

## Effect of Intermittent normobaric hypoxia on sub maximal exercise performance at high altitude (3500 m)

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**Abstract:** *Background:* Intermittent hypoxic exposure (IHE) improves wellbeing and performance by modulating physiological processes. Though the effect of IHE on oxygen saturation (SpO<sub>2</sub>) and submaximal exercise performance (SEP) upon deployment of Indian military personnel at high altitude (HA) has not been studied yet. *Objective:* To observe the effect of IHE on SpO<sub>2</sub> and SEP among Indian military personnel at sea level (SL) and upon rapid induction to 3500 m altitude. The data obtained at HA were also compared with age and gender matched high altitude natives (HAN) and acclimatized lowlanders (ALR). *Methods:* Two hundred thirty three volunteers (age: 22 – 34 years) participated in the study. 210 participants were enrolled at SL and randomly divided into experimental (EXP) or control (CON) group. The EXP group were given IHE at 12% F<sub>I</sub>O<sub>2</sub>, 4 hrs. every day for 4 days at an altitude of 218 m. Both the groups were inducted to 3500 m by air. After IHE at SL and on day 7 at HA heart rate (HR), SpO<sub>2</sub> and SEP were evaluated. 8 HAN and 15 ALR were also participated and their HR, SpO<sub>2</sub> and SEP were evaluated at HA only. *Results:* At SL significant difference between CON and EXP group was noted in resting (HR) and during exercise and recovery (HR and SpO<sub>2</sub>; P<0.05). At HA, HR of CON group during exercise and recovery period was significantly higher than the other 3 groups (P<0.001). Resting SpO<sub>2</sub> of EXP group was higher than other 3 groups but significant difference was noted with CON and HAN group (both P<0.001). During exercise and recovery at HA SpO<sub>2</sub> of CON group was significantly lower than EXP group (P<0.001). *Conclusion:* Intermittent normobaric hypoxia exposure improves SpO<sub>2</sub> and exercise performance during initial days of acclimatization at 3500 m altitude.

**Keywords:** High altitude, intermittent hypoxic exposure, submaximal exercise, arterial oxygen saturation.

### Introduction

The limited availability of atmospheric oxygen due to low barometric pressure is the main causative factor for the altitude related problems observed at high altitude (HA). Individuals living near sea level (SL) when rapidly ascend to HA there is a decrease in their physical working capacity and chances of developing acute mountain sickness (AMS) are high. It has been observed that both maximal and sub-maximal exercise capacity reduces upon induction to HA [1]. Above 5000 feet maximal aerobic capacity ( $\dot{V}O_{2max}$ ) decreases by about 1.5-3.5% for every 1000 feet ascent for both trained and untrained individuals [2].

It has been reported that while inducting from 300 m to 3100 m  $\dot{V}O_{2max}$  was reduced by 26% [3]. At altitude, exercise performance never

reaches its SL value even after several months of acclimatization due to reduced cardiac output (CO) and redistribution of blood flow to the other tissues [4-5]. During a stay at altitude decreased plasma volume (due to low thirst, insensible water and fluid loss from other routes) and increased total peripheral vascular resistance (due to cold) lowers the stroke volume (SV) and ultimately diminishes both maximal and sub-maximal CO [6].

Arterial oxygen saturation (SpO<sub>2</sub>), a predictor of acclimatization and AMS, has also been reported decreased upon induction to HA [7]. The causative factor for lowered SpO<sub>2</sub> at HA might be due to increased dead space ventilation which results from hypobaric hypoxia induced higher breathing frequency, a lower tidal volume and minute ventilation [8].

Intermittent hypoxic exposure (IHE) is a non-invasive, drug free technique reported to improve wellbeing and performance in a low barometric pressure environment and for the treatment of degenerative diseases [9]. This process actually initiates physiological adaptations similar to altitude acclimatization and ultimately helps to increase performance. It has been reported that IHE can decrease the incidence and severity of AMS and improve autonomic control [10-11].

IHE is a well-practiced technique to improve performance at SL and HA both [12-13]. It has also been reported that IHE can improve aerobic capacity, endurance performance, and anaerobic power [13-16]. Rapid deployment of defence personnel at HA by air is required during emergency situations. It has been observed that upon rapid induction of military personnel at HA there is a deterioration of their physical capacity. In these circumstances IHE, that has been reported to improve performance, can be a good strategy to protect the physical capacity of military personnel at HA [17].

