CHAPTER 4

VITAMIN C AND THE COMMON COLD; REVIEW OF A MEGADOSE OF LITERATURE*

Jos Kleijnen, Gerben ter Riet, Paul Knipschild

FOOD SUPPLEMENTS AND THEIR EFFICACY

PROEFSCHRIFT

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Joseph Maria Pieter Kleijnen

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Introduction

Nowadays, many people use extra vitamins, minerals and other products which may cause health improvement. There is a good deal of discussion about which benefits to expect. The question is whether the recommended dietary allowances, which are aimed at the prevention of deficiency symptoms, are also the dosages necessary for optimal health. One of the most extensively investigated claims is the influence of megadosages of vitamin C on the common cold. Despite many publications during the years past, discussions about this topic are still ongoing.
In this article we describe how we retrieved the publications on vitamin C and the common cold, and how we made a selection of those with the highest quality using a criteria list. The results of these studies were used for the assessment of the influence of vitamin C supplementation on the common cold.

Methods

Retrieval of the literature
Many review articles on vitamin C and the common cold only describe a limited number of trials.[1-7] There are, however, many other articles on vitamin C and the common cold which have been published, especially in journals and languages which are not readily accessible. We identified 61 trials by checking of the Index Medicus (1970-1987), and checking of references in all articles found.[8-72] We listed all trials in the reference list. Probably, this is not a complete list of all performed trials. We checked this approach by means of a MEDLINE-computersearch (1963-1988). No additional articles were found using the keywords "ascorbic acid", "common cold", and "respiratory tract infections". Publications were included in this review if a group treated with vitamin C only was compared with a control group.

Selection of the publications
We wanted to answer the following questions:
- Is there an influence of vitamin C in the prevention of colds?
- Is there an influence of vitamin C in the treatment of colds?
- Which dosage is effective?
- In which people are any effects found?

We made a list of criteria of good methodology, because reliable results can only be obtained from trials with sound methodology. Publications were selected for a detailed review using the following criteria list. We think that randomization and blinding are most important:
- Randomized trials could earn 3 points if the method of randomization was described; if the randomization was not described, 2 points were given; and alternate allocations were given 1 point.
- Double-blind trials earned 3 points, and single-blind trials 1 point.
- Furthermore, 1 point each was given if blinding had been checked, if the placebo had been described, if there were at least 100 participants per group, if drop-outs had been described (and if there were no more than 25% drop-outs), if the intervention lasted at least 3 months (for prophylaxis) and if there was a therapeutical follow-up of at least one week. Finally, a point was given if both the endpoints had been described and there was a differentiation between subsequent episodes of symptoms.

In this way, maximally 12 points could be earned. There were 11 trials which earned at least 8 points, and these trials will be described in detail in this review. The trials of Wilson et al.,[44-46] Tyrell et al.[63] and McLean Baird et al.[64] earned 7 points, as well as a

second trial of Ludvigsson et al., which was published in the same article as the trial presented in the table.[61] The other trials scored 6 points or fewer. In order to give an example of the trials involved, we discuss aspects of the trial by Pitt and Costrini in some detail. Together with the trial of Coulehan et al.[53] this trial earned 10 points, which was the highest score.

In the double-blind trial of Pitt and Costrini 862 recruits were treated during an 8 week period. The success of the randomization procedure was checked by comparison of 7 characteristics which were measured at baseline. The were no relevant differences between the intervention and placebo groups. Vitamin C was administered in a dosage of 2.0g/day. The placebo tablets were formulated from citric acid and were indistinguishable in appearance and taste from the vitamin C tablets. The criterions necessary for a cold to be included as an episode were (1) the presence of either runny or stuffy nose, sore throat, or dry or productive cough, (2) at least two days of symptoms, and (3) at least three symptom-free days between episodes. Eight different symptoms were followed-up by means of weekly questionnaires. It was checked whether the pills had actually been taken and the recruits were asked to report side effects and any lapses in pill taking. On the final questionnaire, the recruits were asked to state if they knew which pill they had been taking and how they knew. Sixty-four recruits (34, vitamin C; 30, placebo) were removed from their platoons. An additional 123 recruits (64, vitamin C; 59, placebo) were excluded because they did not continue to take their pills and 1 recruit from the vitamin C group dropped out because of recurrent urticaria related to taking the tablets. Thus, unfortunately, there was no intention-to-treat analysis. There were no apparent differences for the incidence of colds, and the duration and severity of the symptoms. The authors concluded that vitamin C is not effective in the prevention of colds.

Results

The table shows that the treated groups vary from schoolchildren and soldiers to twins and employees of large companies. All 11 double-blind trials presented in the table, assessed the prophylactic as well as the therapeutic effect of vitamin C. The dosage of vitamin C which was used after 1960 is mostly 1 g/day or more. Before 1960, dosages up to 200mg/day were regular.

