Intermittent Normobaric Hypoxic Exposures at Rest: Effects on Performance in Normoxia and Hypoxia

Igor B. Mekjavic, Tadej Debevec, Mojca Amon, Michael E. Keramidas, and Stylianos N. Kounalakis

Introduction: It has been speculated that short (~1-h) exposures to intermittent normobaric hypoxic exposures (IHE) on peak aerobic capacity and performance under both normoxic and hypoxic conditions. Eighteen subjects were equally assigned to either a control (CON) or IHE group and performed a 4 wk moderate intensity cycling exercise training (1 h · d⁻¹, 5 d · wk⁻¹). The IHE group additionally performed IHE (60 min) prior to exercise training. IHE consisted of seven cycles alternating between breathing a hypoxic gas mixture (5 min; ḞO₂ = 0.12–0.09) and room air (3 min; ḞO₂ = 0.21). Normoxic and hypoxic peak aerobic capacity (VO₂peak) and endurance performance were evaluated before (PRE), during (MID), upon completion (POST), and 10 d after (AFTER) the training period. Results: Similar improvements were observed in normoxic VO₂peak tests in both groups [IHE: Δ(POST-PRE) = +10%; CON: Δ(POST-PRE) = +14%], with no changes in hypoxic conditions. Both groups increased performance time in the normoxic constant power test only [IHE: Δ(POST-PRE) = +108%; CON: Δ(POST-PRE) = +114%], whereas only the IHE group retained this improvement in the AFTER test. Higher levels of minute ventilation were noted in the IHE compared to the CON group at the POST and AFTER tests. Conclusion: Based on the results of this study, the IHE does not seem to be beneficial for normoxic and hypoxic performance enhancement.

Keywords: intermittent hypoxemia, endurance training, hypoxic acclimation, performance.

It is not uncommon for athletes to perform innovative training protocols to enhance performance and the use of different hypoxic training protocols is gaining popularity. However, since the most-often used normobaric hypoxic training requires at least 4 wk of daily exposures lasting over 12 h · d⁻¹ (26), there is an ongoing pursuit for new, shorter training regimens. The application of relatively short (1 h · d⁻¹) intermittent normobaric hypoxic exposures (IHE) of relatively high levels of hypoxia at rest (ḞO₂ = 0.13–0.09) has been suggested as a plausible option. IHE has been proposed as a treatment for asthma (32) and hypertension (31,33), as well as a method for enhancing athletic performance (1). The main advantage of the IHE protocol over longer hypoxic-altitude exposures is the shorter exposure time and the simplicity of application. Recent technological advancements have enabled the development of small portable hypoxic devices that made these protocols available to a broad range of users, including athletes (35). The ability of normobaric IHE to enhance both hypoxic and normoxic exercise performance and working ability has direct application in occupational and sports related fields. In particular, it can serve as a preacclimatization strategy for military units and mountain rescue services prior to deployment to high altitude regions (24). Moreover, IHE could be utilized as a method for enhancing the effects of exercise training and subsequently improving sports performance at sea level, with as little disturbance to normal daily lifestyle as possible (≤ 1 h · d⁻¹).

Despite the technological improvements, the effects of IHE on normoxic exercise performance remain ambiguous and controversial. Few studies have reported beneficial improvements following IHE in sprint performance (22), maximal speed (36), or 3000-m time trial performance (10). Moreover, a positive effect of IHE on muscle and systemic oxygenation at maximal exercise intensities has also been suggested (12). However, the majority of the studies have not detected any benefits of IHE on exercise performance in normoxia (1). The reasons for the disparity in the outcomes reported by different studies include different protocol durations, various hypoxia levels used, and a possible placebo/nocebo effect (3). There is an obvious lack of data regarding the effect of IHE on hypoxic performance (11). Hamlin and colleagues (11) reported no beneficial changes for selected performance measures (i.e., 6 × 70 m sprints, maximum speed) at 1550 m altitude following 13 IHE sessions. Since repeated exposures to normobaric hypoxia have been shown to enhance hypoxic ventilatory response (34), we hypothesized that this increase would occur following the tested IHE protocol and would subsequently enhance performance, especially in hypoxic conditions.

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There is also a paucity of data concerning the time course of changes in performance during the deacclimatization following IHE. Wood and colleagues (36) showed that following IHE the substantial beneficial effects on performance were still present 9 d following the cessation of the protocol. A significant decline was shown 3 wk following the continuous intermittent exposures protocol (90 min · d⁻¹ × 3 wk) (18).

We therefore investigated the effects of the IHE protocol on peak aerobic capacity and time to exhaustion under normoxic and hypoxic conditions, during, post-, and 10-d after the protocol. To eliminate the possible effects of the different training activity (i.e., athletic training) on functional test outcomes, all participants performed the same endurance exercise training. We hypothesized that long-term IHE in addition to exercise training would provide benefits for performance; mainly through enhanced chemo-sensitivity induced ventilatory adaptations, in both normoxia and hypoxia, as compared to exercise training alone. To our knowledge, this is the first study to date that investigated the effects of IHE on both hypoxic and normoxic performance during and after the IHE protocol.

