Sleep Breath
DOI 10.1007/s11325-007-0127-9

REVIEW

Preacclimatization in simulated altitudes

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Abstract Acute exposure to high altitude provokes the development of mountain illnesses and decrease of exercise performance. Thus, sufficient acclimatization is of utmost importance for mountaineers, trekkers, and athletes performing at high altitude. The main purpose of this paper was to review existing studies and observations on the effectiveness of preacclimatization at simulated altitude. *Data source*: A PubMed search has been performed and preliminary observations from our laboratory have been included. Although some beneficial effects have been demonstrated, it is not possible to draw firm conclusions from the few available studies dealing with the effects of preacclimatization at simulated altitude on the reduction of acute mountain sickness (AMS) incidence and performance loss at high altitude. For the present, 1–4 h of daily exposures for 1–5 weeks to simulated altitudes of about 4,000 m seem to initiate ventilatory and autonomous nervous system adaptations to high altitude with the potential to reduce AMS development. At least for protocols of short duration, rest during hypoxic exposures seems to be similarly effective as exercise. For the more prolonged protocols, exercise may be included to enhance exercise performance in hypoxia.

Keywords Intermittent hypoxia · Simulated altitude · preacclimatization · Mountaineering · Trekking · Acute mountain sickness · Exercise performance

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Introduction

When going to high altitudes, sufficient acclimatization is necessary to avoid altitude illnesses. The faster the ascent and the more susceptible the individual the greater is the risk of development of altitude illnesses and the lower is the success to reach the summit [1]. On the other hand, prolonged sojourns at high altitude may deteriorate muscle performance and energy stores and also lower the probability of success on the mountain [2]. Thus, efficient preacclimatization at simulated altitude could contribute to the reduced risk for altitude illnesses and reduced loss of performance at altitude. Several studies demonstrated such benefits by various types of preacclimatization in simulated altitudes [3–7]. But the results are far from that we would call "standard preacclimatization".

Therefore, the main purpose of this paper is to review existing preacclimatization studies and observations and to derive at least preliminary recommendations for efficient preacclimatization before going to high altitudes and to raise ideas for further studies.

Materials and methods

Data source Articles were selected from a search of the PubMed database from 1976 to 2007 using the search terms intermittent hypoxia, simulated altitude, acclimatization, adaptation, preparation, mountaineering, trekking, acute mountain sickness (AMS), exercise, performance, and hypoxic ventilatory response (HVR) and articles known to the authors and referenced in review articles. Studies evaluating the AMS incidence after preacclimatization at simulated altitude (intermittent hypoxia) have been included. From those showing preacclimatizing effects like

improved performance in hypoxia, increased HVR, and decreased hypoxic sympathetic activation, we present a balanced selection of studies. In addition, we present preliminary data from our experience with routine preacclimatization and a case report on intermittent hypoxia in a high-altitude pulmonary edema (HAPE) susceptible person.

Results

The main findings of 21 studies and 2 observational reports from our laboratory using intermittent hypoxia for preacclimatization or investigating acclimatizing effects are shown in Table 1. Besides our observations, only two studies focused on AMS prevention by preceding intermittent hypoxia [4, 6] and three on exercise performance in hypoxia [3, 5, 7]. All these studies reported beneficial effects. Whereas we used about 1 h hypoxia per day for 5–7 days, the other authors demonstrating AMS prevention or performance increase in hypoxia used 3 or more hours per day for 6 to 20 days. The degree of hypoxia was about 12% or equivalent to about 4,000 m at least when starting exposures [3–7]. Most studies exposed subjects at rest to hypoxia [8–19]. Those comparing the effects when exposures were at rest or with exercise did not find any differences [5, 6]. Except one study with moderate hypoxia for only 7 days [10], most demonstrated an increase in the HVR [8, 9, 11, 13, 15, 18, 20, 21] and also increased ventilation and/or SaO_2 during exercise when the simulated altitude was higher than 2,500 m [3, 5, 7, 11, 14, 16, 21, 22]. One study found attenuated mood after 3 days with 3 h of hypoxic exposures [17]. Regarding adverse effects after intermittent hypoxia, one study showed reduced cerebral oxygenation [9] and another study found increased exercising blood pressure and lipid peroxidation after more severe hypoxia (12%), which was not observed after moderate hypoxia (15%) [14]. One study reported no differences in SaO_2 during exercise at altitude after 6–7 days for 3 h/day of intermittent hypoxia at an altitude of 4,500–3,000 m but the HVR was not determined [23]. Observations from our laboratory were reported at the hypoxia congress 2005 in Bad Reichenhall.