There are striking differences between the endpoints used: "colds", "symptoms of the nose or throat", "respiratory illness" and "winter illness". Even greater differences are encountered regarding the duration and the severity of the symptoms; sometimes it was not clear whether the endpoint concerned the duration or the severity of the cold. These differences complicate a definitive assessment of the results of these trials. Only Bancalari et al. found a small positive effect on the incidence of colds.[69] Regarding the therapeutical effects of vitamin C we find both for the duration and the severity of the symptoms a small positive effect (approx. 10% or more) in seven trials, and no effect in 4 trials.

From these trials, it is not possible to make a reliable assessment of the optimal dosage needed. It appears that the results for dosages of 1 g/day or more and 200 mg/day are similar. Moreover, it is impossible to establish whether there are any subgroups who might have more or less benefit from vitamin C suppletion, because the differences between trials regarding the intervention and the effect measurement are too large.

authors, year, country	population	number of participants (dropouts)	duration in weeks
Anderson et al. 1972 Canada[39]	employees of several companies	407/411 (182)	9-17
Anderson et al. 1974 Canada[47]	staff of hospitals and several companies	approx. 300 per group total 2349 (1171)	13
Coulehan et al. 1974 USA[49]	schoolchildren	321/320 (13/12)	14
Anderson et al. 1975 Canada[51]	staff of hospitals, large companies and students	tablets 150, capsules 152/ placebo 146 (57,56/61)	15
Karlowski et al. 1975 USA[54]	employees Natl. Inst. Health	totally 311 (more dropouts in placebo group)	39
Coulehan et al. 1975 USA[53,55]	schoolchildren	428/428 combination of 2 trials (88)	15-18
Ludvigsson et al. 1977 Sweden[61]	schoolchildren	304/311 (27)	13
Miller et al. 1977 USA[62]	twins	42 pairs (2 pairs)	22
Pitt & Costrini 1979 USA[65]	recruits	331/343 (99/89)	8
Carr et al. & Martin et al. 1981, 1982 Australia[66-68]	twins	95 pairs (30/30)	14
Bancalari et al. 1984 Chili[69]	schoolchildren	32/30 no dropouts	12

"/" divides vitamin C group from placebo group

daily dosis of vitamin C	symptoms of disease: number of colds per person	severity	duration (days)
prophyl.; therap. 1 g; 4 g	1,1/1,2	vit. C-group less severe	4,6/5,4
prophyl.; therap. 1. 1 g ; 4 g 2. 1 g ; - 3. 2 g ; - 4. - ; - 5. 250 mg; - 6. - ; - 7. - ; 4 g 8. - ; 8 g	no difference	no difference	no difference
1. 1 g 6-10 years 2. 2 g 10-15 years	1. 0.1/0.1 2. 0.1/0.1	vit. C-groups less severe	1. 5.0/5.7 2. 4.4/6.3
prophyl.; therap. 500 mg per week; 1500 mg on day 1 1000 mg on day 2-5	not mentioned	vit. C-groups less severe	1.2, 1.2/1.6
prophyl.; therap. 1. 3 g ; 3 g 2. 3 g ; - 3. - ; 3 g 4. - ; -	 1. 1.3 2. 1.2 3. 1.3 4. 1.4	vit. C-group less severe	 1. 5.9 2. 6.7 3. 6.5 4. 7.1
1 g	0.2/0.2	no difference	5.5/5.8
1 g placebo contains 10 mg vit. C	2.2/2.0	vit. C-group less severe	6.0/5.7
depending on body weight 0.5, 0.75 or 1.0 g (all groups multi-vitamins with additional 50 mg vit.C)	5.0/4.8	vit. C-group less severe	6.9/7.5
2 g	1.8/1.8	no difference	11.2/11.5
1 g (all groups multi-vitamins with additional 50 mg vit.C)	1.6/1.5	vit. C-group less severe	5.2/6.4
2 g	1.2/1.5	vit. C-group less severe	3.4/4.5

"/" divides vitamin C group from placebo group

Discussion

It appears that a great deal of research has been performed on the effects of vitamin C on colds. Of course, we can not exclude the possibility that some trials with "negative" results have remained unpublished.
A look at the populations studied during the years shows us that research on vitamin C and colds has been performed in a great variety of people. This would enable us to draw conclusions about subgroups that might benefit of vitamin C suppletion. However, not only the people participating in these experiments varied, but also many other aspects of the experiments. The same applies to other interesting questions, such as a dose-response effect.
Furthermore, the methodological quality of the earlier trials is disappointing. No trial performed before 1970 attained a high methodological score.
The outcome of the experiments might be summarized as follows: there is no prophylactic effect of vitamin C on the incidence of common colds, but as a therapy it might exert some effect. A positive effect of approx. 10% both on the duration and on the severity of the symptoms cannot be excluded.
The implications for general practice may depend on the perspective from which one looks at this evidence. The patient has to weigh the costs and effort of vitamin C supplementation against the small benefit which can be expected. From the doctor's point of view, there is not much to be gained, because colds are self-limiting. A gain of half a day is not much for a cold that lasts for five days. On the other hand, considering the high incidence of colds, a gain of half a day sick-leave might very well be worthwhile from a larger, nationwide, perspective.
A more comprehensive report of our findings can be found in an earlier published report (in Dutch).[73]

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