METHODS

Subjects

Eighteen healthy, young, male subjects were recruited for this study. All subjects were free of lung and heart diseases, and were not anemic. Subjects gave their written consent after being familiarized with the study design and the experimental protocols, and informed of the risks involved. The protocol was approved by the National Committee for Medical Ethics at the Ministry of Health (Republic of Slovenia) and conformed to the guidelines of the Helsinki declaration. Subjects were instructed to maintain their normal diet and to refrain from alcohol and nicotine during the testing periods. Upon selection, the subjects were balanced according to peak aerobic capacity and age and equally assigned to either the control (CON; N = 9; age = 22.1 ± 4.1 yr; height = 179.3 ± 4.9 cm; body mass = 72.9 ± 9.7 kg; body fat = 10.4 ± 2.9%; VO₂peak = 45.8 ± 6.4 ml · kg⁻¹ · min⁻¹) or intermittent hypoxic exposure group (IHE; N = 9; age = 22.2 ± 3.8 yrs; height = 181.1 ± 7.3 cm; body mass = 74.2 ± 5.7 kg; body fat = 11.3 ± 4.7%; VO₂peak = 49.3 ± 10.1 ml · kg⁻¹ · min⁻¹).

Procedure

The study outline is presented in Fig. 1. The experimental protocol comprised of 20 training sessions performed 5 times per week over a 4-wk period for both groups. Tests were performed before (PRE), following 10 training sessions (MID), at the end of the training (POST), and 10 d after the cessation of training (AFTER) and included the following: a) pulmonary function assessment; b) hematological tests; c) peak aerobic capacity tests (VO₂peak) in normoxia and hypoxia; and d) constant power tests to exhaustion (CPT) in normoxia and hypoxia (Fig. 1). Each exercise test was performed under similar environmental conditions in the same sea level laboratory (Valdoltra Orthopedics Hospital, Ankaran, Slovenia). The CPTs were performed in a random and counterbalanced order. On each test day, subjects performed VO₂peak in the morning and CPT in the afternoon. All tests were conducted at the same time of the day for each individual subject to avoid diurnal variations. During the 10-d post protocol period, subjects refrained from any physical training, and followed their normal daily routines.

Training

The training protocol consisted of endurance exercise training performed by both groups, and IHE protocol performed by the IHE group only. The IHE protocol was performed prior to each exercise training session. All subjects performed endurance exercise training on a cycle ergometer (Bike forma, Technogym, Cesena, Italy). Each training session consisted of a 5-min warm up period, 60-min cycling, and a 5-min cool down period. The intensity of the exercise was maintained so that the exercise heart rate (HR) corresponded to the HR measured at 50% of PRE normoxic peak power output (Wpeak). The warm up and cool down periods were performed at 60 W. During each training session the subject’s HR was constantly monitored and recorded with a telemetric system (Hosand TMpro®, Verbania, Italy). The HR monitoring system provided continuous supervision of the previously determined individual training

![Fig. 1. Study outline. Subjects in the control (CON) and intermittent hypoxic exposure (IHE) groups participated in a series of tests conducted before (PRE), after 10 training sessions (MID), at the end (POST), and 10 d after the training period (AFTER). These included hematology, pulmonary function, anthropometry, VO₂peak, and constant power test (CPT). The latter two were conducted under normoxic and hypoxic conditions at a laboratory situated at sea level. The order of the conditions (normoxia and hypoxia) for the CPT test was counterbalanced.](image-url)
HR range. The individual range was set within \( \pm 4 \) bpm of the targeted HR measured during the first \( V_{O2\text{peak}} \) test in normoxia. In the event that the subject’s HR was outside the set HR interval a visual signal prompted the investigator to either decrease or increase the work rate accordingly. Ratings of perceived exertion (RPE) were also reported during training sessions by all subjects using a modified (0-10) Borg scale (4). The training load was calculated for each individual at each training session using a heart rate based TRIMP score (13).

The IHE protocol consisted of 20 IHE sessions over a 4-wk period. During the IHE sessions subjects rested in a seated position. Each session comprised a 4-min period during which subjects breathed room air, followed by seven IHE cycles. Each IHE cycle consisted of a 5-min period of breathing a hypoxic mixture and a 3-min period of breathing room air. The level of hypoxia used was based on values used in previous studies (10,35) and was gradually reduced every five training sessions (Table 1). The inspiratory side of the mask was connected to a portable hypoxic gas generator (Everest Summit, Hypoxico, New York, NY) with a Universal mask kit and adjustable high altitude adapter. During each session, the level of \( F_{O2} \) in the hypoxic mixture was additionally monitored with an oxygen analyzer (Hypoxico, New York, NY) attached to the \( O_2 \) monitor port on the tube connecting the hypoxic generator with the mask. Capillary oxyhemoglobin saturation (\( S_pO_2 \)) was continuously monitored and recorded with a finger oxy-meter (Nellcor, BCI 3301, Boulder, CO). The finger oxy-metry device had an accuracy of \( \pm 2 \) units across the range of 70–100%, with an acceptable resilience to motion artifact (21). During each hypoxic period of IHE the subjects reported RPE according to a modified Borg scale.

