WILDERNESS & ENVIRONMENTAL MEDICINE, **25,** 263–271 (2014)

ORIGINAL RESEARCH

Sleeping in Moderate Hypoxia at Home for Prevention of Acute Mountain Sickness (AMS): A Placebo-Controlled, Randomized Double-Blind Study

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Objective.—Acclimatization at natural altitude effectively prevents acute mountain sickness (AMS). It is, however, unknown whether prevention of AMS is also possible by only sleeping in normobaric hypoxia.

Methods.—In a placebo-controlled, double-blind study 76 healthy unacclimatized male subjects, aged 18 to 50 years, slept for 14 consecutive nights at either a fractional inspired oxygen (F_{IO_2}) of 0.14 to 0.15 (average target altitude 3043 m; treatment group) or 0.209 (control group). Four days later, AMS scores and incidence of AMS were assessed during a 20-hour exposure in normobaric hypoxia at $F_{IO_2} = 0.12$ (equivalent to 4500 m).

Results.—Because of technical problems with the nitrogen generators, target altitude was not achieved in the tents and only 21 of 37 subjects slept at an average altitude considered sufficient for acclimatization (>2200 m; average, 2600 m). Therefore, in a subgroup analysis these subjects were compared with the 21 subjects of the control group with the lowest sleeping altitude. This analysis showed a significantly lower AMS-C score (0.38; 95% CI, 0.21 to 0.54) vs 1.10; 95% CI, 0.57 to 1.62; $P = .04$) and lower Lake Louise Score (3.1; 95% CI, 2.2 to 4.1 vs 5.1; 95% CI, 3.6 to 6.6; $P = .07$) for the treatment subgroup. The incidence of AMS defined as an AMS-C score greater than 0.70 was also significantly lower (14% vs 52%; $P < .01$).

Conclusions.—Sleeping 14 consecutive nights in normobaric hypoxia (equivalent to 2600 m) reduced symptoms and incidence of AMS 4 days later on exposure to 4500 m.

Key words: acclimatization, acute mountain sickness, hypoxia, prevention, ventilation

Introduction

Ascent to altitudes above 2500 m frequently causes acute mountain sickness (AMS), a syndrome characterized by headache, nausea, dizziness, and insomnia, and ascent to higher altitudes can also occasionally cause potentially lethal high altitude pulmonary edema (HAPE) or high altitude cerebral edema (HACE).[1] The major determinants of the prevalence of these illnesses are altitude, individual susceptibility, rate of ascent, and degree of acclimatization caused by preceding exposures.[2] Slow ascent that would help to reduce severity and incidence of these illnesses is often not possible because of time constraints or financial reasons. Therefore, in a given setting of rapid ascent, preacclimatization or intake of drugs such as acetazolamide[3] or nifedipine[4] are often the only options to avoid or reduce the chance of experiencing AMS or HAPE.

There have been successful attempts to reduce AMS[5] and to improve the rate of ascent on climbing Mt Everest[6] by exposure to hypobaric hypoxia in the weeks preceding the altitude exposure. These studies, however, involved few subjects, were uncontrolled, and used procedures that interfere with regular daily activities. Furthermore, it was shown that staging ascent for 6 days at 2200 m reduces AMS severity at 4300 m by 44%,[7] but a placebo-controlled, double-blind study found only a minor, clinically irrelevant preventive effect on AMS at the same altitude after 8 days of sleeping 7.5 hours in normobaric hypoxia corresponding to an average altitude of 2600 m.[8]

Exposure to hypoxia during sleep is an attractive possibility of acclimatization because it does not interfere with normal daily activities. It is likely that the short duration of total nights accounts for the mostly negative

The study is registered on ClinicalTrial.gov with the title: "Prevention of Acute Mountain Sickness by Intermittent Hypoxia" (NCT 00559832).

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results in the study of Fulco et al.[8] Therefore, we hypothesized that sleeping 14 instead of 8 consecutive nights in a well-tolerated hypoxic environment at home using nitrogen-enriched air would significantly reduce severity and incidence of AMS most likely by inducing ventilatory acclimatization. This hypothesis was tested during a 20-hour exposure in a normobaric hypoxia room at an ambient P_{O_2} corresponding to 4500 m.

