Echinacea, Vitamin C, the Common Cold, and Blinding

Published as:
Hemilä H. Echinacea, vitamin C, the common cold, and blinding [Letter]
Clinical Infectious Diseases 2005;41:762-763
http://dx.doi.org/10.1086/432629

Harri Hemilä
Department of Public Health
University of Helsinki,
Helsinki, Finland
harri.hemila@helsinki.fi
http://www.ltdk.helsinki.fi/users/hemila/

Comments on:
Caruso TJ, Gwaltney JM (2005)
Treatment of the common cold with echinacea: a structured review
Clin Infect Dis 40: 807-810
http://dx.doi.org/10.1086/428061

Sir—Caruso and Gwaltney [1] reviewed the effect of echinacea treatment on the common cold, identifying 9 placebo-controlled trials. A quality score was calculated for each trial, and the main focus was put on 2 trials that received maximum scores and reported negative results. However, the use of quality scores in literature reviews has been strongly discouraged. For example, Greenland [2] commented that quality scoring “introduces an unnecessary and somewhat arbitrary subjective element into the analysis via the scoring scheme. Quality scoring can and should be replaced by direct categorical and regression analyses of the impact of each quality item. Such item-specific analyses let the data, rather than the investigator, indicate the importance of each item in determining the estimated effect” (p. 672). Also, the Cochrane Handbook [3] states that “reviewers should avoid the use of quality scores and undue reliance on detailed quality assessments. It is not supported by empirical evidence, it can be time-consuming, and it is potentially misleading” (p. 66).

Six echinacea trials found positive results, but none of them provided proof that blinding was confirmed, which led Caruso and Gwaltney [1] to propose that the benefit in these 6 trials might be explained by the placebo effect. To support this suggestion, they referred to an old review on vitamin C and the common cold [4] by commenting that the author, Chalmers, “described a study that initially showed a positive therapeutic effect of capsules containing vitamin C on the common cold. However, blinding was not maintained, because many subjects bit through the capsules to taste the contents, which they correctly identified. When data from the unblinded subjects were discarded, ‘there were no differences in the durations of colds’ [p. 534]” [1, p. 810].

The Chalmers review [4] was shown to be erroneous a decade ago; it has data inconsistent with the original study publications, errors in calculations, and other problems [5, 6]. The particular trial referred to by Chalmers [4] was undertaken by Karlowski et al. [7]. It was initiated as a double-blind, placebo-controlled trial, but, after the trial, several participants correctly guessed their treatment, and this led Karlowski to carry out a subgroup analysis according to “correct” and “incorrect” guessing. In this analysis, the benefit of vitamin C was restricted to participants with “correct” guesses. Thus Karlowski concluded that “the effects demonstrated might be explained equally well by a break in the double blind” [7, p. 1038]. Because of such spectacular findings in this subgroup analysis, the
Karlowski trial has often been cited as an example of the placebo effect in action. However, the subgroup analysis excluded 105 episodes of common cold (42% of all episodes of cold), even though the 2 subgroups were presented as if they were complementary [8]. There are numerous additional problems with Karlowski’s placebo effect explanation, and, consequently, it is not a valid interpretation to the study results [8]. Furthermore, a recent meta-analysis of trials comparing placebo and no-treatment groups with respect to diverse medical topics found no or minimal evidence for the placebo effect, which indicates that it is not as large as commonly assumed [9].

A recent Cochrane Review [10] of placebo-controlled trials found that regular vitamin C supplementation reduced the duration of common cold infection in adults by 8% (95% CI, 3%–13%), and in children by 13.5% (95% CI, 5%–21%). Furthermore, although vitamin C showed no effect on the incidence of common cold in the general population (relative risk, 0.98; 95% CI, 0.95–1.00), it reduced the incidence of colds in 6 trials with participants who were under heavy acute physical and/or cold stress (relative risk, 0.50; 95% CI, 0.38–0.66). Even though more studies are needed to evaluate the practical importance of vitamin C supplementation on colds, the Chalmers review [4] and the Karlowski trial [7] should not be cited as evidence that the effects of vitamin C are explained by the placebo effect. Also, the Karlowski trial should not be used as a basis to propose the placebo effect explanation for other potential treatments for the common cold [1]. Echinacea may or may not be practically useful, but the conclusions of its usefulness should not be based on a methodologically unsatisfactory analysis, and mere speculations about placebo effect in placebo-controlled trials.

References
see also: http://www.ltdk.helsinki.fi/users/hemila/reviews/chalmers/
http://helda.helsinki.fi/handle/10250/7979 Links to references are added
http://helda.helsinki.fi/handle/10250/8082 Links to references are added
see also: http://www.ltdk.helsinki.fi/users/hemila/karlowski/