

Ibuprofen Prevents Altitude Illness: A Randomized Controlled Trial for Prevention of Altitude Illness with Nonsteroidal Anti-Inflammatories

BACKGROUND:

- Acute mountain sickness (AMS) can be a very severe and debilitating disease that is common with ascension above 8,250ft and typically occurs within 6 to 12 hours after being at high altitudes.
- While gradual ascent can be an effective means for reducing acute mountain sickness, this approach is not always possible.
- Prescription medications, acetazolamide and dexamethasone, are currently used to prevent and/or treat AMS.
- Inflammatory processes may play a part in the pathophysiology of AMS, which suggests that nonsteroidal anti-inflammatories may be efficacious in AMS prevention and/or treatment.

OBJECTIVE

- Evaluating whether ibuprofen was superior for preventing the incidence and decreasing the severity of AMS compared to placebo

METHODS

- **Design:** Randomized, double blind, parallel, placebo-controlled trial
- **Inclusion criteria:** Healthy, reside at low altitude (<4100ft), and be able to complete moderately strenuous hike at high altitude
- **Exclusion criteria:** Less than 18 years or older than 65 years; pregnant or thought to be pregnant; lived or slept at altitudes greater than 4100ft in the past week; received diuretics, steroids, or acetazolamide or nonsteroidal anti-inflammatory drugs or aspirin; symptoms consistent with acute mountain sickness at baseline; or any history of brain tumor, elevated intracranial pressure, severe asthma, gastrointestinal bleeding, and high altitude cerebral or pulmonary edema
- **Primary outcome measure:** Incidence and severity of acute mountain sickness as calculated on the Lake Louise Questionnaire (LLQ) score
- **Secondary outcome measures:** Headache severity by visual analog scale and peripheral oxygen saturation by fingertip pulse oximetry
- 86 participants were randomized to receive either visually identical ibuprofen 600mg (44 participants) or placebo (42 participants). Participants received 4 doses of the respective treatment during the 24 hour period in which the ascent/hike occurred.
- To achieve 80% power ($\alpha=0.05$), assuming 45% acute mountain sickness incidence, 40 participants were required to detect a significant difference, defined as a reduction in acute mountain sickness incidence by 20%; and 73 participants to detect a clinically significant Lake Louise Questionnaire change of greater than 2 points in the intervention group
- Data handling method was intent-to-treat

RESULTS

- No participant required evacuation; 8 participants did require symptomatic treatment but their high altitude measurements were recorded prior to treatment
- **Primary outcome measure:** Significantly fewer participants randomized to ibuprofen developed acute mountain sickness compared with participants receiving placebo (NNT=3.9; 95% CI: 2-33) (OR 0.3; 95% CI: 0.1-0.8). Although a decrease in severity of acute mountain sickness symptoms was found in the ibuprofen group, statistical significance was not met (OR 0.9; 95% CI: 0.3-3.0).
- **Secondary outcome measures:** There were no statistically significant differences between treatment and control groups for headache severity by visual analog scale (8.7 % difference in

proportions; 95% CI: -0.7-18) or peripheral oxygen saturation change (1.6% difference in proportions; 95% CI: -0.4-3.7).

- **Author's conclusion:** Compared with placebo, ibuprofen was effective in reducing the incidence of acute mountain sickness.

STRENGTHS

- Randomized, double blind trial
- Ibuprofen is an inexpensive and widely available treatment

LIMITATIONS

- Assessment of AMS is subjective
- Exclusion criteria did not account for participants who have a history of living at or being exposed to high elevations
- Only one dose of ibuprofen was studied
- Power was not sufficient to find differences in high altitude headache by visual analog scale
- Symptoms of dehydration or extreme exertion can present the same as symptoms of AMS
- Factors such as ambient temperature, wind speed, rate of ascent, liquid and caloric intake of the participants were not controlled and could play a role in the presentation of AMS symptoms
- Lack of consensus specifying how large a change in the LLQ score grants meaningful benefit

CONCLUSION

- Use of ibuprofen may be an effective treatment option for reducing the incidence of acute mountain sickness. Ibuprofen is a cheap and easily accessible alternative compared to the current prescription treatments for AMS. However, in this study, ibuprofen was only 26% more efficacious than placebo and symptom prevalence was not statistically significantly decreased compared to placebo. Further studies that take into account the high elevation history and physical abilities of the participants as well as control the liquid/caloric intake and rate of ascension during the study could provide a stronger foundation for the use of ibuprofen in acute mountain sickness.
- Further study areas:
 - Higher doses of ibuprofen
 - Comparison of ibuprofen to the known options of acetazolamide or dexamethasone for AMS
 - Use of ibuprofen after symptom presentation
 - The pathophysiology of AMS

Lipman G, Kanaan N, Holck P, Constance B, Gertsch J. Ibuprofen prevents altitude illness: a randomized controlled trial for prevention of altitude illness with nonsteroidal anti-inflammatories. *Ann Emerg Med.* 22 March 2012.

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