Observational study In total, we observed 141 trekkers and climbers. Sixty seven (58 males, 9 females; age 21–67 years) were preacclimatized in our laboratory by 1–2 h of normobaric hypoxia (approximately 3,000–5,500 m) on 5 days close before going to real altitude. All of them and 74 trekkers and climbers without preacclimatization completed a questionnaire on AMS symptoms appearing during the altitude sojourn. Of the mountaineers, 10% with preacclimatization reported mild AMS symptoms and about 30% of those without preacclimatization had mild to severe AMS symptoms. Thus, preacclimatization may have been effective, but there are several limitations: we cannot exclude a placebo effect and we do not have information about the differences of preacclimatization at real altitude between groups.

Case report

A 64-year-old regularly exercising woman had known intolerance to altitudes over 2,000 m. She participated in one of our studies at 3,500 m and developed clear signs of HAPE, which improved after oxygen administration. One year later, she went to the Himalayas for trekking and again suffered from HAPE. She had to be evacuated and recovered. Five years later, she again planned to trek in the Himalayas and visited our laboratory. We exposed her and her partner five times for 30–60 min to simulated altitude and saw a marked increase in SaO_2 from day 1 to 5. During the last 2 days, SaO_2 values were similar to those observed in her partner who tolerated altitudes very well (Table 2). Subsequently, they went to the Himalayas (under medical observation) and tolerated altitudes up to 5,000 m without problems.

Discussion

When going to high altitudes, the human body has to cope with several stressors: hypoxia, hypobaria, cold, exercise, radiation, etc. Undoubtedly, hypoxia is the most important stressor and in certain circumstances, e.g., when going too high too fast, the body is unable to adapt sufficiently and life-threatening illnesses may be the consequences [1]. Therefore, the stepwise and individually designed increase in altitude (hypoxia) allows the body to adapt and to prevent those illnesses. As we know from athletic training, repeated stimuli with adequate recovery periods lead to successful adaptations and performance increase [24]. Thus, one might theoretically deduce that repeated exposures to hypoxia might also be effective for preacclimatization before going to real high altitude. Support for such a strategies comes from some recent successful high-altitude climbers. They prepare by repeated short-term ascents to high altitude with recovery periods at lower altitudes (intermittent hypoxia) and then they climb the highest mountains of the world within a couple of hours (http://www.landderberge.at/biografien/christian-stangl/christian-stangl.htm). Unfortunately, only a few studies evaluated the acclimatizing effects of intermittent hypoxic exposures and nearly all of them used different exposure protocols (Table 1). Therefore, one can draw some cautious con-