**Testing**

Subjects’ body mass (BM), height, and body fat (BF) were measured at PRE and POST testing periods. Body fat was estimated from nine skinfold measurements (subscapular, chest, triceps, suprailiac, abdominal, lower thigh, mid thigh, upper thigh, and inguinal site) according to the equation of Jackson and Pollock (16). Pulmonary function was assessed at each testing period (Fig. 1). Forced vital capacity (FVC), forced expiratory flow (PEF), and maximum voluntary ventilation (MVV) were measured using a pneumotachograph (Cardiovit AT-2plus, Schiller, Baar, Switzerland). All tests were performed according to the guidelines published by Miller et al. (23). The spirometer was calibrated with a 3-L syringe before each test. Tests were repeated three times and the highest of the three acceptable values obtained was used for the subsequent analysis.

The blood samples were taken in the morning of the first test day during each test period, as shown in Fig. 1. Subjects were overnight fasted and blood samples were drawn from the antecubital vein. All samples were analyzed for red blood cell count (RBC), hemoglobin (Hb), hematocrit (Hct), transferrin, and ferritin. For hemogram and transferrin analysis the cytochemical impedance method (Pentra120; Horiba ABX Diagnostics, Montpellier, France) and the turbidimetric method (Hitachi 912; Roche Diagnostics, Basel, Switzerland) were used, respectively. The subjects did not receive iron supplementation, since the levels of all subject’s ferritin were, and remained, above 30 ng·mL\(^{-1}\) throughout the experimental period.

Each subject performed two incremental exercise tests to exhaustion (\( V_{O2\text{peak}} \)) on an electrically braked cycle-ergometer (ERG 900S, Schiller, Baar, Switzerland). During the normoxic test, subjects inspired ambient air (\( F_{O2} = 0.21; V_{O2\text{peak NORMO}} \)) and during the hypoxic test they inspired a humidified hypoxic gas mixture (\( F_{O2} = 0.12; V_{O2\text{peak HYPO}} \)) from a 200-L Douglas bag. During all \( V_{O2\text{peak}} \) tests, the subjects breathed through a two-way valve (Model 2, 700 T-Shape, Hans Rudolph, Shawnee, KS), while their oxygen uptake (\( V_O2 \)) and ventilation (\( V_E \)) were measured by breath using a metabolic cart (CS-200, Schiller, Baar, Switzerland) and averaged over a 10-s period. The pneumotachograph was calibrated with a 3-L syringe prior to each test; the gas analyzers were calibrated with two different standard gas mixtures. During the tests, the subjects provided ratings of peripheral (RPE\(_{\text{leg}}\)) and central (RPE\(_{\text{cen}}\)) sensation of effort on a modified Borg scale (0-10).

The testing protocol consisted of a 10-min resting period, during which subjects breathed room air. During the hypoxic tests, the rest period comprised two 5-min periods, whereby subjects breathed room air during the first period and the hypoxic gas mixture in the second period. The rest period was followed by a 2-min warm-up at a work rate of 60 W. Thereafter, the work rate was increased by 30 W each minute until the subjects could no longer sustain the predetermined pedaling cadence. The criteria for the attainment of the \( V_{O2\text{peak}} \) values that were calculated as the highest average sampled for 60-s were: pedalling cadence < 60 rpm, plateau in \( V_{O2} \), and respiratory exchange ratio > 1.1.

Additionally, two constant power tests (CPT) were performed at each test period. In one, subjects breathed ambient air (CPT\(_{\text{NORMO}}\); \( F_{O2} = 0.21 \)), and in the other a humidified hypoxic mixture (CPT\(_{\text{HYPO}}\); \( F_{O2} = 0.12 \)). After a 2-min resting period (either in normoxia or hypoxia for NORMO or HYPO tests, respectively), the

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**Table 1. Weekly (5 Sessions) Average Fraction of Inspired Oxygen (\( F_{O2} \)), Capillary Oxygen Saturation (\( S_pO_2 \)), Heart Rate (HR), and Ratings of Perceived Exertion (RPE) of the IHE Group During the Intermittent Hypoxic Exposure Sessions.**

