Vitamin C and common cold incidence: a review of studies with subjects under heavy physical stress

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Authors' objectives
To assess the evidence from intervention studies as to whether supplementary vitamin C affects the incidence of the common cold in individuals under heavy physical stress.

Searching
A search from a previous study (see Other Publications of Related Interest) was supplemented by searching MEDLINE and SciSearch for studies published since 1988.

Study selection
Study designs of evaluations included in the review
Randomised placebo-controlled double-blind trials were included.

Specific interventions included in the review
Vitamin C supplements (0.6 to 2.0 g/day), compared with placebo.

Participants included in the review
People under heavy physical stress; more specifically, school children at a skiing camp in the Swiss Alps, military troops training in Northern Canada and in South Carolina, and participants in a 90 km running race.

Outcomes assessed in the review
The incidence of the common cold and, in one study, the incidence of pneumonia.

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

Assessment of study quality
The author does not state that they assessed validity.

Data extraction
The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. However, the proportion of participants catching a common cold infection during the study was calculated for both the vitamin C and placebo groups from the published results. The 95% confidence interval (CI) for the rate ratio (RR) found in each study was calculated using the normal distribution approximation of the binomial distribution.

Methods of synthesis
How were the studies combined?
For three of the studies, the pooled RR and the 95% CI were derived by averaging the individual logarithm values, using the inverses of the variances as the weights. The formulae were given in the paper. The p-value (1-tailed) corresponding to the pooled estimate was derived from the standard normal deviate. Dichotomous data were analysed using Fisher’s exact test.

Data from the fourth, much larger, study was not pooled on the grounds that this study was a few weeks longer than the other three, and vitamin C supplementation did not begin until 3 weeks into the study.
How were differences between studies investigated?
Differences between the studies were not investigated formally. However, with regards to the type of stress, the first three studies were regarded as homogeneous whilst the fourth was treated differently.

Results of the review
Four randomised placebo-controlled double-blind trials were included. There was a total of 475 participants in three of the studies, and at least 1,200 participants in the fourth.

When the three smaller studies were pooled, this gave a pooled RR of common cold infections of 0.50 (95% CI: 0.35, 0.69) in favour of vitamin C groups. The results of a further study, which was originally excluded on the grounds of having no placebo control, were reported post-hoc as having a similar result.

The fourth and largest study, excluded post-hoc, showed no difference in common cold incidence between the vitamin C and placebo groups. However, it did show a significant decrease (p=0.04) in the incidence of pneumonia in the vitamin C group, compared with the placebo group.

Authors’ conclusions
The results of three studies suggested that vitamin C supplementation may be beneficial for some participants who are undergoing heavy exercise and who have problems with frequent upper respiratory infections.

CRD commentary
The review met the criteria to be included as a systematic review since a literature search was carried out to address a predefined question (see Other Publications of Related Interest), and the results of the search were reported, albeit rather incompletely. However, validity was not assessed and no a priori sensitivity analyses were defined. In addition, heterogeneity between the studies was not formally assessed, which leads to problems when pooling the data. There would be no justification for excluding the largest retrieved study from the pooled analysis without a formal heterogeneity assessment, unless justification (from previous literature) had been given a priori for the exclusion of such data in a subsequent sensitivity analysis or subgroup analysis. However, no such analyses were defined a priori. The use of such analyses post-hoc can lead to the introduction of bias. There is no justification for reporting the results from an excluded study to add weight to the result from the pooled analysis. The conclusions drawn from this review are not particularly robust; the inclusion of results from the fourth study in the pooled analysis would give an overall result of no significant difference in common cold incidence between the vitamin C and the placebo groups. Hence, the conclusions should be treated with caution.

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