

## **The effect of vitamin C on the common cold**

Letter to the editor

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### **Comments on**

Mathes A, Bellanger R. Herbs and Other Dietary Supplements: Current Regulations and Recommendations for Use to Maintain Health in the Management of the Common Cold or Other Related Infectious Respiratory Illnesses.

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### **Manuscript version of the paper**

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Proponents of evidence-based medicine (EBM) emphasize that conclusions about medical interventions should be based on controlled trials with clinically relevant outcomes, so that the greatest weight should be given to the systematic reviews of the trials. One of the most comprehensive EBM databases is the Cochrane Library, which contains thousands of systematic reviews on medical interventions.

The Cochrane review on vitamin C and the common cold analyzed 29 trial comparisons on the preventive effects of vitamin C, 29 comparisons on the effect of regular vitamin C on common cold duration and severity, and 7 comparisons on the therapeutic effect of vitamin C [1]. The review concludes: “Implications for practice: The prophylaxis trials found a reduction in common cold duration of 8% in adults and 13% in children. ... So far, therapeutic supplementation has not been shown to be effective. Nevertheless, given the consistent effect of vitamin C on duration and severity in the regular supplementation studies, and the low cost and safety, it may be worthwhile for common cold patients to test on an individual basis whether therapeutic vitamin C is beneficial for them.”

In their review discussing the effect of dietary supplements on the common cold, Mathes and Bellanger refer to 9 papers and state that “various trials have shown no difference in either duration, or severity of symptoms, when vitamin C was compared to placebo. In addition, numerous trials have shown no difference regarding the most commonly studied endpoint: frequency of symptoms” [2]. Since the conclusions of the Cochrane review diverge considerably from the conclusions of Mathes and Bellanger, it is useful to look at the findings of the studies they refer to. Some of the findings are inconsistent with their statements.

Pitt and Costrini found statistically significant ( $P[2\text{-tail}]=0.024$ ), yet small reduction in common cold severity among US Marines who were administered 2 g/day vitamin C [3,4]. Van Straten and Joslin reported a highly significant reduction in the number of participants who had 2 colds during their trial (2/84 vs. 16/84;  $P=0.0004$ ) by 1 g/day vitamin C [4,5]. Ludvigsson et al. found a 14% reduction ( $P = 0.016$ ) in the duration of ‘absence from school because of upper respiratory tract infection’ in their main trial, and a 39% reduction ( $P = 0.004$ ) in the duration of ‘upper respiratory tract infection’ in their smaller trial when schoolchildren were administered 1 g/day of vitamin C [4,6].

Terrence Anderson carried out three vitamin C trials in Canada in the 1970s. In their first trial, Anderson et al. administered 1 g/day vitamin C regularly, and 3 g/day extra when a participant caught the common cold. They found a 30% ( $P = 0.01$ ) decrease in the number of days confined indoors in the vitamin C group [7]. Furthermore, staying free of illness during the study period is also a relevant measure of effect and Anderson et al. found 8 percentage point increase in the proportion of participants who were ‘not ill during the trial’, ‘not confined to the house’, and ‘not off work’ in the vitamin C group ( $P=0.01$ ) [4,7]. In their second trial, Anderson et al. were ambitious and they had 2 placebo arms and 6 vitamin C arms with different dosages [8]. There were technical problems such as the mislabeling of bottles of tablets [4,8], and therefore no firm conclusions can be drawn from the second trial. Nevertheless, in the vitamin C arm which was administered 8 g of vitamin C only on the first day, 6.6 percentage points ( $P=0.046$ ) more participants had colds lasting for only 1 day, compared with the arm administered 4 g of vitamin C, which suggests dose

dependency [4]. In their third trial, Anderson et al. administered 1-1.5 g/day of vitamin C therapeutically so that supplementation was initiated when a person caught a cold. They found a reduction in 'days spent indoors per subject' by 25% (P = 0.048) among the vitamin C participants [4,9].

These 7 controlled trials described above do not support Mathes and Bellanger's statements although the studies are provided as references. Furthermore, Mathes and Bellanger do not describe their rationalization to select the 9 references out of several dozens. In systematic reviews it is important to describe the selection criteria, in order to prevent bias caused by selecting studies that are consistent with the reviewers' preconceptions. If Mathes and Bellanger were not ready to carry out their own systematic review, they should have taken a look at the Cochrane review which used explicit selection criteria and included all studies fulfilling those criteria.

The main findings of the Cochrane review are as follows. In 5 trials with participants under heavy acute physical stress (3 with marathon runners) vitamin C reduced the incidence of colds by 52% (95% CI: 36% to 65%), but there is no evidence that vitamin C prevents colds in the general population. In regular supplementation trials,  $\geq 0.2$  g/day of vitamin C shortened colds in adults by 8% (P=0.0002) and in children by 13% (P=0.0003)[1]. It is possible that the same dose causes greater effect on children and that there is dose-dependency so that higher doses lead to a greater benefit [10]. When the child trials using less than 1 g/day of vitamin C were removed, the pooled estimate of benefit was increased to a 17% (95% CI: 8% to 26%) reduction in the duration of colds of children [1]. Few therapeutic trials have been carried out and none of them with children. Therefore, no firm conclusions about therapeutic vitamin C can be drawn.

Given that dozens of trials on vitamin C and the common cold have been carried out with different populations and different dosages, etc., the interpretation of published studies is not quite simple. For example, there is some evidence indicating that vitamin C may have different effect on males and females [11,12]. The most recent trial on vitamin C and the common cold studied the effect of regular 1 g/day vitamin C on adolescent swimmers. There was significant difference between males and females, so that vitamin C had no effect on females, but shortened the duration of colds in male swimmers by 47% (95% CI: 14% to 80%) [13].

Although there is strong evidence that regular vitamin C shortens the duration of colds, we do not know what is the effect of therapeutic vitamin C, which means starting administration after the onset of symptoms. Also, it is possible that there are variations in the vitamin C effect depending, for example, on dietary vitamin C intake and contact with young children [4,7,9], and sex [11-13]. Although there are a number of important questions remaining, it may be worthwhile for common cold patients to test on an individual basis whether therapeutic vitamin C is beneficial for them.

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