Table 1 Characteristics and effects of exposures to hypoxia

	Characteristics of exposures to hypoxia					Effects			
	Hypoxia	Exposure time		Activity		Increase (time of carry over)		Prophylaxis	Others
Author	FiO_2, altitude	h/day	Total days	Rest, exercise	HVR	VE, SaO_2 (hypoxia) rest (r), exercise (ex)	Performance (hypoxia)	AMS, HAPE	
Bernardi et al. [8]	Approximately 10%	0.4 (4×5–7 min)	14	r	+				Reduced vagal withdrawal
Foster et al. [9]	12%	0.5 (6×5 min)	10	r	+				Reduced cerebral oxygenation in hypoxia
		0.5 (continuous)	10	r	+				
Levine et al. [20]	2,500 m (hb)	0.75	25	ex	+	− (ex) (2,500 m)			
Burtscher et al.	14–12%	1	5	r		+ (r) (14–12%)		+ (HAPE)	
Burtscher et al.	14–12%	1	3–7	r		+ (r) (14–12%)		+ (AMS) ?	
Katayama et al. [10]	15.5%	1	7	r	–	− (ex) (15.5%)			
	12.3%	1	7	r	+	− (ex) (15.5%)			
Katayama et al. [11]	4,500 m	1	7	r	+ (1 week)	+ (ex) (432 Torr) (1 week)			
Katayama et al. [12]	12%	1	10	r		+ (r) (12%) (1 month)			
Lusina et al. [13]	Approximately 12%	1	10	r	+				Increased MSNA
Wang et al. [14]	15%	1	20	r		+ (ex) (sea level)	+ (sea level)		
	12%	1	20	r		+ (ex) (sea level)	+ (sea level)		Increased blood pressure at exercise, lipid peroxidation
Garcia et al. [15]	13%	2	12	r	+ (peak after 5 days)				Increased reticulocytes
Ricart et al. [16]	5,000 m (hb)	2	14	r		+ (ex) (5,000 m)			
Benoit et al. [21]	12.2–10%	2	18	ex (intense)	+	+ (ex) (10.4%)			
Kambis et al. [17]	3,700 m (nb)	3	3	r					Attenuated negative mood
Beidleman et al. [23]	4,500, 3,000 m (nb)	3	6–7	r (2 h), ex (1 h)		− (ex) (4,300 m, 60 h post)			No hemodynamic changes
Jones et al. [3]	4,500, 3,000 m (nb)	3	6–7	r (2 h), ex (1 h)		+ (ex) (4,300 m, 60 h post)	+(4,300 m, foot march)		
Muza et al. [4])	4,500, 3,000 m (nb)	3	6–7	r (2 h), ex (1 h)		+ (r) (4,300 m, 60 h post)		+ (AMS)	
Katayama et al. [18]	12.3%	3	7	r	+				
	12.3%	3	14	r	+				Increased HCVR
Fu et al. [19]	4,000–5,500 m	3	20	r					No sympathoexcitation
Beidleman et al. [5]	4,300 m	4	15	r, ex		+ (r, ex) (4,300 m)	+ (4,300 m)		Exercise in hypoxia did not affect results
Beidleman et al. [6]	4,300 m	4	15	r, ex		+ (r) (4,300 m)		+ (AMS)	Exercise in hypoxia did not affect results
Casas et al. [22]	4,000–5,500 m	3–5	17	ex		+ (ex), sea level			
Richalet et al. [7]	4,350–8,500 m	>9	11	r, ex		+ (ex) (11.5%)	+ (up to 7,800 m)		

Table 2 Changes of hypoxia-dependent SaO_2 values in a HAPE susceptible and a person not susceptible to HAPE during the course of 5 days of intermittent hypoxia

	FiO_2/SaO_2 (%)	
	HAPE	None-HAPE
Day 1	13/59–73	13/85
Day 2	13/77	13/85
Day 3	12/79	12/80
Day 4	12/80	12/81
Day 5	15/89	15/92

clusions about the effectiveness of intermittent hypoxia for preacclimatization but the assessment of the various protocols used remains speculative. All studies investigating the AMS incidence and psychophysical performance after intermittent hypoxia found some beneficial effects [3–7, 14, 22, our observations]. These effects seem to be independent whether exercise has been performed or not during the hypoxic sessions. Duration of 1–3 h/day for at least 1 week seems to be necessary for preacclimatizing effectiveness. These benefits may be preserved after the hypoxic exposures for about 2.5 to 7 days. The degree of hypoxia used was mostly around 12% of FiO_2 or an equivalent altitude of about 4,000 m. Only from one study one could derive that more moderate hypoxia (15.5%) does not increase the HVR after 1 week of exposure [10]. But when exposure time to moderate altitude was more prolonged, e.g., 25 days, the HVR increased [20]. A sufficient HVR and adequate hyperventilation and arterial oxygenation at rest and/or during exercise at altitude seem to be the most important beneficial responses observed after preacclimatization with intermittent hypoxia [3–9, 11–13, 15, 16, 18, 20, 21]. AMS susceptibles and especially HAPE prone mountaineers demonstrate a low HVR [25, 26]. Our case report supports that increasing the low HVR in HAPE susceptibles can prevent HAPE development when subsequently visiting high altitudes. However, acclimatization is a very complex process including several additional responses besides hyperventilation. During short-term exposures to high altitude, when altitude illnesses are most frequent and performance reductions are most pronounced [27], especially changes regarding the autonomic nervous system and possibly accompanied renal responses seem to contribute to acclimatization [28]. Figure 1 shows a schematic overview of the selected main responses to acute and subacute altitude, which may be influenced in an adaptive way by intermittent hypoxia. Hyperventilation and increased sympathetic activation with increases in heart rate and cardiac output are helpful for the improvement of oxygen delivery to tissues. Respiratory and cardiovascular responses to hypoxia display a well-defined pattern, characterized by hyperventilation, increase in heart rate and cardiac output, pulmonary vasoconstriction, a decrease in total systemic resistance, a moderate rise in systemic blood pressure, and a redistribution of blood flow towards the organs with marked metabolic needs, i.e., brain, heart, skeletal muscle [29–31]. In addition, carbohydrate metabolism in acute hypoxia is greatly influenced by the sympathetic nervous system leading to high blood lactate concentrations at exercise [32]. Whereas ventilation progressively increases to a certain level during acclimatization, autonomic activity seem rather to return toward sea level values [33] combined with lowering of heart rate and blood lactate responses to exercise with prolongation of the altitude sojourn [32, 34]. Therefore, a high ventilatory response and reduced sympathetic activation to hypoxic exposure would indicate effective preacclimatization. There is no doubt that the HVR is increased after intermittent hypoxia but the adaptation of the autonomous system with intermittent hypoxia is less clear. Fulco et al. reported that beta blockade had a tendency to reduce the development of AMS [35]. Ledderhos et al. showed a reduced tolerance of simulated altitude (4,200 m) in young men with borderline hypertension [36]. They found an exaggerated response in the sympathetic nervous system, antidiuresis, and enhanced symptoms of AMS in those persons. Scherrer et al. found increased sympathetic activity in persons susceptible to HAPE [37]. Persons susceptible to HAPE could possibly benefit by preacclimatizing intermittent hypoxia from both increased HVR and decreased sympathetic activation. However, Lusina et al. reported increased muscle sympathetic nerve activity (MSNA) and chemosensitivity after 10 daily exposures (1 h/day) of intermittent hypoxia but without hemodynamic changes [13]. Fu et al. found no alterations in autonomic control after 4 weeks of hypobaric intermittent hypoxia in young athletes [19]. But Bernardi et al. demonstrated an increased HVR and a reduced vagal

