Acute mountain sickness: increased severity during simulated altitude compared with normobaric hypoxia

ROBERT C. ROACH, JACK A. LOEPPKY, AND MILTON V. ICENOGLE
Copenhagen Muscle Research Center, Rigshospitalet, DK 2200 Copenhagen N, Denmark; The Lovelace Institutes, and Department of Cardiology, University of New Mexico, Albuquerque, New Mexico 87108

Roach, Robert C., Jack A. Loepky, and Milton V. Icenogle. Acute mountain sickness: increased severity during simulated altitude compared with normobaric hypoxia. J. Appl. Physiol. 81(5): 1908–1910, 1996.—Acute mountain sickness (AMS) strikes those in the mountains who go too high too fast. Although AMS has been long assumed to be due solely to the hypoxia of high altitude, recent evidence suggests that hypobaria may also make a significant contribution to the pathophysiology of AMS. We studied nine healthy men exposed to simulated altitude, normobaric hypoxia, and normoxic hypobaria in an environmental chamber for 9 h on separate occasions. To simulate altitude, the barometric pressure was lowered to 432 ± 2 (SE) mm Hg (simulated terrestrial altitude 4,564 m). Normobaric hypoxia resulted from adding nitrogen to the chamber (maintained near normobaric conditions) to match the inspired PO2 of the altitude exposure. By lowering the barometric pressure and adding oxygen, we achieved normoxic hypobaria with the same inspired PO2 as in our laboratory at normal pressure. AMS symptom scores (average scores from 6 and 9 h of exposure) were higher during simulated altitude (3.7 ± 0.8) compared with either normobaric hypoxia (2.0 ± 0.8; P < 0.01) or normoxic hypobaria (0.4 ± 0.2; P < 0.01). In conclusion, simulated altitude induces AMS to a greater extent than does either normobaric hypoxia or normoxic hypobaria, although normoxic hypobaria induced some AMS.

METHODS

Nine healthy male subjects completed three different 9-h experiments (simulated altitude, normobaric hypoxia, and normoxic hypobaria) in random order at least 1 wk apart in an environmental chamber. All subjects lived between 1,500 and 1,600 m (barometric pressure 630 ± 10 mm Hg). For the simulated-altitude exposure, the chamber was decompressed to 432 ± 2 mm Hg, resulting in an inspired PO2 (PIO2) of 80 Torr (4,564 m). Normobaric hypoxia was achieved by adding nitrogen to the inspired air in the chamber, resulting in an PO2 similar to that of the altitude exposure. To blind the subjects to the experimental conditions during the hypoxic exposure, the chamber was decompressed 15 mmHg below ambient pressure to mimic the noises and atmosphere created in the simulated-altitude and normoxic hypobaria conditions. For normoxic hypobaria, the chamber was decompressed to 432 ± 2 mm Hg and oxygen was added to achieve an PO2 of 115 Torr, similar to the ambient PO2 in our laboratory. During each experiment, we recorded symptoms of AMS and monitored arterial oxygen saturation (SaO2; Criticare 503) after 3, 6, and 9 h in the environmental chamber. All subjects gave informed consent as approved by the Institutional Review Boards of The Lovelace Institutes and the University of New Mexico School of Medicine.

AMS symptoms. We scored symptoms of AMS using the recently adopted Lake Louise Consensus AMS Scoring System (11), which was derived from existing well-accepted clinical scoring techniques (5, 6). In this scoring system, a constellation of symptoms (headache, nausea, dizziness, fatigue, and sleeplessness) is called AMS only when the victim has been exposed to altitude (or hypoxia) for >2 h. A Lake
Hypoxic exposures (83% from normoxic hypobaria. Normobaric hypoxia, AMS symptoms were not significantly different during normobaric hypoxia or normoxic hypobaria (P = 0.7%) and significantly higher during the normobic hypobaric trial (96 ± 0.3%; P < 0.01).

**RESULTS**

The Lake Louise AMS score (average score for hours 6 and 9) was higher during simulated altitude compared with either normobaric hypoxia or normoxic hypobaria (Fig. 1; P < 0.01); symptom scores during normobaric hypoxia and normoxic hypobaria were not significantly different. During the simulated-altitude exposure, five of nine (56%) subjects were ill with AMS by hour 6 compared with only two of nine (11%) in the normobaric hypoxic exposure, and none with normoxic hypobaria. One additional subject became ill with AMS by hour 9 during the normobaric hypoxic exposure. Symptoms of AMS were not associated with greater arterial oxygen desaturation; SaO2 values were similar in the simulated-altitude (83 ± 1%) and normobaric hypoxic exposures (83 ± 0.7%) and significantly higher during the normoxic hypobaric trial (96 ± 0.3%; P < 0.01).

