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ORIGINAL ARTICLE

Preacclimatization in hypoxic chambers for high altitude sojourns

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Abstract
Introduction Since hypoxic chambers are more and more available, they are used for preacclimatization to prepare for sojourns at high altitude. Since there are different protocols and the data differ, there is no general consensus about the standard how to perform preacclimatization by simulated altitude. The paper reviews the different types of exposure and focuses on the target groups which may benefit from preacclimatization.
Discussion Since data about intermittent hypoxia for some hours per day to reduce the incidence of acute mountain sickness differ, it is suggested to perform preacclimatization by sleeping some nights at a simulated altitude which follows the altitude profile of the “gold standard” for high altitude acclimatization.

Keywords Acclimatization · Hypoxia · Simulated altitude · Acute mountain sickness

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Introduction

High altitude sojourns are more and more common for different populations. Besides mountaineers or skiers, there are businessmen traveling to Colorado, South America, and other regions, tourists visiting historic sites in the Andes, scientists working at telescopes in the Andes, in Hawaii, or at the world's highest mines located at 5,300 m in Chile. Several 10,000 trekkers hike the Annapurna Trek every year (Fig. 1), with the highest point of this trek being Thorong La (5,416 m). Time pressure is the reason why Mt. Kilimanjaro (5,860 m) is considered as the most dangerous mountain in the world. More and more people try to climb it within 3–4 days and only a minority reaches the summit healthy [1]. Businessmen are another group with limited time or unforeseen trips to high altitude [2]. Principally, correct acclimatization was, is, and will ever be the “gold standard” for any altitude sojourn [3]. But if immediate ascent or intermittent hypoxia >4,000 m (rsp. 12.5–13% O_2 at 1 bar) cannot be avoided, preacclimatization avoids altitude-related diseases and stabilizes the performance of the persons.

Physiologically, the main problem for the body is the management of the decreased oxygen pressure. If there would be no system to adapt to hypoxic conditions, an altitude of about 1,500 m could not be survived without accidental oxygen [4]. Fortunately, there are multiple systems to manage the problem, some of them reacting within seconds or minutes (e.g., pulse rate, breathing frequency, breathing volume, shift of the oxygen binding curve), some others in days or weeks (e.g., circulation, hemoconcentration, ventilatory acclimatization), or even years or generations (e.g., vascular growth) [5]. The effect of some of these acute adaptations is enormous: the shift of pH by respiratory alkalosis at high altitude from 7.2 to 7.6 at a partial oxygen pressure (pO_2) of 30 mmHg increases O_2 saturation (SaO_2) from 28% to 57% [4].

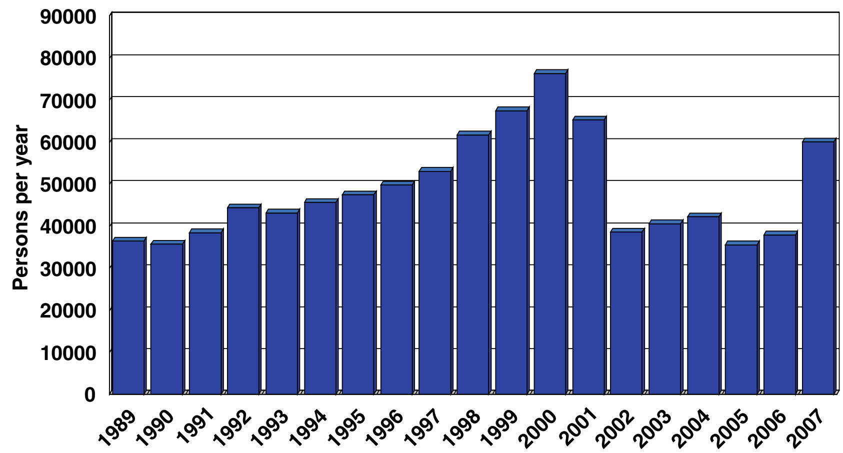

Fig. 1 Number of persons who visited the Annapurna Conservation Area 1989–2007 (courtesy of the National Park Office at Muktinath, Mustang Province, Nepal)

