Acetazolamide or dexamethasone for prevention of acute mountain sickness: a meta-analysis

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Authors' objectives
To evaluate the pharmacologic prophylaxis of acute mountain sickness (AMS) with dexamethasone or acetazolamide.

Searching
A professional librarian searched nineteen databases including MEDLINE (from 1966 to 1990), BIOSIS Previews (from 1969 to 1990) and EMBASE (from 1974 to 1990) using the keywords 'altitude', 'mountain', 'acetazolamide' and 'dexamethasone'. The reference lists of the retrieved articles, reports from personal files, bibliographies of books, and articles related to altitude, were also searched for additional studies. In addition, the primary author of each eligible report, and key investigators in the field, were contacted to identify other eligible reports. Only articles written in the English language were considered.

Study selection
Study designs of evaluations included in the review
The design of the included studies was not explicitly stated, but all studies had to have a placebo control group.

Specific interventions included in the review
Dexamethasone and acetazolamide, compared with placebo controls. The doses of dexamethasone ranged from 0.25 to 4 mg; the doses of acetazolamide were either 250 or 500 mg.

Participants included in the review
The participants were humans, both in the field and hypobaric chambers.

Outcomes assessed in the review
The primary outcomes were the percentage of patients with AMS, and the mean score on AMS measures such as the General High Altitude Questionnaire (GHAQ) and the Environmental Symptoms Questionnaire (ESQ). A secondary measure of interest was the percentage of patients with specific symptoms associated with AMS (e.g. headache, nausea, insomnia, and shortness of breath).

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
Validity was assessed on the basis of the following nine criteria: random assignment of the patients; adequate description of the method of randomisation; the adequacy of protection against bias; investigators blinded to the treatment group; participants blinded to the treatment group; whether the study inclusion and exclusion criteria were well defined; whether the number of excluded patients was reported; whether the regimen was fully described for each group; and appropriate statistical analysis.

Each criteria was scored according to whether it had been addressed completely (2 points), partially (1 point) or not at all (0 points). The possible scores ranged from 0 to 18. Four reviewers independently assessed each study, blinded to study author and journal name. Variation among the reviewers was discussed and arbitrated by a fifth committee member.

Data extraction
The data were extracted independently by four reviewers and any discrepancies were resolved through discussion. For
each study, only the methods, results and discussion section were made available to the reviewers; all details which might bias the reader were removed. An effect size (ES) with 95% confidence intervals (CIs) was calculated for each study.

Methods of synthesis
How were the studies combined?
The frequency-weighted ES, based on sample size, was determined for each individual study. This was then used to calculate the mean weighted ES and its 95% confidence intervals (CIs).

How were differences between studies investigated?
The chi-squared test for homogeneity (Q test) was employed to investigate differences between the studies.

Results of the review
Twenty studies (820 patients) were included.

The quality scores of the included studies ranged from 2.75 to 17.0 (mean 11.5, standard deviation 3.58).

A negative ES indicated that the prophylaxis regimen conferred a protective effect.

When pooling all the drug results, the ES was -0.59 (95% CI: -0.41, -0.77; Q=61.6, p<0.001).

When pooling only the studies of acetazolamide versus placebo, the ES was -0.61 (95% CI: -0.29, -0.93; Q=11.3, p>0.05).

When pooling only the studies of dexamethasone versus placebo, the ES was -0.32 (95% CI: +0.38, -1.02; Q=4.2, p>0.05).

When pooling all of the reported symptoms, the ES was -0.38 (95% CI: -0.23, -0.53; Q=83.3, p>0.05).

Prophylaxis was significantly more effective when conducted in hypobaric chambers, compared with field studies. Acetazolamide was more effective than dexamethasone in the field studies.

Authors' conclusions
Pharmacologic prophylaxis with acetazolamide or dexamethasone was effective against AMS. Acetazolamide appeared to be more effective, but inconsistencies in dexamethasone dosing, environmental conditions, and the rate of ascent, confound interpretation of the results.

CRD commentary
Overall, this was a well reported systematic review with a comprehensive literature search. However, there were some important omissions from the methods section: the type of study design and the method used to select the studies for inclusion were unclear.

The conclusion that dexamethasone is an effective treatment does not appear to be supported by the analysis, which shows that the 95% CI crosses the line of no effect; this indicates that there is no statistically-significant benefit from treatment. The review would therefore appear to indicate, rather than prove, that treatment with acetazolamide is preferential to dexamethasone.

Implications of the review for practice and research
Research: The author identified two areas for further research.

1. A unified and consistent approach to the definition and classification of AMS is required.
2. The influence of study design and other conditions (e.g. sample size, rate of ascent and outcome measure) on the estimate of the effectiveness of drug prophylaxis should be examined.

**Bibliographic details**

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.