

Researchers identify potential risk factors for severe altitude sickness

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Measuring specific, exercise-related responses can help physicians determine who may be more at risk for severe high altitude illness (SHAI), according to a study conducted by researchers in France. The researchers also found that taking acetazolamide (ACZ), a drug frequently prescribed to prevent altitude illness, can reduce some of the risk factors associated with SHAI.

The findings were published online ahead of the print edition of the American Thoracic Society's *American Journal of Respiratory and Critical Care Medicine*.

The three exercise-related factors identified by the researchers include [oxygen desaturation](#) at exercise (Sae), hypoxic cardiac response at exercise (HCRE) and hypoxic ventilatory response at exercise (HVRE). Sae measures the amount of oxygen that is in the blood during exercise; HCRE measures the heart's response to exercise in a hypoxic, or low oxygen, setting, and HVRE refers to respiratory changes (notably rapid breathing) that occur during exercise in a hypoxic setting. The researchers measured these parameters in controlled, hypoxic conditions in a lab setting that mimicked high-altitude conditions.

"These results suggest that HCRE, HVRE and substantial decreases in Sae are independent [risk factors](#) of SHAI, and that decreases in Sae and HVRE can be used to accurately predict the risk of developing SHAI," said Jean-Paul Richalet, MD, PhD, a professor of physiology at Université Paris 13.

"To date, this is the largest epidemiological study of subjects exposed to high altitude-related illness, who were previously evaluated for their responses to hypoxia," he added.

The researchers collected data from 1,326 men and women who were seen prior to high-altitude excursions, which included at least 3 days above 4,000 meters with overnight sleeping above 3,500 meters. Study participants were asked to complete a questionnaire, providing information about their personal and family medical history, usual physical and mountaineering activity and other factors.

Next, study participants went through a routine hypoxic exercise test, which consisted of four, four-minute phases: rest at normal oxygen levels; rest at hypoxic levels; exercise in hypoxia; and exercise in normal levels of oxygen. During the exercise test, the researchers measured heart rate, breathing and blood oxygen levels.

Following their excursions, study participants were asked to complete a questionnaire to determine if they had experienced any symptoms of high altitude pulmonary edema (HAPE), or swelling of the lung tissue; high altitude cerebral edema (HACE), which refers to swelling of the brain tissue; or severe acute mountain sickness (AMS), which can include a variety of symptoms, including headache, nausea, fatigue and dizziness. Participants were also asked to indicate if they had used ACZ.

Among the 1,326 questionnaire respondents, 318 reported that they had experienced a severe altitude illness during their high-altitude excursion, including 105 who used ACZ and 213 who did not.

Using these results, the researchers were able to identify which factors, reported both before and during the excursions, were associated with SHAI. They were also able to determine the effect of ACZ on the development of SHAI.

"We found that among those who did not use ACZ, factors including young age, female gender, history of migraine, regular physical activity, previous history of severe altitude illness, rapid ascent, HCR_e, substantial changes in Sae and HVRe were significantly associated with SHAI," Dr. Richalet said. "Geographically, the area of Ladakh, India, was associated with a higher risk of SHAI among non-ACZ users."

In those respondents who used ACZ preventively, young age, female gender, history of migraine, regular physical activity, HCR_e, substantial changes in Sae and the Alps were no longer significantly associated with SHAI, Dr. Richalet noted, but Ladakh retained borderline significance. A history of SHAI, rapid ascent and HVRe were still associated with SHAI in those who used ACZ, but the associations were not as strong as those noted in non-ACZ users.

They also found that preventive use of ACZ resulted in a 44 percent reduction in the risk of developing SHAI.

"Although it was not double-blinded and placebo-controlled, this study confirms in a large number of subjects the efficacy of the preventive use of ACZ in high-altitude-related illness," Dr. Richalet said. "These results indicate that preventive use of ACZ may reduce the risk of SHAI in susceptible subjects to the same level as that of non-susceptible subjects."

The study also linked frequent physical activity to an increased risk of SHAI, a result which Dr. Richalet said supports the common belief among mountaineering experts that increasing the body's ability to absorb oxygen during exercise is not a predictor of success in high-altitude expeditions.

"Of course, that does not mean that those who visit high altitudes should stop training before an expedition, but they should realize that intense

aerobic training is not a protective factor against altitude-related disorders," he said.

The study is the first to suggest an independent association between the geographical location of ascent and SHAI.

"When adjusted for all other risk factors, especially rate of ascent, one location – Ladakh – remained associated with a higher risk of SHAI in both ACZ and non-ACZ users," Dr. Richalet said. "No clear explanation, linked to the climate or the difficulty of the terrain, is available, although many informal reports mention the higher risk of this location."

Dr. Richalet said that although previous episodes of SHAI are still the best predictor of new episodes, results of the study support the use of hypoxic [exercise](#) testing, especially in individuals who are planning their first high-altitude excursions.

"Ideally, testing should be aimed both at subjects with no previous experience of high altitude, who therefore lack information about potential risk factors, and those who have experienced severe symptoms in the past, in order to determine if those episodes of SHAI were due to physiological characteristics," he said. "And of course, during a visit to [high altitude](#) regions, it must be emphasized that the best way to avoid severe symptoms is to ascend slowly – less than 400m of altitude difference between two consecutive nights above 3000 meters during the acclimatization period."

Provided by American Thoracic Society

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