Methods

SUBJECTS AND STUDY DESIGN

We recruited 84 healthy, nonsmoking male subjects who did not take any medication and who had not stayed above 2000 m during the last 2 months before the study. Seventy-six of them were found eligible, agreed to participate, and were randomly assigned to one of the study groups. Three dropped out during the study and 73 finished the study protocol (Figure 1). They had a mean age of 26.5 years (range, 18 to 48 years) and a mean body mass index of 23.6 kg/m^2 (range, 19.1 to 35.2 kg/m^2). History of AMS was not assessable in all but 3 subjects because of lack of appropriate altitude exposures. Subjects were randomly assigned in blocks of 6 to normoxic or hypoxic treatment, which consisted of sleeping for 14 consecutive nights at home under a tent that was ventilated by either normoxic (control group) or hypoxic (treatment group) air. A few days before the

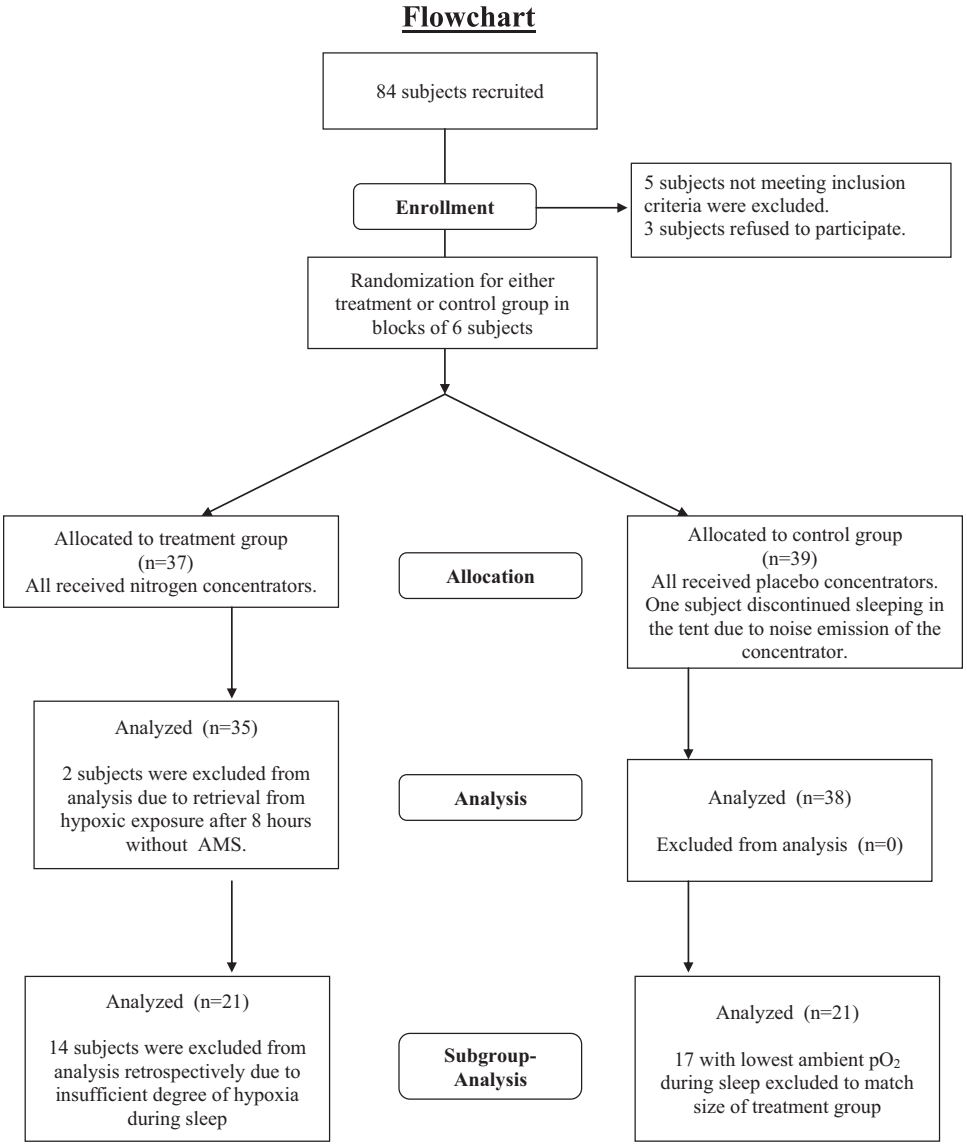

Figure 1. Cohort flow diagram. Flowchart of enrolment and randomization of the subjects and overview of data analysis.