<table>
<thead>
<tr>
<th>IHE Sessions</th>
<th>1 - 5</th>
<th>6 - 10</th>
<th>11 - 15</th>
<th>16 - 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>( F_{O2} ) (%)</td>
<td>0.12</td>
<td>0.11</td>
<td>0.10</td>
<td>0.09</td>
</tr>
<tr>
<td>( S_pO_2 ) (%)</td>
<td>81 ± 3</td>
<td>75 ± 1*</td>
<td>73 ± 1*</td>
<td>72 ± 1*</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>78 ± 2</td>
<td>78 ± 2</td>
<td>78 ± 1</td>
<td>78 ± 3</td>
</tr>
<tr>
<td>RPE</td>
<td>2 (1–4)</td>
<td>2 (1–5)</td>
<td>3 (1–8)*</td>
<td>3 (1–7)*</td>
</tr>
</tbody>
</table>

Values are mean ± SD. RPE values are median (range).  
* Significantly different from wk 1 (\( P < 0.05 \)).  
† Significantly different from wk 2 (\( P < 0.05 \)).
TABLE II. RESULTS OF PULMONARY FUNCTION AND HEMATOLOGICAL TESTS CONDUCTED BEFORE (PRE), IN THE MIDDLE (MID), AT THE END (POST), AND 10 DAYS AFTER (AFTER) THE TRAINING PERIOD FOR THE CONTROL (CON) AND EXPERIMENTAL (IHE) GROUP.

<table>
<thead>
<tr>
<th></th>
<th>CON Group</th>
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<th>IHE Group</th>
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<tr>
<td></td>
<td>PRE</td>
<td>MID</td>
<td>POST</td>
<td>AFTER</td>
<td>PRE</td>
<td>MID</td>
<td>POST</td>
<td>AFTER</td>
<td></td>
</tr>
<tr>
<td>FVC (L)</td>
<td>5.6 ± 0.9</td>
<td>5.5 ± 1.2</td>
<td>5.6 ± 1.1</td>
<td>5.5 ± 1.7</td>
<td>5.7 ± 0.8</td>
<td>5.7 ± 0.9</td>
<td>5.8 ± 0.7</td>
<td>5.7 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>4.9 ± 0.5</td>
<td>4.6 ± 0.9</td>
<td>4.7 ± 0.8</td>
<td>4.7 ± 1.3</td>
<td>5 ± 0.6</td>
<td>4.9 ± 0.7</td>
<td>4.8 ± 0.6</td>
<td>4.8 ± 0.8</td>
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<tr>
<td>SVC (L)</td>
<td>5.1 ± 0.8</td>
<td>5.0 ± 0.8</td>
<td>5.6 ± 1.3</td>
<td>5.4 ± 1.6</td>
<td>5.5 ± 0.8</td>
<td>5.3 ± 0.8</td>
<td>5.6 ± 0.8</td>
<td>5.1 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>PEF (L)</td>
<td>8.9 ± 2.2</td>
<td>10.3 ± 1.7</td>
<td>10.1 ± 1.5</td>
<td>9.7 ± 1.4</td>
<td>10.9 ± 1.3</td>
<td>10.5 ± 1.3</td>
<td>11.1 ± 1.7</td>
<td>10.4 ± 1.6</td>
<td></td>
</tr>
<tr>
<td>MVV (L · min⁻¹)</td>
<td>183 ± 34</td>
<td>187 ± 34</td>
<td>185 ± 29</td>
<td>172 ± 75</td>
<td>199 ± 32</td>
<td>204 ± 36</td>
<td>205 ± 39</td>
<td>200.9 ± 36</td>
<td></td>
</tr>
<tr>
<td>RBC (10¹²·L⁻¹)</td>
<td>5.0 ± 0.5</td>
<td>5.1 ± 0.3</td>
<td>4.8 ± 0.2</td>
<td>5.0 ± 0.2</td>
<td>5.1 ± 0.3</td>
<td>5.1 ± 0.3</td>
<td>5.1 ± 0.2</td>
<td>5.2 ± 0.15</td>
<td></td>
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<tr>
<td>Hb (g · L⁻¹)</td>
<td>15.1 ± 1.0</td>
<td>15.5 ± 0.9</td>
<td>14.3 ± 1.2</td>
<td>14.7 ± 1.3</td>
<td>15.1 ± 0.8</td>
<td>14.5 ± 0.9</td>
<td>15.0 ± 0.7</td>
<td>15.1 ± 0.6</td>
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<tr>
<td>Hct (%)</td>
<td>45 ± 3.0</td>
<td>47 ± 2.2</td>
<td>44 ± 3.0</td>
<td>46 ± 4.0</td>
<td>46 ± 3.0</td>
<td>46 ± 2.0</td>
<td>46 ± 3.0</td>
<td>46 ± 2.0</td>
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<tr>
<td>Transferrin (g · L⁻¹)</td>
<td>2.7 ± 0.3</td>
<td>2.5 ± 0.4</td>
<td>2.7 ± 0.2</td>
<td>3.2 ± 1.5</td>
<td>2.8 ± 0.2</td>
<td>2.6 ± 0.1</td>
<td>2.6 ± 0.1</td>
<td>2.6 ± 0.2</td>
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<tr>
<td>Ferritin (ng · mL⁻¹)</td>
<td>71.1 ± 33.4</td>
<td>67.9 ± 66.1</td>
<td>62.2 ± 30.8</td>
<td>68.2 ± 42.1</td>
<td>79.5 ± 44.4</td>
<td>81.6 ± 27.8</td>
<td>82.6 ± 44.6</td>
<td>89.7 ± 36</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SD; †Significant (P < 0.05) differences between groups; *Significantly (P < 0.05) different from PRE test values.
FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; SVC, slow vital capacity; PEF, peak expiratory flow; MVV, maximum voluntary ventilation; RBCs, Erythrocytes; Hb, Hemoglobin; Hct, Hematocrit.