It is well established that the strength of the overall acclimatization process is assessed by the decrease in AMS incidence and reduction in heart rate (HR) during exercise in association with maintenance of SpO<sub>2</sub> level. In our earlier study we have found that the IHE significantly reduces the AMS on acute induction to HA [18]. However, the effect of IHE on SpO<sub>2</sub> and submaximal exercise performance (SEP) upon rapid deployment of Indian military personnel at HA has not been studied yet. The present study was undertaken to observe the effect of IHE on SpO<sub>2</sub> and SEP of Indian military personnel at SL and HA (3500 m). SpO<sub>2</sub> and SEP of high altitude natives (HAN) and acclimatized lowlanders (ALR) in the same altitude were also evaluated at HA to observe the effectiveness of IHE with them.

### Material and Methods

*Participants:* A total 233 healthy males volunteered for the study.

*Inclusion criteria were;*

- (i) Healthy and within age range: 21 to 35 years.
- (ii) Medical category SHAPE-I.

*Exclusion criteria were;*

- (i) Presence of systemic hypertension
- (ii) Any pre-existing/ concurrent illness
- (iii) Under any medication.

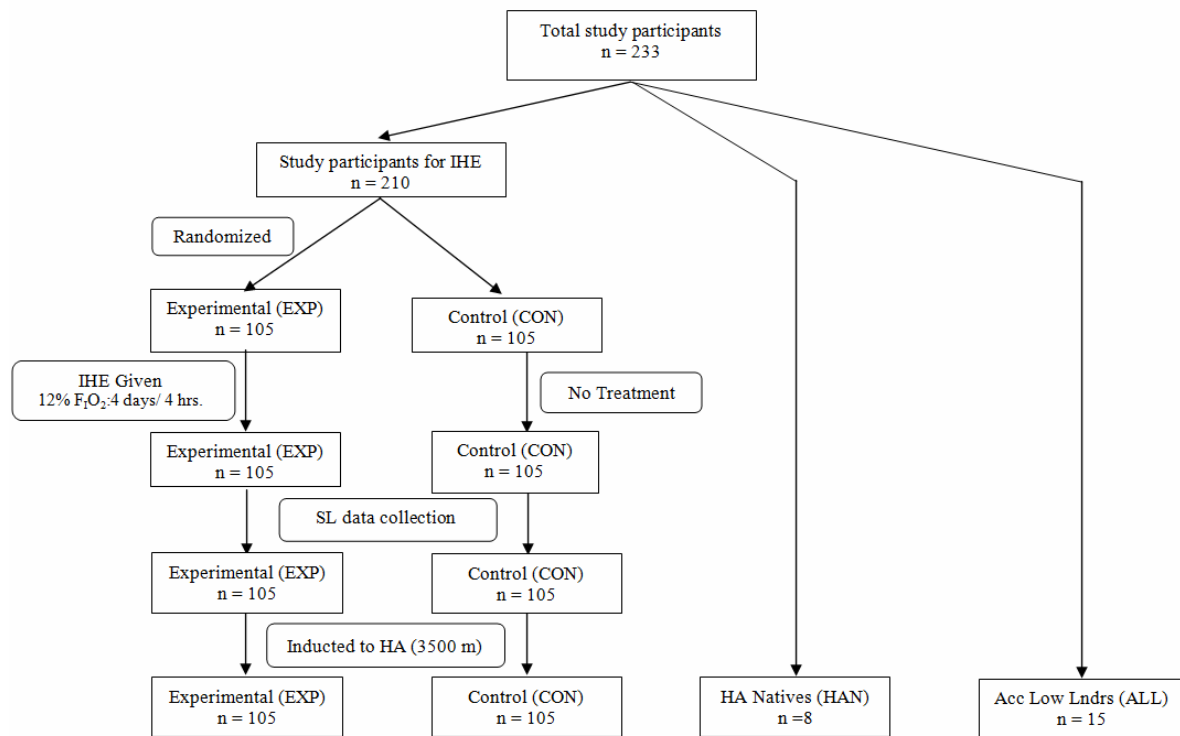
Two hundred and ten soldiers from Indian Armed Forces recruited for the study at SL. They were randomly divided into 2 groups – Experimental (EXP) and Control (CON). Age and gender matched 8 HAN, who were born and brought up at an altitude ranging from 3000 – 3600 m, and 15 ALR, who are posted around Leh area (3100 – 3600 m) for the last 30 days, were also included in the study.