The vulnerability of a person to acute mountain sickness (AMS), high altitude pulmonary edema (HAPE), and high altitude cerebral edema is influenced by the hypoxic pulmonary ventilatory drive (HVD), although this correlation is not strong enough to use HVD as a predictor of a person's ability to cope with high altitude conditions. HVD is genetically determined. But there are other important factors which are responsible for the individual fitness at altitude and the risk of altitude-related diseases as the limitation of diffusion capacity of the alveolar membrane or of minute breathing volume [6], the erythrocytes form, plasticity, size, and age [7], or increased plasma volume or low hematocrit, respectively [8].

A central role for the regulation of many of these mechanisms has a substance called hypoxia-inducible factor 1α (HIF1α) [9]. HIF1α is produced permanently and metabolized via hydroxylation and proteasomal lysis. If hypoxia occurs, the system switches to another pathway within seconds: by a massive phosphorylation, HIF1α becomes the active metabolite which joins the hypoxic binding sites and induces the increased transcription of the HIF1α-dependent genes [10–12].

To answer the questions listed below, an extensive literature research was performed in international databases (e.g., PubMed) with the keywords "intermittent hypoxia, simulated altitude, acute mountain sickness, hypoxic ventilatory response, mountaineering, trekking, acclimatization, hypoxic chambers, and isobaric hypoxia." Papers cited in reviews but not listed in the databases and other papers which were known to the authors but also not listed in the databases were also included if there was a substantial contribution to the topic of this paper.

Who may benefit from preacclimatization?

Most knowledge about acclimatization strategies and ascent profiles are mainly based on empirical data, but these include >1,000 years of high altitude sojourns (military operations in the region today called Tibet, sacrifices in the Andes, and modern mountaineering and research for about 200 years). Nevertheless, there is no doubt that proper acclimatization according to the "gold standard" (recommendations published in [3], and a multitude of other papers) is the best way to prepare the body for high altitude. There is no evidence that this will change in the next 100 or so years, since any genetic adaptation, if there is some interbreeding between lowlanders and highlanders in the course of the so-called globalization, will take several generations.

Acclimatization is of special importance for any lowlander who will sleep at an altitude >2,500 m or who will stay at >4,000 m for >1–3 h. Persons with pre-existing conditions may need special advice or, in some cases, restrictions [13]. The "gold standard" includes slow ascent (+500 m sleeping altitude every second day or a maximum of +1,000 m/week, beginning at 2,500 m), sleep with slight upper body increases, no breathing with pressure, and workload below the anaerobic threshold during the acclimatization phase [3].

In some situations, such an ideal acclimatization profile cannot be realized. It may be impossible if the person has to fly to airports at high altitude (e.g., in the Andes or Tibet), if urgent and unexpected work has to be done at high altitude (e.g., for industrial maintenance and services at high altitude facilities or for some special rescue purposes), or "critical" mountains where a good altitude profile is difficult to be realized (e.g., Ruwenzori Mountains). While a preacclimatization for 24–48 h should be possible for most industrial or business tasks, the setting for most rescue operations is different. For normal alpine (helicopter) rescue, preacclimatization is not necessary, mainly because the crews stay too short at altitude and most of them are partially acclimatized. But if international operations should be assisted by a backup team of unacclimatized lowlanders, the time necessary to organize such operations should be used to preacclimatize the team members.

But there are even more people who may benefit from preacclimatization: persons with known problems of acclimatization, although the altitude profile was perfect ("slow acclimatizers"), or elite sport teams who are facing competitions at high altitude. The latter was first discussed for the Olympic Games at Mexico City in 1968.

Preacclimatization—how should it be performed?

