Letters to the Editor

Acetazolamide (Diamox) may cause frostbite at extreme altitude

To the Editor:

Acetazolamide is a drug frequently used by climbers to prevent acute mountain sickness and insomnia at extreme altitude. Numerous studies have clearly established the value of acetazolamide in the prevention and treatment of acute mountain sickness and sleep hypoxia, including periodic breathing.^{1,2} Its beneficial effect at high altitude is to diminish the degree of alkalosis with a higher arterial PO₂ and to increase ventilation.³ However, it should be remembered that part of this effect is due to an increase in the urinary excretion of bicarbonate, which will increase the loss of water and could contribute to serious dehydration.

Dehydration at extreme altitude is a common problem due to increased respiratory water loss, which is caused by the cold dry air and increased respiratory rates. A diminished sensation of thirst, apathy, and listlessness to prepare fluid, together with the practical difficulties of melting snow or ice to produce water, result in an inadequate fluid intake. The use of acetazolamide could reinforce the negative water balance because of its diuretic effect.

Dehydration causes a loss of plasma volume. Blood viscosity will increase and slow down peripheral blood flow and oxygen transport to the muscles. Because of the decrease in oxygen transport, performance is reduced and therefore the ability to increase heat production through exercise diminishes as well. In addition, a lower peripheral blood flow and high blood viscosity will raise the chance of local cold injuries because of a lower warming of the peripheral tissue and a higher risk of thrombosis.⁴

Concerning these facts, I made several observations on expeditions to Denali (6193 m), Cho Oyu (8201 m), and Mt Everest (8850 m). My observations indicate a correlation between the intake of acetazolamide and the

appearance of local cold injuries at extreme altitude. Four of 23 climbers suffered from frostbite (grade 2–3/ fingers and toes) on their way from the last high camp to the summit and back. All of them took acetazolamide (Diamox, 250 to 500 mg) only once on the evening before attempting to reach the summit. The climbers who did not use any drugs and the ones who took acetazolamide (2 × 125 to 250 mg daily) on a regular basis for several days had no problems with local cold injuries. It is possible that there is a difference between a single intake of acetazolamide and its long-term use. A single dose, as opposed to long-term use, may provoke greater diuresis and dehydration, resulting in the problem mentioned.

If these observations are confirmed in future controlled studies, high-altitude climbers should be informed about the higher risk of cold injuries when taking acetazolamide for the first time at extreme altitude. To minimize the risk of cold injuries, it seems to be safer to start the prophylactic intake of acetazolamide 2 to 3 days in advance of an attempt to reach the summit, while in an environment where enough fluid is available (eg, base camp).

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References

1. Sutton J, Houston C, Mansell A, et al. Effect of acetazolamide on hypoxemia during sleep at high altitude. *N Engl J Med.* 1979;301:1329–1331.
2. Green M, Keer A, McIntosh I, Prescott R. Acetazolamide in prevention of acute mountain sickness. *Br Med J.* 1981; 283:811–813.
3. Larsen E, Roach R, Schoene R, Hornbein T. Acute mountain sickness and acetazolamide: clinical efficacy and effect on ventilation. *JAMA.* 1982;248:328–332.
4. Ward M, Milledge J, West J. Frostbite and altitude. In: Ward M, Milledge J, West J, eds. *High Altitude Medicine and Physiology.* London, England: Arnold Publishers; 2000:313.