Flow chart of the randomized controlled trial – participant recruitment and study design is depicted in figure 1. The study protocol was approved by the Institute's Ethical Committee (IEC/DIPAS/09/DIP-251) and informed consent from all the participants was taken as per Declaration of Helsinki (WMA, 2000).

*Experimental Design:* The SL study was carried out at Delhi (740 mm Hg) where the laboratory temperature was maintained between 20 and 24° C and relative humidity at 40-50%. EXP group of subjects were exposed to normobaric intermittent hypoxia exposure at 12% F<sub>1</sub>O<sub>2</sub> (altitude equivalent to 4350m, final SpO<sub>2</sub> in blood was around 87-88%) for 4 hours per day for four consecutive days at an altitude of 218m.

CON group of subjects breathed ambient air sitting in a separate room for the same duration. On the following day, all the volunteers were inducted to Leh (altitude 3,500 m and barometric pressure 483 mmHg) in the Western Himalayas, by a pressurized aircraft. At SL arterial oxygen saturation level and submaximal exercise data of 210 participants were recorded after IHE. At 3500 m altitude resting and exercise testing was conducted on day 7, after acclimatization for 6 days, in the morning hour and in a temperature controlled room where the temperature was maintained between 20 - 25° C and relative humidity was 40%. Similar experiments were also conducted on HAN and ALR group at HA.

**Fig-1:** Flow chart of the randomized controlled trial-participant recruitment and study design. IHE: Intermittent hypoxic exposure; SL: sea level, HA: high altitude.



The resting parameters were recorded in sitting condition. HR was recorded with a Polar HR Belt (T34, Polar Electro OY, Kempele, Finland) and monitored at Polar Heart Wrist Receiver (S810i), connected telemetrically. SpO<sub>2</sub> was recorded using digital fingertip pulse oximeter (MD300C1, Choicemmed, Europe). Submaximal exercise was performed on a wooden stool for a total duration of 2 minutes where participants were asked to step up and down as rapidly as possible [19]. HR and SpO<sub>2</sub> were recorded at 1<sup>st</sup> and 2<sup>nd</sup> minute of exercise. Participants were instructed to sit immediately after exercise and recovery data were recorded at 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> minute after cessation of the exercise. Data were presented as Mean ± SD and statistical analysis carried out

using SPSS (v21.0, SPSS. Inc., Chicago, IL, USA). Repeated measure ANOVA has been used to test the significant difference ( $p \leq 0.05$ ), followed by Tukey Test to see the pair wise differences.

**Results**

Mean age, height and weight of the 4 groups (CON, EXP, HAN and ALR) are shown in Table 1. There was no significant difference in age and weight among the 4 groups. However significance difference was observed in height of HAN group from other groups (CON vs. HAN:  $P < 0.001$ ; EXP vs. HAN:  $P < 0.001$ ; ALR vs. HAN:  $P < 0.01$ ).

Group	Age (Years)	Height (cm)	Weight (kg)
CON	27.2 ± 4.0	173.2 ± 4.7 <sup>***</sup>	72.9 ± 5.4
EXP	27.3 ± 3.9	172.2 ± 4.8 <sup>###</sup>	71.9 ± 5.9
HAN	26.5 ± 3.4	165.4 ± 3.0 <sup>€</sup>	68.1 ± 4.3
ALR	26.7 ± 1.9	172.3 ± 3.7	71.5 ± 7.6

Values are expressed as Mean ± SD.  
 CON: Control group; EXP: Experimental group; HAN: High altitude native; ALR: Acclimatized sea level residents.  
<sup>\*</sup>  $p < 0.05$ , as compared from CON vs. HAN; <sup>#</sup>  $p < 0.05$ , as compared from EXP vs. HAN; <sup>€</sup>  $p < 0.05$ , as compared from HAN vs. ALR.