### Results

#### Training

The mean absolute workload (IHE = 160 ± 26 W; CON = 159 ± 19 W) and HR (IHE = 145 ± 9 bpm; CON: 143 ± 8 bpm) during the training period were similar for both groups. The average training power output increment between the first and the last training session was 6% and 7% for the IHE and CON group, respectively. The calculation of the training load based on the TRIMP scores showed no differences between groups, with average values of 31.1 ± 3.1 for the CON and 29.9 ± 5.9 for the IHE group.

**Statistical Analysis**

All analyses were performed using Statistica 5.0 (StatSoft, Inc., Tulsa, OK). Training variables and group characteristics were compared using a Student’s t-test. The differences in the protocol outcomes were assessed using a 3-way analysis of variance (ANOVA) (group × condition × testing period). A 4-way ANOVA was employed to analyze the relative values of selected variables during the VO2 peak and CPT tests (group × condition × testing period × time). A post hoc test (Tukey HSD) was used to identify the specific differences when a significant main effect or interaction was noted. Due to technical problems encountered on four hypoxic PRE VO2 peak tests, we used a regression model to predict the missing PRE VO2 hypoxic values from the power output–VO2 relationship produced from the normoxic and the available hypoxic tests. All data are reported as means ± SD unless otherwise indicated. The alpha level of significance was set a priori at 0.05.

**RESULTS**

**Training**

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The average $S_pO_2$ was 75.5 ± 5% during the hypoxic exposure bouts, and 95 ± 2% during the normoxic bouts. The values of $S_pO_2$ during IHE decreased throughout the training period, concomitantly with the decreasing $F_pO_2$ in the inspired breathing mixture (Table I). The ratings of perceived exertion were significantly higher during the last 10 training sessions ($t < 0.05$). No changes were observed in HR during sessions.

**Testing**

There were no changes in the %BF between or within both groups. The CON group had significantly higher BM in the POST compared to the PRE test ($t < 0.05$). It is noteworthy that the CON group had significantly lower BM compared to the IHE group before the training protocol. PEF was significantly elevated during the MID test in the CON group ($F = 4.5; P < 0.05$). No other significant changes in pulmonary function were noted during and after the protocol (Table II).

No significant differences were found within the groups at different testing periods in any of the measured hematological variables (Table II). Also, there were no significant interactions between groups.

$V_O2peak$ results are presented in Fig. 2. There was no difference between groups in $V_O2peak$ NORMO and $V_O2peak$ HYPO prior to the training protocol. $V_O2peak$ NORMO was significantly increased in both groups over the course of the training regimen ($F = 3.1; P < 0.05$). No significant changes were observed in the $V_O2peak$ HYPO during the training in either group.

Peak values of the measured cardio-respiratory variables during the $V_O2peak$ tests are presented in Table III. The only significant increase in $V_Epeak$ was noted in the AFTER $V_O2peak$ NORMO test for the IHE group ($F = 4.2; P < 0.05$). HR peak decreased significantly during $V_O2peak$ NORMO in the IHE group only at the MID test ($F = 3.8; P < 0.05$). $W_peak$ increased significantly during $V_O2peak$ NORMO in both groups in the POST and AFTER tests ($F = 7.1; P < 0.05$). No changes were observed in the $W_peak$ during the $V_O2peak$ HYPO test. No significant differences were observed between or within groups in $S_pO_2$ and $RPE_{leg peak}$, $RPE_{cen peak}$ was significantly lower in the IHE group at the MID testing only during both $V_O2peak$ NORMO and $V_O2peak$ HYPO tests ($F = 3.9; P < 0.05$).

There was no difference between groups in time to exhaustion for both $CPT_{NORMO}$ and $CPT_{HYPO}$ before the training protocol (Fig. 3). Both groups significantly improved $CPT_{NORMO}$ time at the POST test ($F = 13.9; P < 0.01$). Only the IHE group maintained this improvement in the AFTER test ($F = 13.9; P < 0.01$) (Fig. 3). No significant differences were noted in the $CPT_{HYPO}$ results of both groups during the course of the protocol (Fig. 3).

