symptoms of acute mountain sickness such as headache.¹²

Our study is among the largest randomised trials of acetazolamide for prophylaxis against acute mountain sickness, and the 250 mg twice daily regimen exhibited a robust and predictable clinical effect similar to previous studies.^{13–14} These results validate acetazolamide therapy as the standard of care for pharmacological prevention of acute mountain sickness, which may be used as an adjunct to behavioural strategies for avoiding altitude sickness.

Our study had several limitations. Firstly, baseline was at a high elevation (4280 m or 4358 m); many participants will have acute mountain sickness below this altitude. Although it may be argued that participants who achieve ascent to this altitude are relatively resistant to acute mountain sickness, our testing conditions were adequate because these individuals were protected from acute mountain sickness using acetazolamide in a manner consistent with previous studies.^{13–14} Secondly, over a fifth of participants were lost to follow up, and the outcome among these people may have affected the significance of our findings. However, participants in all groups were equally likely to drop out, and a reasonable degree of attrition is expected owing to the setting and the low incentive to follow up at the end point.^{13–15} Thirdly, participants were recruited at two villages in close proximity (around 78 m difference in elevation), which may differentially influence the degree of exposure to hypoxia. Lastly, although we studied a diverse population in typical trekking conditions, these results may not be generalisable to other high altitude trekking environments with different ascent rates and different baseline or final elevations.

We thank Pharmaton of Lugano; Deurali-Janta Pharmaceuticals of Kathmandu, Nepal for randomisation of the drugs and packaging; Eric Johnson for clinical support; Anna Donahue, Joel Meyer, and Sabina Yamamura for their translations of study materials into Italian and Spanish, French, and German, respectively; and the trekkers for their participation. See bmj.com for members of the Prevention of High Altitude Illness Trial (PHAIT) Research Group.

Contributors: See bmj.com

Funding: Pharmaton provided financial support for study expenses. Representatives of Pharmaton provided limited statistical support by generating the power calculation.

Competing interests: JHG and JO have been funded by Pharmaton to attend a research symposium. All authors except BB, EWJ, JO, and PSH have received reimbursement for on-site living costs incurred during the implementation period of the study.

Ethical approval: This study was conducted under the auspices of the Himalayan Rescue Association and received ethical approval from the Nepal Health Research Council.

What is already known on this topic

Ginkgo biloba, an experimental prophylactic agent against acute mountain sickness, has shown mixed efficacy in several small randomised controlled trials

Acetazolamide is the standard pharmaceutical prevention of acute mountain sickness

The minimum effective dose of acetazolamide is under debate

What this study adds

This large randomised controlled clinical trial showed that ginkgo was not effective in decreasing the incidence or severity of acute mountain sickness

The efficacy of acetazolamide for preventing headache was decreased when combined with ginkgo

Acetazolamide at 500 mg daily had a robust clinical effect

Acetazolamide could be used as an adjunct to behavioural strategies for avoiding altitude sickness

- Moraga F, Flores A, Zapata J, Ramos P, Madariaga M, Serra J. Ginkgo biloba decreases acute mountain sickness (AMS) at 3700 m. Abstracts from the 13th international hypoxia symposium, Banff, Alberta, Canada, February 19–22, 2003. *High Alt Med Biol* 2003;3:453.
- Le Bars PL, Katz MM, Berman N, Itil TM, Freedman AM, Schatzberg AF, for the North American EGB Study Group. A placebo-controlled, double-blind, randomized trial of an extract of Ginkgo biloba for dementia. *JAMA* 1997;278:1327–32.
- Bailey DM, Davies B. Acute mountain sickness: prophylactic benefits of antioxidant vitamin supplementation at high altitudes. *High Alt Med Biol* 2001;2:21–9.
- Roach RC, Bartsch P, Hackett PH, Oelz O. The Lake Louise AMS Scoring Consensus Committee. The Lake Louise acute mountain sickness scoring system. In: Sutton JR, Coates G, Huston CS, eds. *Hypoxia and molecular medicine: proceedings of the 8th international hypoxia symposium*, 9–13 Feb, 1993; Lake Louise, Alberta, Canada. Burlington, VT: Queen City Printers, 1993: 272–4.
- Bartsch P, Muller A, Hofstetter D, Maggiorini M, Vock P, Oelz O. AMS and HAPE scoring in the Alps. In: Sutton JR, Houston CS, Coates G, eds. *Hypoxia and molecular medicine: proceedings of the 8th international hypoxia symposium*, Lake Louise, Canada. Burlington, VT: Queen City Printers, 1993:265–71.
- Maggiorini M, Muller A, Hofstetter D, Bartsch P, Oelz O. Assessment of acute mountain sickness by different score protocols in the Swiss Alps. *Aviat Space Environ Med* 1998;69:1186–92.
- Chen X, Salwinski S, Lee TJ. Extracts of Ginkgo biloba and ginsenosides exert cerebral vasorelaxation via a nitric oxide pathway. *Clin Exp Pharmacol Physiol* 1997;24:958–9.
- Hackett PH, Rennie D, Levine HD. The incidence, importance, and prophylaxis of acute mountain sickness. *Lancet* 1976;2:1149–54.
- Basnyat B, Gertsch JH, Johnson EW, Castro-Marin F, Inoue Y, Yeh C. Efficacy of low-dose acetazolamide (125 mg BID) for the prophylaxis of acute mountain sickness. *High Alt Med Biol* 2003;4:45–52.
- Murdoch DR. Symptoms of infection and altitude illness among hikers in the Mount Everest region of Nepal. *Aviat Space Environ Med* 1995;66:148–51.

(Accepted 23 January 2004)

doi 10.1136/bmj.38043.501690.7C

Endpiece

On healing

Let no one come to you without leaving better and happier.

Mother Teresa (1910–1997).
The Quotation Page.
[www.quotationspage.com/
quotes/Mother_Teresa/](http://www.quotationspage.com/quotes/Mother_Teresa/)

Neesav Goyal,
Department of Surgical Gastroenterology,
Sir Ganga Ram Hospital, New Delhi

- Roncin JP, Schwartz F, D'Arbigny P. EGB 761 in control of acute mountain sickness and vascular reactivity to cold exposure. *Aviat Space Environ Med* 1996;67:445–52.
- Gertsch JH, Seto TB, Mor J, Onopa J. Ginkgo biloba for the prevention of severe acute mountain sickness starting one day before rapid ascent. *High Alt Med Biol* 2002;2:110.
- Leadbetter GW, Maakestad K, Olson S, Hackett PH. Ginkgo biloba reduces incidence and severity of acute mountain sickness. Abstracts from the 12th international hypoxia symposium, Jasper, Alberta, Canada, March 10–14, 2001. *High Alt Med Biol* 2001;2:110.
- Chow TK, Browne VA, Heileson HL, Wallace DR, Anholm JD. Comparison of Ginkgo biloba versus acetazolamide in the prevention of acute mountain sickness. *Med Sci Sports Exerc* 2002;34:S246.
- Leadbetter GW, Hackett PH, Maakestad K, Tissot-Van Patot M, Olson S, Keyes L, et al. Comparison of Ginkgo biloba, acetazolamide, and placebo for prevention of acute mountain sickness. Abstracts from the 13th international hypoxia symposium, Banff, Alberta, Canada, February 19–22, 2003. *High Alt Med Biol* 2003;3:455.