	Heart rate (bpm)		SpO <sub>2</sub> (%)	
	CON	EXP	CON	EXP
<b>Resting</b>	69.0 ± 7.5	67.2 ± 4.8*	98.4 ± 0.5	98.5 ± 0.5
<b>Exercise</b>				
1 min	116.2 ± 3.2	115.5 ± 3.5	97.7 ± 0.5	97.5 ± 0.5**
2 min	136.0 ± 2.7	130.1 ± 3.0***	97.7 ± 0.4	97.5 ± 0.5**
<b>Recovery</b>				
1 min	110.3 ± 3.4	103.2 ± 1.8***	97.7 ± 0.5	97.8 ± 0.4*
2 min	95.0 ± 1.7	92.2 ± 1.5***	97.7 ± 0.5	97.8 ± 0.4*
3 min	90.2 ± 2.0	88.7 ± 1.6***	97.8 ± 0.4	97.8 ± 0.4

Values are expressed as Mean ± SD.  
 CON: Control group; EXP: Experimental group.\* p<0.05, as compared from CON vs. EXP.

Table 2 depicts the HR and SpO<sub>2</sub> of the CON and EXP groups during resting condition, in response to SEP and recovery at SL. Resting HR of CON group was significantly higher (P<0.05) than EXP group. During exercise at 2<sup>nd</sup> min. and recovery period HR of CON group was significantly higher (P<0.001) than EXP group. SpO<sub>2</sub> of CON group was higher during SEP (P<0.01) and recovery period (min 1 and min 2: P<0.05) was significantly lower from EXP group. HR and SpO<sub>2</sub> of the CON, EXP, HAN and ALR groups during resting condition, in response to SEP and recovery at HA were presented in Table 3. No significant difference was observed in resting

heart rate among the 4 groups. Resting SpO<sub>2</sub> of EXP group was significantly higher than CON and HAN group (both P<0.001) at HA. SpO<sub>2</sub> of HAN group was significantly lower from CON and ALR groups (both P<0.001). SpO<sub>2</sub> of ALR group was significantly higher from CON group (P<0.05). During 1<sup>st</sup> min of exercise test HR of CON group was significantly higher from EXP, HAN and ALR groups (all P<0.001). During the same time HR of EXP group was significantly higher from HAN and ALR groups (both P<0.001).

	Heart rate (bpm)				SpO <sub>2</sub> (%)			
	CON	EXP	HAN	ALR	CON	EXP	HAN	ALR
<b>Resting</b>	76.2 ± 3.6	75.0 ± 6.5	74.5 ± 11.2	75.9 ± 7.5	95.2 ± 0.9***	96.1 ± 0.9@@@	93.3 ± 1.2 sss	95.9 ± 1.4 €yyy
<b>Exercise</b>								
1 min	134.1 ± 4.7***	129.7 ± 8.1@@@	109.8 ± 9.2 sss y	119.1 ± 16.5### €€€	89.3 ± 1.4***	91.8 ± 1.2###	91.0 ± 0.8 ss	93.3 ± 2.2 €€€yy
2 min	158.5 ± 5.9***	147.4 ± 9.0@@@	128.9 ± 12.9 sss	138.4 ± 17.2 ## €€€	85.3 ± 1.4***	88.4 ± 2.0	89.4 ± 1.9 sss	89.5 ± 3.0 €€€
<b>Recovery</b>								
1 min	131.1 ± 6.4***	122.4 ± 6.57@@@	106.9 ± 13.6 sss	120.5 ± 16.2 €€€ yyy	90.0 ± 1.1***	91.3 ± 1.8@	93.1 ± 1.1 sss	90.6 ± 2.6 yy
2 min	116.1 ± 7.8***	108.8 ± 8.2@@@	94.3 ± 12.3 sss	105.3 ± 12.3 €€€ y	93.3 ± 1.1***	95.0 ± 1.2	95.9 ± 0.8 sss	95.2 ± 1.3 €€€
3 min	97.8 ± 5.4***	90.0 ± 5.2	87.4 ± 10.4 sss	89.7 ± 9.2 €€€	95.2 ± 0.9***	96.0 ± 0.9	96.1 ± 1.0 s	96.1 ± 1.1 €€

Values are expressed as Mean ± SD.  
 CON: Control group; EXP: Experimental group; HAN: High altitude native; ALR: Acclimatized low altitude residents.  
 \* p<0.05, as compared from CON vs. EXP; @ p<0.05, as compared from EXP vs. HAN; # p<0.05, as compared from EXP vs. ALR; \$ p<0.05, as compared from CON vs. HAN; € p<0.05, as compared from CON vs. ALR; y p<0.05, as compared from HAN vs. ALR.