Peak values of $V_O2$, $S_pO_2$, $RPE_{leg}$ and $RPE_{cen}$ during both $CPT_{NORMO}$ and $CPT_{HYPO}$ were comparable between groups throughout the experimental protocol (Table IV).

Significant differences were noted in $HRpeak$ during the POST $CPT_{NORMO}$ and MID $CPT_{HYPO}$ in the CON and IHE group ($F = 5.2; P < 0.05$), respectively.

During the POST and AFTER $CPT_{NORMO}$ tests, a significantly greater $V_E$ was noted in the IHE compared to the CON group at 60%, 80%, and 100% relative CPT time ($F = 4.6; P < 0.05$), respectively (Fig. 4). Comparable increases in $V_E$ of both groups were noted at MID, POST, and AFTER $CPT_{NORMO}$ at 20% relative CPT time ($F = 7.3; P < 0.01$). A significant decrease in $V_E$ at 80% and 100% of relative $CPT_{NORMO}$ time during the POST testing was noted in the CON group only ($F = 7.3; P < 0.01$) (Fig. 4). No differences in relative $V_E$ values were observed within or between groups during the $CPT_{HYPO}$ tests.

**DISCUSSION**

The present study investigated the effect of repeated intermittent hypoxic exposures at rest, combined with moderate intensity exercise training on $V_O2peak$, and CPT

| TABLE III. PEAK VALUES OF MINUTE VENTILATION ($V_Epeak$, $HRpeak$), POWER OUTPUT ($Wpeak$), CAPILLARY OXYGEN SATURATION ($S_pO_2$), AND PERIPHERAL ($RPE_{leg peak}$) AND CENTRAL ($RPE_{cen peak}$) RATINGS OF PERCEIVED EXERTION DURING NORMOCYME AND HYPOXYC $V_O2peak$ TESTS BEFORE (PRE), IN THE MIDDLE (MID), AT THE END (POST), AND 10 DAYS AFTER (AFTER) THE TRAINING PERIOD FOR THE CONTROL (CON) AND EXPERIMENTAL (IHE) GROUP |

<table>
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<th>CON Group</th>
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<tr>
<td></td>
<td>PRE</td>
<td>MID</td>
<td>POST</td>
<td>AFTER</td>
<td>PRE</td>
<td>MIDDLE</td>
<td>POST</td>
<td>AFTER</td>
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<tr>
<td>$V_O2peak$ NORMO</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>$V_Epeak$ (L·min⁻¹)</td>
<td>132 ± 18</td>
<td>140 ± 19</td>
<td>139 ± 21</td>
<td>141 ± 13</td>
<td>113 ± 30*</td>
<td>143 ± 30</td>
<td>147 ± 28</td>
<td>153 ± 30*</td>
</tr>
<tr>
<td>$HRpeak$ (bpm)</td>
<td>190 ± 8</td>
<td>187 ± 4</td>
<td>186 ± 6</td>
<td>188 ± 7</td>
<td>189 ± 8</td>
<td>181 ± 7.3*</td>
<td>186 ± 7</td>
<td>187 ± 8</td>
</tr>
<tr>
<td>$Wpeak$ (W)</td>
<td>294 ± 35</td>
<td>309 ± 29</td>
<td>322 ± 34*</td>
<td>327 ± 31*</td>
<td>314 ± 54</td>
<td>324 ± 45</td>
<td>337 ± 53*</td>
<td>342 ± 59*</td>
</tr>
<tr>
<td>$S_pO_2$ (%)</td>
<td>89 ± 8</td>
<td>94 ± 2</td>
<td>93 ± 6</td>
<td>95 ± 2</td>
<td>91 ± 3</td>
<td>92 ± 5</td>
<td>92 ± 6</td>
<td>91 ± 5</td>
</tr>
<tr>
<td>$RPE_{leg peak}$</td>
<td>8 (6-10)</td>
<td>9 (7-10)</td>
<td>9 (8-10)</td>
<td>9 (7-10)</td>
<td>10 (7-10)</td>
<td>8 (7-10)</td>
<td>9 (7-10)</td>
<td>10 (7-10)</td>
</tr>
<tr>
<td>$RPE_{cen peak}$</td>
<td>7 (4-9)</td>
<td>7 (4-9)</td>
<td>8 (3-10)</td>
<td>8 (3-10)</td>
<td>9 (7-10)</td>
<td>7 (5-9)*</td>
<td>8 (5-10)</td>
<td>8 (5-10)</td>
</tr>
<tr>
<td>$V_O2peak$ HYPO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V_Epeak$ (L·min⁻¹)</td>
<td>130 ± 20</td>
<td>121 ± 23</td>
<td>125 ± 20</td>
<td>125 ± 17</td>
<td>114 ± 16</td>
<td>137 ± 19</td>
<td>142 ± 23</td>
<td>145 ± 26</td>
</tr>
<tr>
<td>$HRpeak$ (bpm)</td>
<td>182 ± 8</td>
<td>177 ± 6</td>
<td>176 ± 5</td>
<td>174 ± 4</td>
<td>181 ± 7</td>
<td>175 ± 7</td>
<td>177 ± 7</td>
<td>178 ± 11</td>
</tr>
<tr>
<td>$Wpeak$ (W)</td>
<td>250 ± 19</td>
<td>247 ± 28</td>
<td>247 ± 34</td>
<td>244 ± 25</td>
<td>271 ± 38</td>
<td>263 ± 37</td>
<td>280 ± 36</td>
<td>283 ± 43</td>
</tr>
<tr>
<td>$S_pO_2$ (%)</td>
<td>76 ± 6</td>
<td>73 ± 4</td>
<td>74 ± 5</td>
<td>74 ± 5</td>
<td>73 ± 6</td>
<td>74 ± 5</td>
<td>73 ± 5</td>
<td>74 ± 6</td>
</tr>
<tr>
<td>$RPE_{leg peak}$</td>
<td>7 (1-10)</td>
<td>8 (2-10)</td>
<td>8 (6-10)</td>
<td>8 (7-10)</td>
<td>10 (7-10)</td>
<td>8 (7-10)</td>
<td>8 (7-10)</td>
<td>9 (5-10)</td>
</tr>
<tr>
<td>$RPE_{cen peak}$</td>
<td>7 (3-10)</td>
<td>8 (5-10)</td>
<td>8 (3-10)</td>
<td>9 (2-10)</td>
<td>8 (7-10)</td>
<td>7 (4-10)*</td>
<td>8 (5-10)</td>
<td>9 (7-10)</td>
</tr>
</tbody>
</table>

