a growing tendency from 1.71 $\pm$ 1.02 to 2.19 $\pm$ 1.35 l/min%*kg$^{-1}$ ($p=0.60$). However, the increased values in 4 subjects, decreased values in 2 and similar values in 1 subject only showed a tendency of correlation ($r = 0.58, p>0.05$) with
changes in $\dot{V}_E$ at 180 W.

The only significant change in blood gas parameters was a decrease in $P_{CO_2}$ by about 0.5 kPa ($p<0.05$) in HYP (Table 2) which, with unchanged $[HCO_3]$ increased pH by about 0.04 ($p<0.05$) (Table 2). By applying a parabola model, a significant correlation ($r = 0.70$, $p<0.05$) existed between $\Delta SaO_2$ and $\Delta pH$ at 180 W. The attempt to describe changes of $SaO_2$ using a multiple linear regression model, by adding the changes in $\dot{V}_E$ and $P_{CO_2}$ to the changes in pH, was not successful. After correcting for small samples, the results showed $R^2 = 0.65$ (NS).

### Table 1

| Variable | $P_{LT}$ (W) | $LA_{LT}$ (mmol/l) | $HR_{LT}$ (min⁻¹) | $P_{VT}$ (W) | $\dot{V}_{EVT}$ (l/min) | $HR_{VT}$ (min⁻¹) |
|----------|---------------|--------------------|-------------------|--------------|------------------------|-------------------|
| PRE-NOR  | 151 ± 19      | 1.5 ± 0.4          | 125 ± 14          | 162 ± 35     | 54 ± 10                | 129 ± 17          |
| POST-NOR | 155 ± 18      | 1.3 ± 0.4          | 122 ± 12          | 145 ± 23     | 53 ± 6                 | 122 ± 12          |
| PRE-HYP  | 117 ± 14*     | 1.6 ± 0.5          | 117 ± 11          | 125 ± 20*    | 60 ± 12                | 118 ± 15          |
| POST-HYP | 137 ± 31      | 1.5 ± 0.6          | 125 ± 18          | 135 ± 29     | 60 ± 9                 | 125 ± 16          |

* Statistically significant when PRE-NOR vs. PRE-HYP and POST-NOR vs. POST-HYP values were compared ($p<0.05$)

### Figure 1

The influence of high-altitude acclimatization on $P_{LT}$ PRE and $P_{LT}$ POST expedition (left graph) during NOR (filled circles) and HYP (open circles), and the influence of high-altitude acclimatization on $P_{VT}$ PRE and $P_{VT}$ POST expedition (right graph) during NOR (filled circles) and HYP (open circles)
Table 2

Blood LA, pH, \( P_{\text{CO}_2} \), HCO\(_3\), SaO\(_2\) and VE measured at 180 W before (PRE) and after (POST) the high-altitude expedition in normoxic (NOR) and hypoxic (HYP) conditions. Values are mean ± SD

| Variables | LA (mmol·l\(^{-1}\)) | VE (l·min\(^{-1}\)) | Blood pH | \( P_{\text{CO}_2} \) (kPa) | HCO\(_3\) (mmol·l\(^{-1}\)) | SaO\(_2\) (%) |
|-----------|----------------------|----------------------|----------|-----------------------------|-----------------------------|--------------|
| PRE - NOR | 2.1 ± 1.1            | 68 ± 7               | 7.39 ± 0.03 | 5.1 ± 0.5 | 23 ± 2 | 97 ± 1 |
| POST - NOR| 2.3 ± 1.0            | 77 ± 11              | 7.39 ± 0.03 | 4.8 ± 0.4 | 21 ± 4 | 97 ± 1 |
| PRE - HYP | 4.3 ± 1.8            | 104 ± 9              | 7.34 ± 0.04 | 5.0 ± 0.5 | 20 ± 3 | 86 ± 4 |
| POST - HYP| 3.6 ± 2.6            | 113 ± 13*            | 7.38 ± 0.04* | 4.5 ± 0.4* | 20 ± 2 | 91 ± 2* |

*Significantly different between PRE-HYP and POST-HYP (p≤0.05)

Figure 2

The result of acclimatization: the increase of SaO\(_2\) (\( \Delta \text{SaO}_2 \)) observed at 180 W accompanied increases in \( P_{\text{LT}} \) (\( \Delta P_{\text{LT}} \)) in hypoxic conditions.

The exponential model (\( r = 0.98; \ p=0.01 \)) showed that \( \Delta P_{\text{LT}} \) in the range of 0 to 40 W was accompanied by small \( \Delta \text{SaO}_2 \) (2 to 4%; low-steep part of the curve). Differently, large \( \Delta \text{SaO}_2 \) from 4 to 12% occurred when \( \Delta P_{\text{LT}} \) reached values from 40 to 60 W (steeper part of the curve).
Figure 3

The individual alterations in $\Delta E$ and $\Delta P_{VT}$ that resulted from the high-altitude alpinist expedition were correlated with each other at 120 and 180 W, but not at 140 W due to the larger scatter of data. These relationships showed a tendency whereby increased $\Delta E$ (positive values of $\Delta E$) at a similar absolute power output predicted a decrease in $P_{VT}$. At decreased values of $\Delta E$ (a decrease towards negative values of $\Delta E$), the regression curve did not accurately predict a further increase in $P_{VT}$.