Some of the mechanisms listed above prevent altitude diseases in the early stage of altitude exposure, while others are responsible for the metabolic stabilization of the body for long stays at altitude with some of them developing over several generations [5]. Preacclimatization is performed by an exposure of the body to real or simulated altitude, either isobaric or hypobaric hypoxia, but ever for a limited duration. Therefore, any preacclimatization will influence exclusively those mechanisms which are responsible for the early stage of high altitude sojourns, i.e., to avoid AMS. Already, Paul Bert found 140 years ago that there are minor differences between data obtained in the laboratory and those from "real" high altitude in the mountains [14]. But these differences do not have any consequences for the tactics of acclimatization, neither in isobaric conditions nor in the mountains.

The main difference between preacclimatization at "real" altitude or in a hypoxic chamber is that, normally, real altitude means that the person will stay at a given altitude for some time (continuous exposure), while in most cases, the stay in a hypoxic chamber will last some hours per day or an overnight stay. Unfortunately, there is not yet much knowledge about acclimatization by intermittent hypoxia and, therefore, there is actually no standard for preacclimatization in hypoxic chambers by intermittent hypoxia of some hours. As Burtscher et al. mentioned in detail, studies performed so far show a benefit if the persons are exposed 1–4 h/day at a corresponding altitude of about 4,000 m (FiO_2=12%) [15]. On the other hand, Bärtsch et al. did not find any difference in the incidence of AMS in persons ascending to Margherita Hut (4,560 m) after some days with 12% O_2 for 4 h (personal communication, May 2009). But as stated by Mutschler, the subjects of Bärtsch's study did not exactly follow the altitude profile of the study for several reasons (weather, etc.; Mutschler, personal communication, July 2009), which is a major limitation of the study.

Several other recent studies deal with the topic of simulated altitude, in contrast to the legendary "Operation Everest II" in most cases with intermittent hypoxia. Most studies available so far deal with limited numbers of subjects and with significant differences in exposure (altitude, duration of hypoxia, and duration normoxia between the hypoxic phases). This prevents a direct comparison of the results. Nevertheless, since Richalet used a hypoxic chamber when he was preparing the Everest expedition in the early 1990s [16], some other studies indicate the benefit of preacclimatization by intermittent hypoxia to minimize the risk of suffering from AMS [17–19]. In most cases, the hypoxic exposure was equivalent to an altitude of 4,000 m, but the duration per day and the total period of exposure was very different (three or more hours per day for 6–20 days) [16–20]. There was reportedly no difference between exposure combined with some or without activity [18, 19]. At moderate altitude, there was no significant influence on several physiological factors by intermittent hypoxia [21], but several changes as usual in normal ("real") hypoxia in the mountains were found when the exposure exceeded a corresponding altitude of 2,500 m [16, 18, 20, 22, 23]. In some investigations, an increase of performance [16, 18, 20] or mood status was found [24]. Intermittent hypoxia also increased vagotonus [25]. Some data indicate that at least 1 week of exposure may be necessary to induce significant preacclimatization [21]. In contrast to Katayama's study, significant acclimatization was found after 25 days of exposure only [26]. The most prominent effects of intermittent hypoxia with simulated altitude were found for HVD, hyperventilation, and arterial oxygen saturation [16–20, 22, 23, 25–28].

In summary, the knowledge about the influence of intermittent hypoxia and here especially the optimal "profile" of equivalent altitude, duration of exposure, number of exposures, pause between them on acclimatization AMS, and other factors is not yet clear. Therefore, we would suggest to follow "traditional" rules for acclimatization and to sleep in hypoxic conditions for some nights. Although there are no double-blind controlled studies, there is evidence that the interruption of hypoxia during the day (when the subjects sleep in hypobaric hypoxia only) is of minor effect compared to 24 h hypoxia. Our nonsystematic data of about 30 mountaineers do not indicate a significant lesser acclimatization (indicated by higher incidence of AMS or failing to reach the summit of Kilimanjaro) when compared to others who spent days for acclimatization all the time at altitude.

