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1471-4906/$ - see front matter
doi:10.1016/j.it.2003.09.010

Letters

Vitamin C, respiratory infections and the immune system

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Almost a century ago, several authors suggested that vitamin C might affect respiratory infections. However, not much attention was paid to this topic until 1970, when Nobel laureate Linus Pauling wrote the bestseller 'Vitamin C and the Common Cold.' His claim that gram-dose vitamin C supplementation would prevent and alleviate colds was not based on any studies of his own but on previously published trials. One result of his activity was that a series of placebo-controlled trials was carried out to determine whether large doses of vitamin C would affect colds [1–3]. The new trials found that ≥ 1 g day^{-1} vitamin C supplementation had no consistent effect on common cold incidence (Figure 1). Consequently, these trials did not support the suggestion that regular vitamin C ingestion would increase the resistance of the general Western population to colds. However, some evidence indicated that vitamin C could have moderate preventive effects in restricted groups, such as subjects with particularly low dietary intake or those suffering from acute physical stress [1,3].

However, the placebo-controlled trials found that the duration and symptoms of colds were reduced by ≥ 1 g day^{-1} vitamin C, although, the quantitative results diverge sharply (Figure 1). In most of the trials, the decrease in morbidity was between 5% and 35%, with a mean of 23%. Evidently, the main question should not be to decide whether a decrease of 23% is clinically important but to identify the factors that could affect the magnitude of the benefit. For example, even in the gram-dose region, there is a trend for trials with 2–4 g day^{-1} doses to show greater benefit when compared to trials using 1 g day^{-1} [1,2]. All trials summed up in Figure 1 used regular daily vitamin C supplementation. If the main goal is to alleviate the symptoms, it appears more rational to administer vitamin C therapeutically, starting immediately after the early symptoms; however, few such trials have been carried out.

Vitamin C could also affect lower respiratory tract infections. Several early reports suggested that vitamin C might hasten convalescence from pneumonia, a hypothesis that was supported by one placebo-controlled trial [3]. Three controlled trials with human subjects reported a significantly lower incidence of pneumonia in vitamin C supplemented groups [3,4], suggesting that under certain conditions, vitamin C might affect susceptibility to pneumonia. Studies with guinea pigs and other animals have also found that vitamin C modifies susceptibility to various viral and bacterial infections, including pneumococcal infections [3,4]. Recently, a new coronavirus was identified as the cause of the severe acute respiratory syndrome (SARS), and two reports of vitamin C studies are of particular interest in this regard. Vitamin C increased

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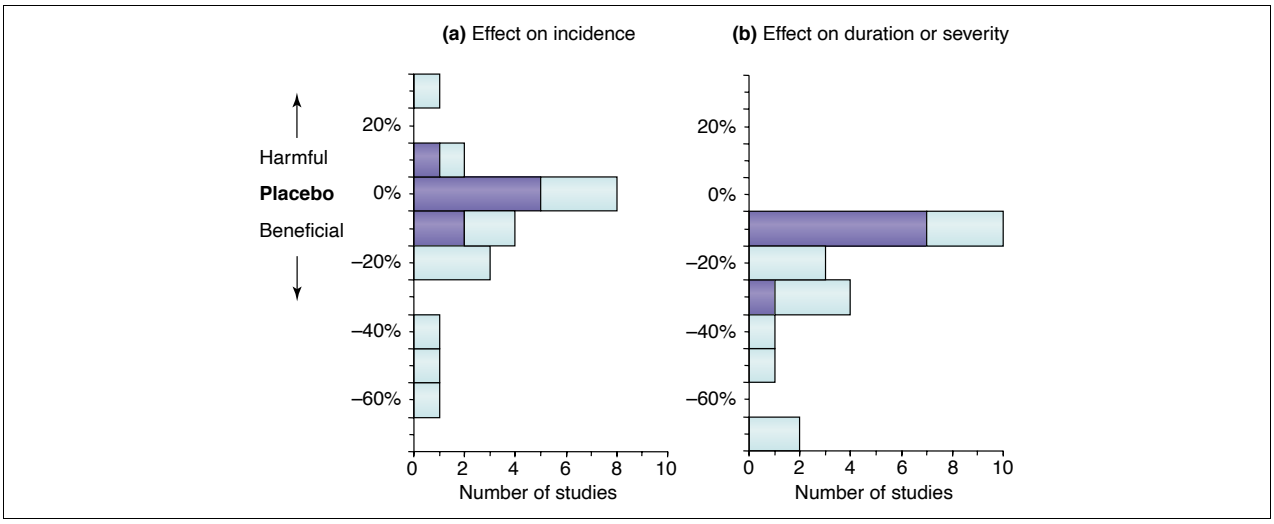

Figure 1. Vitamin C supplementation does not affect the incidence of the common cold **(a)** but decreases its duration and alleviates its symptoms **(b)**. The vertical scale shows the relative effect of vitamin C compared to the placebo. The horizontal bar indicates the number of trials reporting the effect falling within the vertical limits of the bar. Black bars indicate trials with ≥400 subjects. All trials used 1–4 g day^{-1} of vitamin C, all were placebo-controlled, and all except one were double-blind. For details and original references, see Ref. [1], from which the figure is reproduced with permission.

the resistance of chick embryo tracheal organ cultures [5] and broiler chicks [6] to infection caused by an avian coronavirus.

The mechanisms whereby vitamin C affects the immune system are poorly understood, although there are several reports indicating that it might affect, for example, functions of phagocytes, proliferation of T lymphocytes, production of interferon and gene expression of monocyte adhesion molecules [3,7–10]. Nevertheless, in the intensive search for molecules participating in the defence against viruses and bacteria, vitamin C has not been particularly interesting because it is not specifically and firmly linked to any single immunological mechanism. Still, it is possible that, as a major physiological antioxidant, vitamin C has nonspecific protective effects on diverse parts of the immune system [1,7]. During infections, phagocytes generate a set of oxidizing agents that have antimicrobial effects but if released into the extracellular medium, the oxidants can be harmful to the host [1,11]. The oxidizing agents seem to have an important role in the pathogenesis of certain viral infections [11]. A number of studies have found that vitamin C levels are decreased in plasma, leucocytes and in urine during various infections, including the common cold and pneumonia [1,3]. These findings support the notion that oxidants generated during infections react with vitamin C, and the vitamin could thereby protect the host against the potential harm done by the oxidants.

Vitamin C is an essential nutrient, which complicates the interpretation and generalization of study results because the 'control' groups always continue to receive vitamin C in their diet. The control group levels have varied greatly in different studies and there is some evidence that the benefits of supplementation might be greater for subjects with low dietary vitamin C intakes [2–4]. The essential nutrient character of vitamin C makes the question of its effects on the immune system a particularly interesting issue, even though the effects on the immune system seem to be nonspecific.

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1471-4906/$ - see front matter
doi:10.1016/j.it.2003.09.004