HR of HAN was also significantly lower ( $P < 0.05$ ) from ALR group. A similar trend was also observed in the 2<sup>nd</sup> min of SEP. HR of CON group was significantly higher from EXP, HAN and ALR groups (all  $P < 0.001$ ). HR of EXP group was significantly higher from HAN ( $P < 0.001$ ) and ALR (all  $P < 0.01$ ) groups. During 1<sup>st</sup> and 2<sup>nd</sup> min of recovery, HR of CON group was significantly higher from rest of the 3 groups (all  $P < 0.001$ ). In the same time HR of EXP group was significantly higher ( $P < 0.001$ ) from HAN group. In these 2 minutes HR of HAN group was significantly lower from ALR (1<sup>st</sup> min:  $P < 0.001$  and 2<sup>nd</sup> min:  $P < 0.05$ ) group. In the 3<sup>rd</sup> min of recovery period only the HR of CON group was significantly higher from the EXP, HAN and ALR groups (all  $P < 0.001$ ).

No significant difference was noted among the other groups in this period. In the 1<sup>st</sup> min of exercise test SpO<sub>2</sub> of CON group was significantly lower from EXP group ( $P < 0.001$ ), HAN group ( $P < 0.01$ ) and ALR group ( $P < 0.001$ ). SpO<sub>2</sub> of EXP group was significantly lower ( $P < 0.001$ ) than ALR group. In the 2<sup>nd</sup> min of SEP the SpO<sub>2</sub> of CON group was significantly lower from the other 3 groups ( $P < 0.001$ ). No significant difference was noted among the EXP, HAN and ALR groups in this period.

In the 1<sup>st</sup> min of recovery period SpO<sub>2</sub> of CON group was significantly lower from EXP and HAN groups ( $P < 0.001$ ). In the same time SpO<sub>2</sub> of EXP group and ALR group was statistically lowered from HAN group ( $P < 0.05$  and  $P < 0.01$  respectively). In the 2<sup>nd</sup> and 3<sup>rd</sup> min of recovery period the SpO<sub>2</sub> of CON group was significantly higher from EXP group ( $P < 0.001$ ), HAN group (2<sup>nd</sup> min:  $P < 0.001$  and 3<sup>rd</sup> min:  $P < 0.05$ ) and ALR group (2<sup>nd</sup> min:  $P < 0.001$  and 3<sup>rd</sup> min:  $P < 0.01$ ). In the same periods no significant difference was noted among the other 3 groups.

### Discussion

In the present study the effect of IHE on oxygen saturation and exercise response were assessed both at SL and at HA (3,500 m). Moreover, the effectiveness of IHE, on the same parameters, was also compared with HAN and ALR at HA. The important finding that we observed from this study was IHE for 4 days at 12% F<sub>I</sub>O<sub>2</sub> improved resting SpO<sub>2</sub> and exercise performance at HA. It

has been reported by various authors that IHE improves exercise performance by modifying various physiological pathways.

Bonetti *et al* (2006) reported that following intermittent hypoxic training physical performance in terms of peak power and repeat sprint speed was improved by changing the oxygen transport [20]. It has also been observed that after 3 weeks of intermittent normobaric hypoxic exposure there was an improvement in 3-km performance in multi-sport athletes [12].

It was observed that height of HAN group was lowest among 4 groups (4.5% from CON group, 3.9% from EXP and 4% from ALR). The difference in height might be due to the larger leg length of the other 3 groups, different food & nutrition pattern, genetic and environmental factors [21]. After IHE at SL resting HR of CON group was 2.6% higher from EXP group. The lower HR of EXP group might be due to change in the autonomic nervous system towards more parasympathetic by IHE [11].

During 2<sup>nd</sup> min of SEP, HR of CON group was increased by 14.6% whereas in EXP group it was 11.2% only. During exercise at HA, HR of CON group was increased by 75% and 108% in 1<sup>st</sup> and 2<sup>nd</sup> min respectively. In the same period HR of EXP group was increased by 72.9% and 96.5%, in HAN group 47.4% and 73% and in ALR group 56.9% and 82% respectively. Though there was no difference in resting HR at HA between CON and EXP group. But during exercise HR of CON group was lower than EXP group by 3.4% and 7.5% respectively.