Values are mean ± SD. RPE values are median (range). *Significantly ($P < 0.05$) different from PRE test values.
in normoxia and hypoxia. The results demonstrate no effect of IHE per se on aerobic capacity and endurance performance in normoxia and hypoxia.

Improvements in normoxic $V_{\text{O}_2\text{peak}}$ following similar or even lower (45% $HR_{\text{peak}}$) training intensity protocols have already been demonstrated in healthy young adults (9). Our results show similar improvements in $V_{\text{O}_2\text{peak, NORMO}}$ for both the CON and IHE groups (Fig. 2), thus indicating that IHE did not provide any additional benefits for sea level aerobic capacity compared to endurance training per se. Similarly, we observed no additive effect of IHE on endurance performance compared to the exercise training per se at the MID and POST training periods. This is in line with the results of studies using trained athletes showing no additive effects of IHE on normoxic $V_{\text{O}_2\text{peak}}$, running economy (17,35), and 5000-m running performance (15). On the other hand, the study by Hamlin (10) showed improvements in 3000-m running time, likely to be beneficial for non-elite athletes. Nevertheless, their conclusions have also been questioned by Bartsch (1), who attributed the measured effects to the inhomogeneous distribution of performance level and gender between the groups, rather than the IHE effects per se. The intriguing finding of this study is the retention of the improved performance at the AFTER testing that was only seen in the IHE group. Our findings regarding the postprotocol period are in accordance with the findings of Wood (36), who showed that benefits of IHE were still present 9 d after cessation of IHE. They showed improved sprint performance, reduced exercise blood lactate ([La]) and HR levels POST and AFTER the IHE protocol, thus indicating that IHE can provide benefits for high intensity running performance. Although these results were promising, they were not confirmed in a subsequent study performed by the same research group (14) that showed no benefit of IHE over comparable training and a placebo IHE protocol. On the other hand, Katayama et al. (18) showed that 3 wk after a IHE protocol (90 min $\times$ 3 wk$^{-1} \times$ 3 wk at ~4500 m), all benefits were diminished. Therefore, according to our results and those of Katayama et al. (18), we assumed that the potential benefits of IHE could be present for 10 d, but no more than 20 d after the cessation of the intervention.

Although some studies investigating the effects of different intermittent hypoxic protocols on performance showed possible benefits for hypoxic performance (2), this was not confirmed by our study. Namely, no significant improvements in $V_{\text{O}_2\text{peak, HYPO}}$ or CPT$_{\text{HYPO}}$ tests were found in either group during and after the protocol. Our results are in agreement with the findings of Hamlin (11), who tested the effects of a similar IHE protocol on performance at altitude. The tests were performed at a moderate altitude (1550 m), but sufficiently high to significantly impair performance in game specific tests of rugby players. They found that the IHE protocol provided some benefits on submaximal HR and [La] during hypoxic exercise, but induced no changes in the game specific test performance variables. Our results do not support the rationale that IHE provides benefits for performance and working ability in hypoxic conditions and thus cannot be recommended as a preacclimatization model prior to high altitude deployment. Moreover, a recent study also confirmed that 1 h of continuous severe normobaric hypoxia ($F_{\text{O}_2} = 0.12$), even if combined with low intensity exercise training, does not provide benefits for hypoxic performance (6).