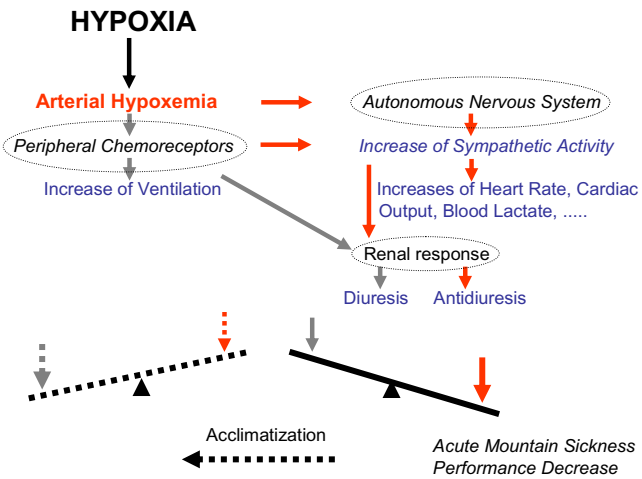

Fig. 1 Schematic overview of selected responses to acute hypoxia (altitude), which may adapt during preacclimatization

withdrawal during progressive hypoxia after 2 weeks of intermittent hypoxia [8]. In contrast to sleep apnea, the presented protocols of intermittent hypoxia seem to be safe without evidence for sustained physiologically significant sympathoexcitation. At least from the study of Bernardi et al., one could assume that some autonomic adaptation occurs with intermittent hypoxic exposure [8].

In addition, sympathetic activation and the ventilatory response to hypoxia affect renal function [28]. Whereas the enhanced sympathetic outflow to the kidney promotes antidiuresis, diuresis increases with an increasing ventilatory response to hypoxia. Antidiuresis has sometimes been reported to be associated with AMS development, therefore, one could speculate that a high sympathetic activity and a low HVR favors AMS, as shown by Ledderhos et al. [36], whereas a high HVR and low sympathetic activity would indicate acclimatization with good toleration of hypoxia. If this is true, high altitude exposure after intermittent hypoxia should be accompanied not only by a reduced incidence of AMS but also by increased diuresis.

Although some beneficial effects may exist, it is not possible to draw firm conclusions from the few available studies dealing with the effects of prior intermittent hypoxia on the reduction of AMS incidence and performance loss at high altitude. For the present, 1–4 h of daily exposures for 1–5 weeks to simulated altitudes of about 4,000 m seem to initiate ventilatory and autonomous nervous system adaptations to high altitude. At least for protocols of short duration, rest during hypoxic exposures seems to be similarly effective as exercise. For the more prolonged protocols, exercise may be included to enhance exercise performance in hypoxia. More well-designed and controlled studies are necessary for adequate recommendations on how to use intermittent hypoxia for preacclimatization.

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