Principally, any preacclimatization should follow the recommendations of the "gold standard" [3]. This can be done in hypoxic chambers as well as during some days in a mountain hut. The latter is more charming, but unfortunately not always realistic. The special advantages of hypoxic chambers will be discussed later. The next questions are how high the final altitude will be and whether the preacclimatization shall be combined with activity. What's your goal? Just to preacclimatize to avoid

AMS or to improve your performance? For the latter, planning is crucial: vascular endothelial growth factor and mitochondriosis increase only by high intensive training at about 3,650 m [29] and the "threshold" for erythropoietin increase is at about 2,100–2,500 m [30, 31]. An increase of +5% of erythrocyte volume may need at least 400 h (3–4 weeks) at 2,500–3,000 m and the anaerobic system provide more benefit by altitude than the aerobic system [32, 33].

The so-called slow acclimatizers are a special problem for preventive altitude medicine, as there are no procedures available which allow detecting them with a positive predictive value which is acceptable. For example, HVD, well known to be inversely correlated with an increased risk for problems of acclimatization and AMS, cannot be used as predictor because its positive predictive value is only about 60% [34, 35]. The monitoring of SaO_2 is limited by the same problem. Pulse frequency cannot be used as a predictor, but it may be used to monitor acclimatization: although there are no data, there is evidence that slow acclimatizers should have normal pulse rate as normal persons have when they are completely acclimatized to the respective altitude. Actually, the only chance to identify "slow acclimatizers" is a careful and detailed history of the person's altitude sojourns and the problems which have arised. Any person who suffered significantly from AMS symptoms although the altitude profile was acceptable or who complained about sleep disturbances significantly more than his or hers companions at the same altitude should be suspected to be "slow acclimatizers." The same should be suspected if a person suffered from HAPE at surprisingly low altitude (2,500–3,000 m) or if a person suffered from recurrent HAPE. It is well accepted that slow acclimatizers should follow a more "defensive" altitude profile than other mountaineers—but unfortunately, there are no data or any consensus what "more defensive" is. Until more detailed data are available, we suggest adding at least one more day to every altitude of the profile until an altitude of 4,000 m is reached. Above this altitude, the acclimatization process of slow acclimatizers is highly individual and should be monitored clinically (pulse rate, AMS symptoms, or Lake Louise Score [36]).

The final altitude of preacclimatization depends partially on the altitude profile later in reality. If a person wants to climb a mountain, the days of ascent can be included in the altitude profile of preacclimatization. This is impossible if the person has to go to altitude at once, e.g., the business-men or tourists to destinations in the Andes. For high destinations, work, or "critical" altitude profiles, the ideal altitude to be reached by preacclimatization is the same (or a bit more to get a "safe zone") than the destination. Risk groups ("slow acclimatizer") should preacclimatize to a final altitude which is a bit higher than the highest place planned for sleeping, but a much more "defensive" altitude profile should be chosen. As mentioned above, athletes should preacclimatize to the height of the competition +300 m. Both risk group and athletes get a safe margin by doing so with a technique which is not yet evaluated in detail.

For the timing of preacclimatization, data are limited. Possibly, the best scheme for altitude up to 4,000 m and healthy persons is as follows: first night at 2,500 m equivalent altitude, two (to three) nights at 3,000 m, and 1 week later, two (to three) nights at 3,000 and 3,500 m. This can be done during weekends and, therefore, can be easily combined with normal life. It should be as near as possible, but not longer as two (to three?) weeks before departure.

Conclusion

Preacclimatization decreases the risk of altitude diseases significantly, if acute ascent cannot be avoided. The special advantage of hypoxic chambers is the well-controlled environment, the safety for persons with individual risks or pre-existing conditions, and the easy coordination of the exposure with normal daily life and work. Nevertheless, it must be planned carefully and performed within a short period before departure. Going "not too high too fast" for optimal acclimatization is the "gold standard" to avoid health risks and to provide optimal performance at high altitude.

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