**DISCUSSION**

Rapid ascent to high altitude often causes a collection of symptoms widely known as AMS. We will discuss the differences in the onset of AMS due to simulated altitude (hypobaric hypoxia) and AMS at sea level caused by normobaric hypoxia. We found that simulated altitude induces AMS to a greater extent than either normobaric hypoxia or normoxic hypobaria, although normobaric hypoxia induced some AMS. The relative lack of AMS when subjects are exposed to normobaric hypoxia has been reported previously. Meehan (10) exposed seven men to 6 h of mild exercise at 12.5% oxygen. None of the subjects developed any symptoms of AMS, although their arterial Po2 averaged 42 ± 3 Torr. In another study using a similar degree of normobaric hypoxia, Swenson et al. (12) exposed 16 subjects to 12% oxygen for 6 h and reported only very mild symptoms of AMS. These studies support our findings that AMS is worse after several hours at altitude than after similar exposure to normobaric hypoxia. How the combination of hypoxia and hypobaria accelerates or exacerbates AMS is not known.

The symptoms of AMS usually begin several hours after ascent to altitude and often are worse after the first night; therefore, it is reasonable to question whether our subjects were at altitude long enough to develop AMS. Our goal was to study the role of normobaric hypoxia and normoxic hypobaria in the onset of AMS in contrast to studying their role in late-stage AMS. Fulminant late-stage AMS may take several days to develop. Supporting our ability to induce AMS within several hours of simulated-altitude exposure is the observation that one of the nine subjects left the chamber after 7 h during the altitude exposure because of severe AMS. On exposure to either normobaric hypoxia or normoxic hypobaria, this subject did not become ill with AMS. Also, our subjects ill with AMS appeared as incapacitated as climbers ill with AMS after 1–2 days at a similar altitude in the mountains.

One possible explanation for the differences in AMS symptom responses between simulated altitude and normobaric hypoxia comes from the observation by Tucker et al. (13) that ventilatory drive was depressed at altitude compared with normobaric hypoxia. They reported a greater increase (63%) in resting ventilation when six subjects were exposed to hypoxia with inspired oxygen fraction = 0.14 compared with when they were exposed to the same P02 at simulated altitude (25%). Although a low ventilatory response to hypoxia is not thought to cause AMS directly (7), the decrease in oxygen transport secondary to depressed ventilation will likely cause AMS symptoms to worsen. Additionally, normoxic hypobaria causes sodium and fluid retention in humans (4) and increased blood-brain barrier permeability in rabbits (3). How hypobaria and hypoxia interact in the pathophysiology of AMS is likely a combination of these factors.

In summary, when we combined normobaric hypoxia and normoxic hypobaria to simulate altitude, the symptoms of AMS were worse than during hypoxia with normal pressure. Further investigations are necessary to explore these findings, with careful physiological measurements of the mechanisms likely to contribute to AMS. Such studies would examine ventilation and fluid balance, as well as factors that contribute to the regulation of these responses. The question of the effect of hypobaria on the etiology of AMS remains open.

The enthusiasm and perseverance of our volunteer subjects made this difficult study possible. Thanks to Dr. P. Scotto for medical assistance and R. Gonzales, D. Maes, and D. Sandoval for technical assistance and R. Gonzales, D. Maes, and D. Sandoval for technical assistance.
assistance. Our thanks are also due to Dr. Charles Houston and Dr. Niels Olsen for constructive criticism of the manuscript. This study was conducted at the Hypobaric Chamber Facility, University of New Mexico, Dr. R. A. Robers, Director.

This project was supported by National Aeronautics and Space Administration Grant NAG 9–375 from the Johnson Space Center, Houston, TX.

Address for reprint requests: R. C. Roach, Copenhagen Muscle Research Center, Rigshospitalet, Section 7652, 20 Tagensvej, DK 2200, Copenhagen N, Denmark.

Received 29 January 1996; accepted in final form 17 June 1996.

REFERENCES