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Letter to the Editor re: Use of Statins for Prophylaxis Against Acute Mountain Sickness

Dear Editor:

We read with great interest the article titled “Statin use and the development of acute mountain sickness.”³ The authors do present some interesting data regarding the potential benefits of statin therapy for prevention of acute mountain sickness (AMS). We would, however, like to highlight some issues in the article which we feel need clarification. A) The authors have administered the Lake Louise questionnaire for diagnosis of AMS for the first 7 d at high altitude. We presume that the scores presented in the paper are mean scores recorded over these 7 d. It would be nice to know the day-wise break-up of the scores since symptoms of AMS usually subside within 72 h at a particular altitude.⁸ Mean scores, in our opinion, may not be an appropriate method of reporting AMS incidence. B) The time course of onset of the actions of the statins, such as their anti-inflammatory effect, is debatable and there is data to suggest that some of these effects may take weeks to develop.⁴⁻⁷ In this scenario, do the authors envisage a practical use of this drug for the pharmaco-prophylaxis against AMS? C) The role of progesterone in the proposed beneficial effects of statin therapy is not supported by the data presented in the paper. Despite higher progesterone levels in the statin group, the oxygen saturation values are lower than those in the non-statin group. Measurement of end-tidal CO₂ might have provided some interesting data in this regard. D) The incidence of AMS at the given altitude (2835 m; physiological altitude of ~3200 m) appears to be higher than that reported by other studies, even after accounting for a possibly lower barometric pressure at the poles.^{1,2}

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REFERENCES

1. Bärtsch P, Swenson ER. Acute high-altitude illnesses. *N Engl J Med*. 2013; 368:2294–302.
2. Harrison MF, Anderson P, Miller A, O'Malley K, Richert M, et al. Physiological variables associated with the development of acute mountain sickness at the South Pole. *BMJ Open*. 2013; 3(7):e003064.

3. Harrison MF, Johnson BD. Statin use and the development of acute mountain sickness. *Aerosp Med Hum Perform*. 2015; 86(2):97–102.
4. Nissen SE, Tuzcu EM, Schoenhagen P, Crowe T, Sasiela WJ, et al. Statin therapy, LDL cholesterol, C-reactive protein, and coronary artery disease. *N Engl J Med*. 2005; 352(1):29–38.
5. Pearson T, Ballantyne C, Sisk C, Shah A, Veltri E, Maccubbin D. Comparison of effects of ezetimibe/simvastatin versus simvastatin versus atorvastatin in reducing C-reactive protein and low-density lipoprotein cholesterol levels. *Am J Cardiol*. 2007; 99(12):1706–1713.
6. Ridker PM, Rifai N, Pfeffer MA, Sacks F, Braunwald E. Long-term effects of pravastatin on plasma concentration of C-reactive protein. *Circulation*. 1999; 100(3):230–235.
7. van Wissen S, Trip MD, Smilde TJ, de Graaf J, Stalenhoef AF, Kastelein JJ. Differential hs-CRP reduction in patients with familial hypercholesterolemia treated with aggressive or conventional statin therapy. *Atherosclerosis*. 2002; 165(2):361–366.
8. Wagner DR, Teramoto M, Knott JR, Fry JP. Comparison of scoring systems for assessment of acute mountain sickness. *High Alt Med Biol*. 2012; 13(4):245–251.

In Response:

Thank you for the opportunity to engage in further academic discourse related to our work. We offer the following responses:

1. The values presented represent the group means of the individual peak scores for each individual during the first 72 h. The break-up of the peak scores were similar to what has been previously presented from the larger population as a whole,¹ with symptoms peaking within the first 72 h as expected.
2. The motivation for the present analysis stems from our previous report that LDL cholesterol itself may be associated with a decreased incidence of acute mountain sickness (AMS).³ As summarized in our current publication, statins as a drug class have a number of theoretical protective properties, including increased anti-inflammatory activity and decreased development of hypoxia-induced pulmonary hypertension;⁵ statins also represent the most commonly prescribed class of medications for cholesterol-lowering

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DOI: 10.3357/AMHP:4497.2016

treatment.² Recent reports indicate that nearly 30% of adults over the age of 40 in the United States are currently taking a statin² and recent changes in the guidelines would increase the number of U.S. adults who are eligible to take a statin by nearly 13 million.⁶ All of the current participants continued to take their prescribed medications in their usual manner and none of these prescriptions were new. Thus, our proposal would be that individuals already taking a statin and traveling to altitude (either recreationally or professionally) may have previously unreported or unexpected protective factor(s) against the development of AMS. These numbers may make this finding of further interest to those conducting AMS research in the future who should be aware of these potentially confounding factors. We hypothesize that adults with hyperlipidemia who are taking a statin may in fact have two protective factors that may confound high altitude research results if investigators are not aware.^{3,5}

3. Progesterone has been a hormone of interest to AMS and another of our recent publications is available to summarize.⁴ Where it is a respiratory stimulant that would increase ventilation, we agree that the measurement of end-tidal CO₂ may be an interesting variable to measure and monitor in the future.
4. The conditions experienced by our participants provide a number of unique factors that may have influenced the incidence of AMS at increased rates compared to other publications. Our participants were transported in a rapid passive manner from a coastal location at sea level directly to a cold and dry environment at high altitude. Upon arrival, many of our participants engaged in moderate manual labor as a

function of their regular operational duties at the South Pole. Furthermore, none of our participants were able to descend for sleep or other sojourns after their arrival. More importantly, this was strictly controlled for every participant simply by the nature of the deployment and the geography.

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REFERENCES

1. Anderson PJ, Miller AD, O'Malley KA, Ceridon ML, Beck KC, et al. Incidence and symptoms of high altitude illness in South Pole workers: Antarctic Study of Altitude Physiology (ASAP). *Clin Med Insights Circ Respir Pulm Med.* 2011; 5:27–35.
2. Gu Q, Paulose-Ram R, Burt VL, Kit BK. Prescription cholesterol-lowering medication use in adults aged 40 and over: United States, 2003-2012. *NCHS Data Brief.* 2014; 2014(177):1–8.
3. Harrison MF, Anderson P, Miller A, O'Malley K, Richert M, et al. Physiological variables associated with the development of acute mountain sickness at the South Pole. *BMJ Open.* 2013; 3(7):e003064.
4. Harrison MF, Anderson P, Miller A, O'Malley K, Richert M, et al. Oral contraceptive use and acute mountain sickness in South Pole workers. *Aviat Space Environ Med.* 2013; 84(11):1166–1171.
5. Harrison MF, Johnson BD. Statin use and development of acute mountain sickness. *Aerosp Med Hum Perform.* 2015; 86(2):97–102.
6. Pencina MJ, Navar-Boggan AM, D'Agostino RB Sr, Williams K, Neely B, et al. Application of new cholesterol guidelines to a population based sample. *N Engl J Med.* 2014; 370(15):1422–1431.