The unchanged hematological parameters outcome of our study is in line with other studies (1,17,35), even though increases in Hb, Hct, and reticulocyte concentrations following short term intermittent hypoxia have been shown in one study (10). It would appear that short intermittent hypoxic exposures do not provide hematological benefits (29), most probably due to the insufficient hypoxic dose (1). Although hypoxic training modalities mostly focus on erythropoiesis augmentation and subsequent increased total hemoglobin mass, considering this as the main aspect accountable for improved performance, other beneficial factors have also been proposed (8). These include: ventilatory adjustments, improved muscle efficiency, greater muscle buffering capacity and improved lactic acid tolerance (1,8).

**Fig. 3.** A) Normoxic and B) hypoxic endurance times determined with a constant power (CP) test before (PRE), after 10 training sessions (MID), at the end (POST), and 10 d after the training period (AFTER) for the control (CON) and intermittent hypoxic (IHE) groups. Values are means ± SD. ** Indicates statistically significant differences from PRE values ($P < 0.01$).
The effect of IHE on ventilatory regulation and chemosensitivity seem to be the main underlying mechanism for the potential beneficial adjustments (34). According to our findings, the prolongation of improved performance at sea level can be attributed to ventilatory adaptation resulting in increased $V_{E}$ in the POST and AFTER CPT NORMO tests (Fig. 4). However, this finding is in contrast with the results of Katayama (20). They showed that continuous IHE did not provide any ventilatory benefits during consequent sea level exercise, whereas in our study we found significant increases in maximal and submaximal $V_{E}$ during the normoxic CPT test following IHE. The different results can probably be ascribed to the different hypoxic doses, since both the

![Fig. 4](image-url)
above-mentioned studies used only seven continuous 1-h exposures performed during 1 wk. In addition, the increases in maximal normoxic exercise \( V_{\text{E}} \) have also been shown following nine 3-5 h exposures to 4000 m (27). This is consistent with the findings of Sheel et al. (34), indicating that longer exposure periods, and/or more severe hypoxia, are required to elicit a change in sea level exercise ventilation. However, it seems that no clear link exists between increases in hypoxic ventilatory response and changes in sea level exercise ventilation (7). In particular, Foster et al. (7) did not observe any differences in normoxic and hypoxic exercise ventilatory responses between different IHE protocol durations. Currently, the functional effects of increased chemosensitivity following IHE on sea level exercise ventilation are not clear (34). Even though our results showed benefits in submaximal and maximal ventilation following IHE, they have to be interpreted as a reflection of concomitant IHE and exercise training compared to IHE alone.

Even more interesting is the fact that we did not note any benefits of IHE in the ventilatory responses to hypoxic exercise. This is indeed intriguing, since previous studies have shown that increased hypoxic chemosensitivity following short hypoxic exposures provides increases in \( V_{\text{E}} \) and \( S_{\text{O}_2} \) during exercise in hypoxia (19,25). While these discrepancies could be explained by the shorter duration and the intermittent nature of the hypoxic exposures, since both above mentioned studies used continuous exposures (\( \geq 1 \)-h), the exact mechanisms remain to be elucidated.

As can be seen from the results, \( S_{\text{O}_2} \) decreased concomitantly with decreasing \( F_{\text{O}_2} \) in the inspired air (Table I). \( F_{\text{O}_2} \) levels used during our IHE protocol are comparable to those of other studies investigating the effects of IHE on performance and aerobic capacity, although the tested hypoxic stimulus was more intense in the last sessions. In particular, the \( F_{\text{O}_2} \) in our study was 9.5% compared to 10% used by Tadibi et al. (35). The duration of hypoxic and normoxic bouts between the IHE was shorter (5:3 min) compared to those (6:4 min) used in previous studies (35,36), although the total number of sessions was higher (20 vs. 15 sessions).

With regards to the findings of the effect of IHE on hypoxic performance, it should be emphasized that this refers to performance conducted under normobaric hypoxic conditions. Recent evidence suggests that ambient pressure per se may influence the physiological responses to hypoxia (5,28,30), thus providing support to the challenge of the Equivalent Air Altitude Model.

The novelty of the present study arises from a strictly controlled and identical training of both groups. Although the possible benefits induced by IHE could be masked by the training responses per se, we aimed at eliminating the possible performance outcome differences as a result of different exercise training performed concomitantly with the IHE; a possible occurrence in studies where subjects perform their normal training during the testing protocol (35,36).

In conclusion the tested IHE protocol did not enhance performance or peak aerobic capacity in hypoxia or normoxia during and immediately following the protocol. However, the prolongation of improved performance (CPT\text{NORMO}) 10 d after the IHE protocol cessation might indicate a potential IHE benefit. Further studies investigating the de-acclimatization period following IHE combined with exercise training seem warranted in order to determine the existence, duration, and the magnitude of those benefits.

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