HR of EXP group, during exercise, was higher than HAN and ALR group. During exercise, at 1<sup>st</sup> min SpO<sub>2</sub> of EXP was 1.6% higher than ALR group. During recovery period the difference in HR between EXP and CON group was 7.1%, 6.7%, and 8.7% in 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> min respectively. HR of EXP group during recovery period (1<sup>st</sup> and 2<sup>nd</sup> min) was higher than HAN group only. At HA the resting SpO<sub>2</sub> of EXP group was highest among all the other groups, thus proving the effectiveness of IHE for less fall of SpO<sub>2</sub> upon

rapid induction to HA. Our observation is similar with other published reports [10-11, 22].

It has also been reported that at HA assessment of SpO<sub>2</sub> after light exercise estimates the level of acclimatization among healthy subjects [23]. During SEP in the present study SpO<sub>2</sub> of CON group was reduced by 6.2% and 10.4% in the 1<sup>st</sup> and 2<sup>nd</sup> min respectively. Whereas during the same time fall of SpO<sub>2</sub> in EXP group was 4.5% and 8%, in HAN 2.5% and 4.2%, in ALR group 2.7% and 6.7%. The maintenance of oxygen saturation of HAN group during exercise might be due to their higher diffusion capacity for oxygen [24].

During exercise SpO<sub>2</sub> of EXP group was lower than the CON group by 2.7% and 3.5% respectively. In recovery period also the difference in SpO<sub>2</sub> between the 2 groups was 1.4%, 1.8%, and 0.8% in the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> min respectively. It has been proved that those who can maintain their resting and exercise induced SpO<sub>2</sub> at HA do not develop AMS [25].

In this study the higher resting SpO<sub>2</sub> at HA and lesser fall of SpO<sub>2</sub> during exercise test at SL and HA both in EXP group than CON group might be due to higher arterial oxygen content, total haemoglobin mass and haemoglobin concentration due to IHE [26]. IHE might also increase SV that improves oxygen pulse and ultimately exercise performance [12]. Hypoxic training can also increase serum erythropoietin syntheses which in turn increase the haematocrit, synthesis of red blood cells, haemoglobin, reticulocytes and ultimately improve supply of oxygen to the working muscle during exercise and thus improve performance [27-28].

Less increase in HR and fall of SpO<sub>2</sub> of HAN group during exercise testing might be due to their higher gas exchange efficiency with low minute ventilation and smaller alveolar-arterial partial pressure differences during exercise [29]. It has been reported that HAN have significantly higher  $\dot{V}O_{2max}$  than their SL counterparts and decrement of  $\dot{V}O_{2max}$  was also smaller with increasing altitude. It was also found that during exercise HAN people have lower pulmonary ventilation and higher SpO<sub>2</sub> than SL participants

[30]. Lower HR and higher SpO<sub>2</sub> during exercise as observed in the ALR group in comparison to CON and EXP groups might be due to their higher haemoglobin level that may be increased with stay at HA [31].

In recovery period increase in SpO<sub>2</sub> in HAN group was observed 4.1%, 2.9% and 0.2 % and in ALR group 1.2%, 4.8% and 0.9% in the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> min respectively. It has been reported that though during acclimatization of lowlanders at HA there is an improvement in pulmonary gas exchange but that always remain lower than the HAN people [32].

After IHE at SL resting HR and exercise performance of EXP group was better than CON group. At HA resting SpO<sub>2</sub> of EXP group was higher than other 3 groups but their exercise performance was better than the CON group only. Observing the effectiveness of normobaric IHE in the improvement of oxygen saturation and exercise performance in our study and others [33] it can be concluded that IHE could be an effective way to improve performance for maintaining operational effectiveness for the personnel, such as army, mountaineers, trekkers and tourists, who require rapid induction to HA.

### Conclusion

Intermittent normobaric hypoxia exposure improves arterial oxygen saturation and also increases exercise performance during initial days of acclimatization at HA, thus can be used as a tool during emergency rapid induction. Future studies with larger subject cohort, other physiological and biochemical parameters are required for further analysis on the effectiveness of IHE on human health and performance.

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