Discussion

The most important finding of our study is a significant correlation of two characteristics of acclimatization during exercise: the increase in $SaO_2$ and $\Delta E$, with two characteristics of submaximal performance during hypoxic exercise: changes of $P_{LT}$ and $P_{VT}$ between the POST and PRE expedition. The increase in $SaO_2$ during hypoxic exercise as an acclimatization effect, resulting from the high-altitude acclimatization, may correlate with increased $P_{LT}$. In contrast, increased $\Delta E$ during hypoxic exercise correlated with the decrease in $P_{VT}$. This negative correlation may show a detrimental effect of increased $\Delta E$ during high-intensity exercise in hypoxia.

An alpinist climbing at a high altitude is influenced by two groups of stressors originating from exercise and environmental characteristics. Small and inconsistent changes in $P_{LT}$ and $P_{VT}$, as two indirect measures of endurance performance (Usaj and Starc, 1996), in the NOR testing conditions show that mountain climbing as a training stimulus does not appear to be sufficient for larger and consistent changes in endurance performance, probably due to small mechanical power output during high-altitude climbing. Oeltz et al. (1986) supported this assumption with their results: relatively low values of $P_{O2max}$ for world-class, high-altitude alpinists. Boutellier et al. (1990) reported a decrease in $P_{O2max}$ as a result of altitude exercise when testing in normoxic conditions. In our study, subjects with a higher $P_{LT}$ and $P_{VT}$ PRE showed a tendency for reducing their $P_{LT}$ and $P_{VT}$ values POST in contrast to those subjects with lower initial $P_{LT}$ and $P_{VT}$ values who revealed a tendency to increase both values. This is partially supported by the findings of Hoppeler and Vogt (2001). They reported that alpinists who had the highest pre-expedition mitochondrial
volume also had the greatest reduction in muscle oxidative capacity during an expedition. Since the exercise adaptations in our study were negligible, acclimatization effects seem to be dominant in changes in performance in HYP. Of the seven subjects, four increased $P_{\text{ET}}$ and $P_{\text{VT}}$ in HYP. The acclimatization effects were mostly related to haematological alterations (Groover and Bartch, 2001). However, our interest was related to blood oxygen saturation and ventilatory adaptations during HYP exercise. Namely, in our study, clear acclimatization effects increased $\text{SaO}_2$ and $\dot{V}_E$ during the high-altitude expedition. Increased $\text{SaO}_2$ correlated with the increase in $P_{\text{ET}}$, which supported the already established importance of acclimatization (Hornbein and Schoene, 2001; Sheel et al., 2009). Of the acclimatization effects which potentially determine $\text{SaO}_2$ changes during a high-altitude expedition, only a combination of changes in blood $P_{\text{CO}_2}$ and pH explained about 65% of the variance, which still represents an insignificant amount of variance, probably due to the small number of subjects in our study. Although changes in $\dot{V}_E$ are simultaneously influenced by an increase stimulated by increased sensitivity of baroreceptors (Lahiri and Cherniak, 2001; Lahiri et al., 2003) and a decrease due to lower sensitivity of baroreceptors with endurance-type training (Byrne-Quinn et al., 1971), we could not explain the $\dot{V}_E$ increase with these two phenomena in our study. Namely, the $\dot{V}_E$ sensitivity during the similar relative exercise intensity only showed a tendency for increasing, and the influence of exercise training on endurance seems negligible in our study. The results of our study support the idea that increased $\dot{V}_E$ during hypoxic exercise is not an important adaptation which may explain changes in endurance performance in HYP. Despite this, a rise in $\dot{V}_E$ (hypoxic ventilatory response) is an important acclimatization effect which helps increase $\text{SaO}_2$ while resting (Dempsey and Forster, 1982; Sheel et al., 2009). Therefore, the expected correlation between the hypoxic ventilator response during exercise and $\text{SaO}_2$ was absent during the hypoxic exercise in our study. The increase in $\dot{V}_E$ was correlated with the decrease in $P_{\text{VT}}$ in HYP (left part of the diagram, below 0 W in Figure 3) and there was a low correlation between these two variables in the right part of the diagram (Figure 3) where $\Delta P_{\text{VT}}$ increased above 0 W. The increase in ventilation represents an increase in the work of respiratory muscles during exercise in HYP (Sheel et al., 2009). Therefore, these muscles consume more oxygen which should be transported via blood redistribution from the exercising leg muscles (Amann et al., 2007; Harms et al., 1997; Amann, 2012). The competition for the blood flow and oxygen may lead to detrimental exercise performance and cause fatigue during exercise in hypoxia (Amann, 2012).

In conclusion, our results show that a high-altitude alpinist expedition (climbing in hypoxic environmental conditions) may increase, decrease or retain one’s endurance performance in hypoxic conditions, predominantly via acclimatization effects. In our study, we observed effects on $\text{SaO}_2$ and $\dot{V}_E$ at a similar absolute exercise intensity of 180 W. Increased $\text{SaO}_2$ might enhance endurance performance in HYP, mostly when the $\text{SaO}_2$ increase exceeded values of 2-3%. The increased $\dot{V}_E$ correlated with decreased endurance performance, especially when $\dot{V}_E$ exceeded 10 l/min.

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